



# WSI-LLaVA: A Multimodal Large Language Model for Whole Slide Image

## Supplementary Material

**Abstract.** In this supplementary material, we provide additional information about the proposed WSI-Bench, WSI-LLaVA, WSI Metrics. Appendix 1 illustrates additional experiments of the proposed WSI-LLaVA on the proposed WSI-Bench and supplementary details that complement the main experiments in the paper. Appendix 2 includes further discussion with key insights about WSI evaluation. Appendix 3 demonstrates the details of WSI-Bench. Appendix 4 provides the details of the WSI metrics. Appendix 5 provides the implementation details of the proposed method.

### 1. Additional Experiments

#### 1.1. Quantitative Evaluation across Each Task

To quantitatively evaluate each pathological task across three capabilities, we demonstrate the performance of existing MLLMs and our proposed WSI-LLaVA in Table 1. As shown in the results, WSI-LLaVA achieves superior overall performance with the highest average scores in both WSI-Precision (0.601) and WSI-Relevance (0.608). Specifically, in morphological analysis capability, WSI-LLaVA demonstrates leading WSI-Precision scores across all sub-tasks, with particular strength in specific feature description (0.760). For diagnostic capability, it exhibits robust performance in histological typing (0.410), grading (0.570), and staging (0.830), although Quilt-LLaVA shows slightly better results in molecular subtyping. Regarding treatment planning capability, WSI-LLaVA excels in treatment recommendations with the highest scores in both metrics (0.790 and 0.881), while maintaining competitive performance in prognosis. These comprehensive results validate WSI-LLaVA’s balanced and reliable performance across diverse pathological tasks compared to existing MLLMs.

#### 1.2. Qualitative Evaluation across Each Task

To qualitatively evaluate each task, we demonstrate the visual results of existing methods and our proposed WSI-LLaVA for 11 pathological tasks, as shown in Table 18 to 28. We use color green to highlight content that matches the ground truth and red to indicate content that contradicts it. In these Tables, we can observe that WSI-LLaVA’s answers are more consistent with the ground truth and exhibit higher accuracy across all tasks. While Quilt-LLaVA’s responses are similar in form to the ground truth, they contain more errors in specific content, especially in morphological description tasks. This may be due to its inability to extract the rich morphological features in WSI im-

ages. WSI-VQA’s answers often include repeated invalid information, and some sentences have grammatical errors, indicating the fundamental disadvantages of Transformer-based models compared to LLMs. GPT-4o provides a large amount of irrelevant information, likely because it cannot be trained to read WSI images.

In the radar chart displaying WSI-Precision metrics (Figure 6), WSI-LLaVA (our model) dominates with broader coverage and higher peaks in most diagnostic categories, particularly excelling in “Specific Feature Description,” “Staging,” and “Prognosis.” This suggests an excellent ability to accurately identify and describe critical pathological features and outcomes. Meanwhile, models like GPT-4o show considerably lower precision, particularly in detailed descriptions, which may limit their utility in nuanced diagnostic scenarios.

The WSI-Relevance radar chart reveals that WSI-LLaVA also leads in relevance (Figure 6), with outstanding performance in “Staging” and “Treatment Recommendations,” underscoring its capability to deliver clinically pertinent information that aids in treatment planning and prognosis estimation. In contrast, while GPT-4o and WSI-VQA provide valuable insights in specific areas such as “Prognosis” and “Regional Structure Description,” they exhibit a balanced but generally lower relevance compared to our model, indicating a need for targeted improvements to enhance their practical application in clinical settings.

#### 1.3. Ablation Studies Details

**Effectiveness of WSI Encoder.** To prove the effectiveness of WSI encoder in extracting WSI features, we ablate the WSI encoder in our proposed WSI-LLaVA framework, as listed in Table 2. When ablating WSI encoder, across all three pathological capabilities and both report generation tasks, the model with WSI encoder consistently outperforms the variant without it. Notable improvements are observed in the WSI-R metrics for morphological analysis (0.447 to 0.610) and treatment planning (0.816 to 0.845). The overall average performance increases from 0.632 to 0.680, representing a 4.8% improvement. These results clearly validate the effectiveness of the WSI encoder in extracting meaningful features from whole slide images, contributing to better performance across all evaluation metrics.

**Effectiveness of the three-stage training scheme.** To demonstrate the necessity of the three-stage training scheme for the WSI-LLaVA framework, we ablate the first or second stage to compare performance. As shown in Table 2, when ablating the first stage, the overall performance de-

Table 1. Quantitative comparison among MLLMs across three capabilities by using WSI-Precision and WSI-Relevance metrics.

Methods	Morphological Analysis				Diagnosis				Treatment Planning		Average
	Global Morph. Desc.	Key Diag. Desc.	Reg. Struct. Desc.	Spec. Feat. Desc.	Hist. Typing	Grading	Mol. Subtyping	Staging	Treat. Recom.	Prognosis	
WSI-Precision											
Quilt-LLaVA	0.338	0.314	0.389	0.752	0.339	0.505	0.675	0.824	0.764	0.812	0.571
GPT-4o	0.221	0.243	0.153	0.263	0.282	0.363	0.578	0.655	0.498	0.493	0.375
WSI-VQA	0.322	0.313	0.389	0.554	0.377	0.430	0.388	0.550	0.708	0.874	0.490
WSI-LLaVA	0.390	0.350	0.450	0.760	0.410	0.570	0.630	0.830	0.790	0.830	0.601
WSI-Relevance											
Quilt-LLaVA	0.289	0.363	0.404	0.732	0.333	0.453	0.708	0.922	0.858	0.773	0.584
GPT-4o	0.171	0.326	0.216	0.103	0.177	0.312	0.169	0.745	0.792	0.889	0.390
WSI-VQA	0.383	0.370	0.511	0.586	0.475	0.514	0.476	0.634	0.444	0.746	0.514
WSI-LLaVA	0.333	0.382	0.465	0.766	0.380	0.511	0.675	0.882	0.881	0.808	0.608

Abbreviation: Global Morph. Desc. (Global Morphological Description), Key Diag. Desc. (Key Diagnostic Description), Reg. Struct. Desc. (Regional Structure Description), Spec. Feat. Desc. (Specific Feature Description), Hist. Typing (Histological Typing), Grading (Grading), Mol. Subtyping (Molecular Subtyping), Staging (Staging), Treat. Recom. (Treatment Recommendations), Prognosis (Prognosis).

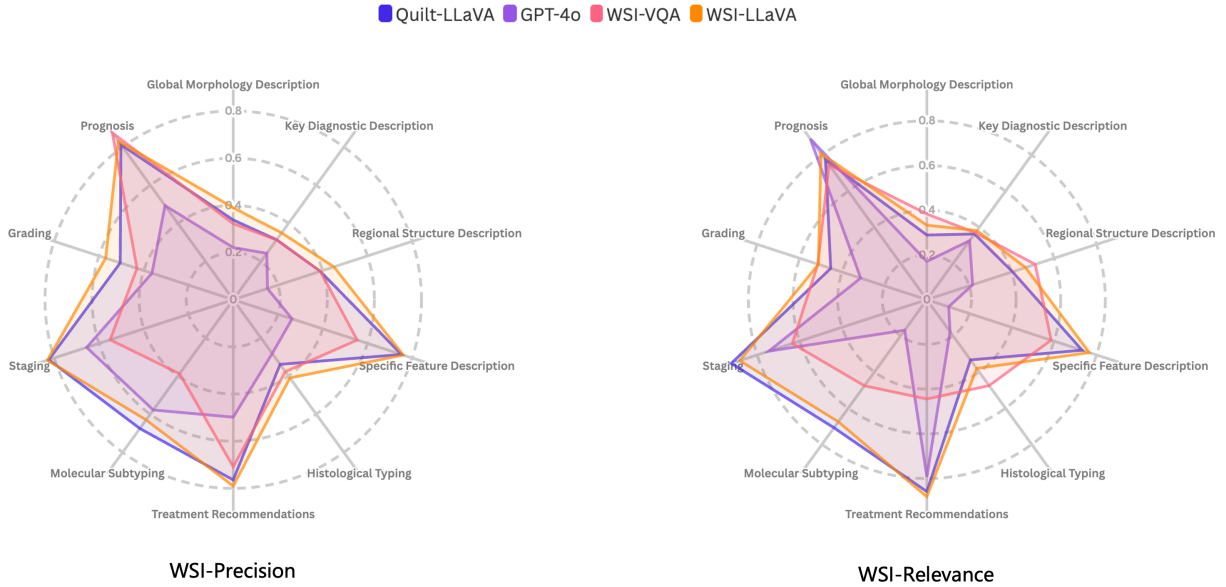


Figure 6. Radar charts of WSI-Precision and WSI-Relevance for MLLMs across different tasks.

clines by 2.2% in average score. When ablating both the first and second stages, the performance decreases significantly by a large margin with an average score of 3.3%, indicating that each stage contributes to improving performance to different extents. This highlights the effectiveness of three-stage training in mitigating the cross-modal gap.

#### 1.4. External Validation Details

**WSI-VQA Dataset.** From the original WSI-VQA dataset [4], we removed clinically unreasonable questions.

Specifically, we excluded survival time predictions, as these cannot be reliably determined from histological images alone; estimations of 3D tumor size, which exceed the analytical scope of 2D pathology slides; and immunohistochemistry evaluations that depend on specialized staining techniques.

**SlideBench-VQA(BCNB).** From the SlideBench dataset [5], we excluded questions that require information on immunohistochemical markers, such as PR, ER, and HER2 status.

WSI Encoder	Stage 1	Stage 2	Morphological Analysis			Diagnosis			Treatment Planning			Report Generation		Average
			Open		Close	Open		Close	Open		Close	WSI-P	WSI-R	
			WSI-P	WSI-R	Acc	WSI-P	WSI-R	Acc	WSI-P	WSI-R	Acc			
✗	✓	✓	0.435	0.433	0.940	0.565	0.577	0.847	0.739	0.803	1.000	0.290	0.326	0.632
✓	✗	✗	0.425	0.483	0.945	0.561	0.541	0.837	0.761	0.798	1.000	0.356	0.367	0.643
✓	✗	✓	0.442	0.478	0.945	0.589	0.602	0.856	0.744	0.776	1.000	0.380	0.377	0.654
✓	✓	✓	0.488	0.487	0.951	0.610	0.612	0.863	0.810	0.845	1.000	0.380	0.429	0.680

Table 2. Combined ablation studies on WSI encoder and training stages of WSI-LLaVA. WSI-P: WSI-Precision, WSI-R: WSI-Relevance, Acc: accuracy, Open: open-ended questions, Close: close-ended questions.

**CPTAC-NSCLC Dataset.** For ease of evaluation, based on the classification labels of the CPTAC-NSCLC dataset, we constructed the question: "Which carcinoma type is indicated by the tissue slide? Choose the correct option: A) Lung Adenocarcinoma; B) Lung Squamous Cell Carcinoma." The final test set consisted of 1,091 WSIs, with 546 labeled as LUAD (Lung Adenocarcinoma) and 545 as LSCC (Lung Squamous Cell Carcinoma).

## 2. Discussion

From the above results, three key insights have been deduced as follows:

1) **WSI-LLaVA demonstrates superior morphological understanding across all dimensions.** As illustrated in Fig. 5, our model consistently outperforms existing approaches in critical morphological analysis tasks. WSI-LLaVA achieves notable advantages in specific feature detection (0.76 vs. 0.752 for Quilt-LLaVA), cellular morphology analysis (0.46 vs. 0.404 for WSI-VQA), and infiltration pattern recognition (0.45 vs. 0.40 for Quilt-LLaVA). The performance gap is particularly pronounced when compared with general-purpose models like GPT-4o, which averages only 0.193 across morphological tasks versus WSI-LLaVA's 0.473. This superiority stems from our model's dual-encoder architecture that effectively captures both local details and global context, combined with a three-stage training approach that ensures proper alignment between visual and textual representations. Such comprehensive morphological understanding directly translates to improved diagnostic accuracy, as demonstrated in our qualitative analysis in Table 4.

2) **Morphological understanding enables robust cross-dataset generalization.** External validation results reveal a striking pattern: models with stronger morphological capabilities demonstrate substantially better generalization to unseen datasets. This relationship is most evident in tasks requiring nuanced morphological assessment, where WSI-LLaVA outperforms the next best model by substantial margins on histological grading (46.33% vs. 23.11%) and molecular subtyping (29.2% vs. 18.1%). Unlike previous approaches that may learn dataset-specific correla-

tions, WSI-LLaVA's focus on fundamental morphological principles provides a more transferable form of knowledge. This finding has significant implications for clinical deployment, suggesting that morphology-aware models can maintain consistent performance across diverse institutional settings and patient populations without requiring extensive re-training or adaptation.

3) **Traditional NLU metrics fail to capture clinical accuracy in pathology language tasks.** Table 5 shows that both Hist-Gen and WSI-LLaVA achieve similar scores on standard NLU metrics (e.g., BLEU-1: 0.531 vs. 0.521, ROUGE-L: 0.536 vs. 0.534), despite evident differences in their clinical accuracy. This is because traditional NLU metrics focus on surface similarity, such as lexical overlap, rather than the correctness and relevance of key pathological findings. For example, Hist-Gen's response—"There is no evidence of vascular invasion ..."—is structurally similar to the ground truth and thus receives high NLU metric scores, but its meaning is completely opposite. In contrast, WSI-LLaVA accurately identifies these features, achieving superior WSI metrics (WSI-P: 0.800, WSI-R: 0.830). This demonstrates the limitations of conventional NLU metrics in evaluating pathology language tasks, where capturing clinically relevant information is essential. Our proposed WSI-Precision and WSI-Relevance metrics address these limitations by focusing on factual correctness and clinical relevance rather than linguistic similarity. These metrics provide a more reliable and clinically meaningful assessment of model performance in pathological contexts. WSI-LLaVA demonstrates substantially higher clinical precision and relevance (WSI-Precision: 0.800 vs. 0.233, WSI-Relevance: 0.830 vs. 0.520), highlighting the inability of traditional metrics to reflect clinical utility.

This discrepancy stems from three key limitations of conventional metrics:

1) **Surface Similarity:** High word overlap between generated text and references inflates scores without considering clinical accuracy. For example, phrases like "Microscopic observation reveals poorly differentiated squamous cell carcinoma" appear in both Hist-Gen and WSI-LLaVA, leading to similar scores despite differences in factual cor-

rectness.

2) **n-gram Matching:** Shared terms such as "nuclear pleomorphism" and "prominent nucleoli" contribute to high scores, even when these terms are used in incorrect or contradictory contexts.

3) **Semantic Insensitivity:** Conventional metrics fail to penalize clinically significant errors, such as Hist-Gen's incorrect statement that "there is no evidence of vascular invasion or necrosis," which directly contradicts the reference text.

Our proposed WSI-Precision and WSI-Relevance metrics address these limitations by focusing on factual correctness and clinical relevance rather than linguistic similarity. These metrics provide a more reliable and clinically meaningful assessment of model performance in pathological contexts.

### 3. WSI-Bench

To establish a comprehensive and large-scale WSI-Bench, we include an automated data construction process using GPT-4o and a subsequent validation process by clinical experts.

#### 3.1. Data Distribution

In Fig. 7, we illustrate the distribution of WSI across various cancer types as categorized in the Cancer Genome Atlas (TCGA) database. Cancer types are commonly identified by standardized abbreviations. Specifically, TCGA-ACC refers to Adrenocortical Carcinoma; TCGA-BLCA is Bladder Urothelial Carcinoma; TCGA-BRCA denotes Breast Invasive Carcinoma; TCGA-CESC stands for Cervical Squamous Cell Carcinoma and Endocervical Adenocarcinoma; TCGA-CHOL represents Cholangiocarcinoma; TCGA-COAD is Colon Adenocarcinoma; TCGA-DLBC refers to Lymphoid Neoplasm Diffuse Large B-cell Lymphoma; TCGA-ESCA denotes Esophageal Carcinoma; TCGA-HNSC stands for Head and Neck Squamous Cell Carcinoma; TCGA-KICH represents Kidney Chromophobe; TCGA-KIRC is Kidney Renal Clear Cell Carcinoma; TCGA-KIRP denotes Kidney Renal Papillary Cell Carcinoma; TCGA-LGG refers to Brain Lower Grade Glioma; TCGA-LIHC stands for Liver Hepatocellular Carcinoma; TCGA-LUAD represents Lung Adenocarcinoma; TCGA-LUSC is Lung Squamous Cell Carcinoma; TCGA-MESO denotes Mesothelioma; TCGA-OV refers to Ovarian Serous Cystadenocarcinoma; TCGA-PCPG stands for Pheochromocytoma and Paraganglioma; TCGA-PRAD represents Prostate Adenocarcinoma; TCGA-READ is Rectum Adenocarcinoma; TCGA-SARC denotes Sarcoma; TCGA-SKCM refers to Skin Cutaneous Melanoma; TCGA-STAD stands for Stomach Adenocarcinoma; TCGA-TGCT represents Testicular Germ Cell Tumors; TCGA-THCA is Thyroid Carcinoma; TCGA-THYM denotes Thymoma;

TCGA-UCEC stands for Uterine Corpus Endometrial Carcinoma; TCGA-UCS represents Uterine Carcinosarcoma; and TCGA-UVM refers to Uveal Melanoma.

#### 3.2. Training and Testing Distribution

We strictly separated training and testing sets by cancer type to evaluate model generalization. For each cancer type, we allocated 2% of WSIs for testing (at least 2 WSIs for smaller cancer types). The final distribution includes 9,642 WSIs with 175,450 VQA pairs for training and 208 WSIs with 4,119 VQA pairs for testing. Figure 8 shows the distribution of VQA pairs across training and testing sets for each cancer type.

#### 3.3. Reverse-Engineer Scheme

To enrich morphological descriptions, we introduce a reverse-engineer scheme to provide a morphological description extension. It uses diagnostic labels to identify the corresponding morphological characteristics according to tumor classification standards like the Nottingham grading system. This extension is included in the WSI reports that are then refined by clinical experts. This reverse-engineering process is supported by the breadth of medical literature included in GPT-4o's training data, ensuring a high level of precision that mirrors the expertise of professional pathologists.

Specifically, we take the instance of breast cancer where reports utilize the Nottingham grading system [7], a method frequently used in TCGA datasets. The grading system assesses three critical aspects: gland formation, nuclear pleomorphism, and mitotic count, assigning each a score from 1 to 3. Consider a report that assigns a score of 3 for both gland formation and nuclear pleomorphism. This high score indicates minimal gland formation and substantial variation in nuclear size and shape, suggestive of aggressive tumor characteristics. Furthermore, if the pathology report confirms a diagnosis of invasive ductal carcinoma, it characterizes the cancer cells as having breached duct walls and forming invasive clusters. Such diagnostic details are crucial as they provide clear visual markers that can be directly observed in WSIs. We incorporate these specific findings into our dataset to enrich the morphological descriptions, ensuring that they reflect real-world pathological assessments and are tightly aligned with established diagnostic criteria.

Table 6 presents an example of the Nottingham grading system applied to breast cancer, a method derived from the WHO Classification of Tumors [7]. This system is recognized for its rigor and authority in classifying tumor severity. It systematically scores three critical histological features: gland formation, nuclear pleomorphism, and mitotic count. Each feature is evaluated based on specific morphological characteristics observable in tissue samples. The



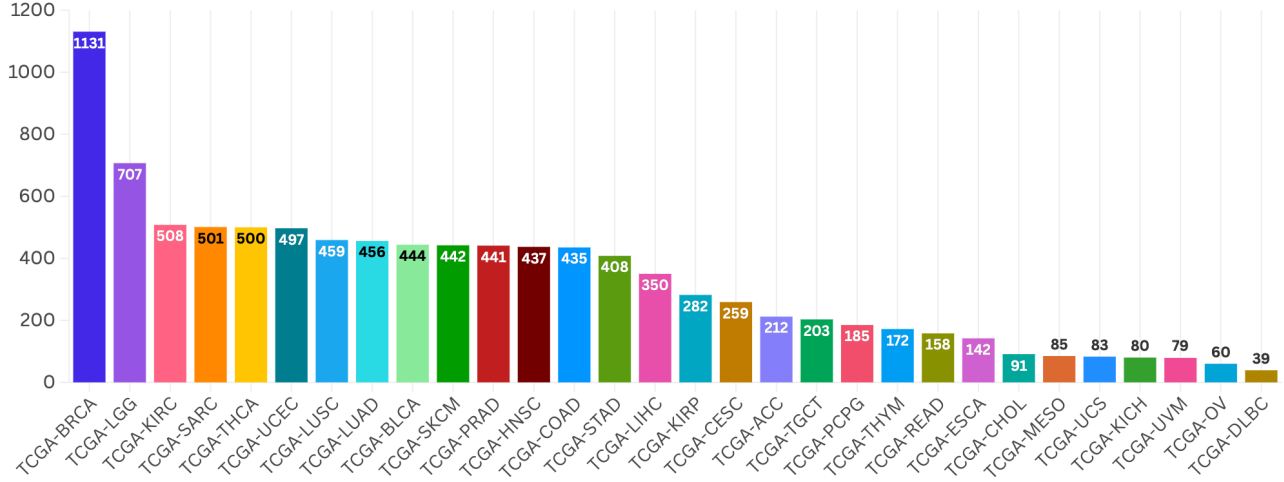


Figure 7. Data distribution of WSI samples across various TCGA cancer types.

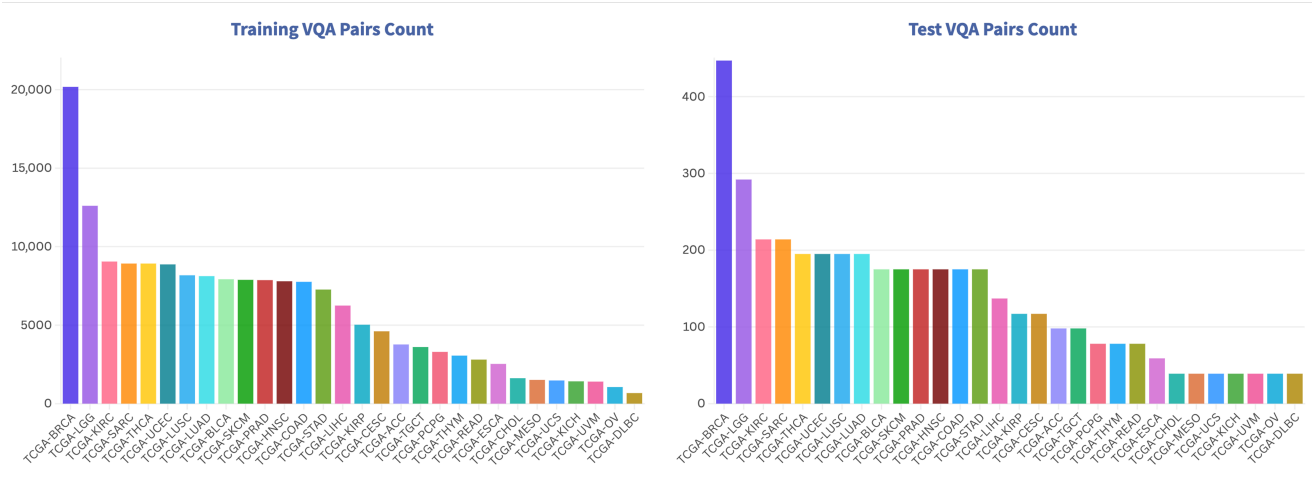


Figure 8. Distribution of VQA pairs across training and testing sets by cancer type.

scores correlate directly with these features, ensuring that the derived descriptions are not only standardized but also clinically meaningful. By adhering to this methodology, the descriptions generated are both accurate reflections of the histopathological findings and relevant for clinical assessment and treatment planning.

To address **hallucinations**, we generate three versions of each report and use another LLM to verify if the content aligns with the original reports. The model performs five iterations of selection, and if one version is selected three or more times, it is deemed accurate. If none achieve this threshold, a pathologist reviews and selects the appropriate content. Furthermore, to avoid the pitfalls of incomplete filtering, especially concerning immunohistochemical data and macroscopic descriptions, we use regular expressions to identify and exclude 30 keywords, with any flagged text

revised by a pathologist.

### 3.4. Data Construction

**Report Generation Task.** Fig. 13 illustrate how prompts are utilized to guide GPT-4o in generating textual reports that encompass critical histopathological assessments. Table 7 shows the example of the WSI and the corresponding report. These examples demonstrate the process of crafting prompts that effectively elicit comprehensive and clinically relevant reports from the model, ensuring essential diagnostic information is accurately captured.

**Other Pathological Tasks.** We present detailed examples for other pathological tasks showcasing how each prompt is crafted to elicit precise responses from the model, aligning with clinical expectations and diagnostic standards. The prompts, referenced in Fig. 14 to 23, are pivotal in defining

the scope and focus of each pathological task. Tables 8 to 17 visualize the examples for each task.

### 3.5. Expert Review and Quality Control

To ensure medical accuracy, clinical applicability, and educational effectiveness of the generated VQA pairs, we employed a structured expert review process with a proportional sampling strategy due to the extensive dataset size. The expert panel comprised two senior pathologists and five junior physicians with diverse clinical experience.

The detailed quality control workflow was systematically organized as follows:

- **Sampling Strategy:** For open-ended VQA pairs, we randomly selected 10% of the generated pairs for thorough expert review. This sampling aimed to statistically ensure at least 90% accuracy across all pairs. For close-ended VQA pairs, we randomly reviewed 5% to verify their quality.
- **Medical Accuracy Check:** Senior pathologists rigorously validated the sampled pairs by cross-checking the diagnostic accuracy and alignment between answers and visual evidence presented in Whole Slide Images (WSIs), strictly adhering to established clinical guidelines and diagnostic criteria.
- **Clinical Relevance Evaluation:** Both senior and junior reviewers assessed the clinical practicality of sampled VQA pairs, ensuring that they reflected realistic clinical scenarios frequently encountered in pathological diagnosis.
- **Educational Clarity Review:** Junior physicians specifically evaluated whether the VQA pairs were clearly phrased, comprehensible, and effective as educational resources suitable for learners at varying stages of medical training.

If significant inaccuracies or issues were identified during the review, prompts were adjusted accordingly, and affected VQA pairs were regenerated. For close-ended pairs, we randomly reviewed 5% using the same rigorous criteria. This structured sampling and iterative review ensured high-quality, clinically accurate, and educationally valuable VQA pairs across the entire dataset.

## 4. WSI Metrics

We introduce two key metrics developed to evaluate WSI MLLMs: *WSI-Precision* and *WSI-Relevance*. These metrics are essential for assessing the accuracy and relevance of model-generated responses in a clinical context.

### 4.1. WSI-Precision

WSI-Precision measures the accuracy of model responses by comparing them directly to claims derived from the ground-truth response. As shown in Table 4, it includes

three main steps to compute the evaluation result for the model response and ground-truth response, including the claims extraction, individual score calculation, and final score calculation.

**Claims Extraction.** To break down complex medical information into assessable units, we extract distinct claims from the ground-truth response by using GPT-4o. As shown in Fig. 10, we design the prompt to guide GPT-4o for claims extraction. The second row in Table 4 shows the extracted claims for the ground-truth response.

**Individual Score Calculation.** With the extracted claims, we compare them with the generated response using our scoring criterion, which is defined as follows:

- **Score 1:** The information in the model’s response is completely accurate with respect to the claim. The response perfectly aligns with established facts, correctly addressing all elements of the claim.
- **Score 0.7:** The information is mostly correct and closely aligns with the claim, with minor discrepancies that do not fundamentally alter the truth or clinical significance of the response.
- **Score 0.3:** The claim is acknowledged, but the response contains significant errors in critical content areas, such as the degree of differentiation or malignancy status, affecting the core message.
- **Score 0:** The information in the model’s response is completely incorrect or unrelated to the claim, indicating a fundamental misunderstanding or misrepresentation of the clinical facts.

Following this scoring criterion, we design the prompt to guide GPT-4o to compute the individual score for each claim, as demonstrated in Fig. 11. In Table 4, the third row shows the score of each claim.

**Final Score Calculation.** With the individual score for each claim, we calculate the overall WSI-Precision score by averaging all the individual claim scores.

### 4.2. WSI-Relevance

WSI-Relevance assesses the relevance of the claims extracted from model responses in relation to the ground-truth response. Similarly, it also includes three main steps to evaluate the model response and ground-truth response, including the claims extraction, individual score calculation, and final score calculation, as shown in Table 5.

**Claims Extraction.** To extract the claims from the model response, we design the prompt to guide GPT-4o for claims extraction, as illustrated in Fig. 10. Table 5 visualizes the extracted claims of model response in second row.

**Individual Score Calculation.** With the extracted claims, we compare them with the ground-truth response using our scoring criterion which is the same as that for WSI-Precision. Based on the scoring criterion, we devise the prompt to guide GPT-4o to compute the individual score

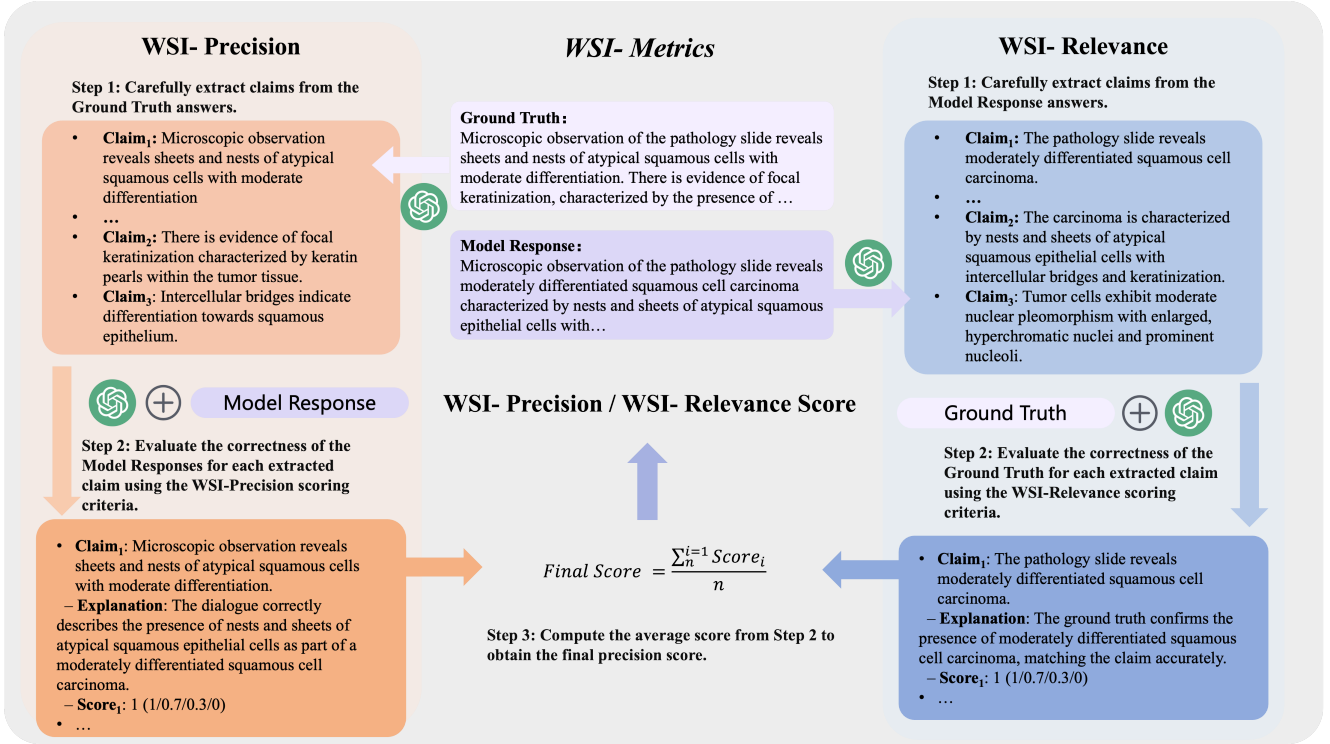


Figure 9. Evaluation workflow for WSI-Precision and WSI-Relevance metrics

for each claim, as shown in Fig. 12.

**Final Score Calculation.** With the individual scores for each claim, we average them and obtain the final WSI-Relevance score.

By utilizing both WSI-Precision and WSI-Relevance, we aim to provide a comprehensive assessment of the diagnostic accuracy and clinical relevance of model outputs. This structured evaluation ensures that models are not only producing factually correct responses but are also providing information that is pertinent and useful in real-world medical settings.

#### 4.3. Evidence for WSI Metrics Validation

To rigorously validate our proposed WSI-specific metrics (WSI-Precision and WSI-Relevance), we conducted a systematic sampling-based evaluation comparing automated metric scores against human expert judgments. Due to the large volume of data in our test set (124,011 open-ended responses), we randomly sampled 2% of the test set from each pathological capability (morphological analysis, diagnosis, treatment planning, and report generation), resulting in 2488 representative WSI-LLaVA model responses for evaluation. For automated evaluation, we tested multiple large language models including GPT-4o, GPT-4o-mini, Claude-3.5-Sonnet, and Gemini-1.5-flash. Considering cost, response speed, and consistency, we ultimately selected GPT-4o. While Claude-3.5-Sonnet demonstrated slightly better

performance, it was more expensive and slower than GPT-4o. GPT-4o-mini and Gemini-1.5-flash were faster and more cost-effective but provided lower quality evaluations. A panel of five medical doctors with extensive clinical experience independently assessed each response for precision and relevance using the same four-point scoring system employed by our automated metrics.

The comparative analysis demonstrated strong alignment between automated WSI metrics and human expert evaluation, with a Pearson correlation of 0.87 for WSI-Precision and 0.82 for WSI-Relevance. Table 3 shows the average performance of different models compared to human expert evaluation across all evaluated samples. As shown in the table, expert scores were consistently slightly higher than automated metrics, suggesting that automated metrics are marginally more conservative.

Model	WSI-Precision	WSI-Relevance
GPT-4o	0.572	0.624
GPT-4o-mini	0.539	0.602
Claude-3.5-Sonnet	0.580	0.631
Gemini-1.5-flash	0.535	0.597
<b>Human</b>	0.636	0.689

Table 3. Comparison of LLM-based evaluation with human expert evaluation.

The inter-rater reliability between pathologists showed a Cohen’s kappa of 0.78, indicating substantial agreement. Discrepancies between automated and human evaluations were most pronounced in cases involving complex morphological descriptions requiring subtle interpretations, instances where clinical context significantly influenced relevance judgment, and cases where semantic variations in terminology had different clinical implications.

Our sampling-based validation study also revealed several key advantages of WSI metrics over traditional NLU metrics: (1) focus on clinical significance rather than linguistic similarity, (2) interpretability through the claims-based approach, (3) superior contextual understanding within specialized pathology domains, and (4) robustness to stylistic variations. These findings strongly support the validity of our proposed WSI metrics as clinically relevant evaluation measures for assessing model performance in whole slide image analysis tasks.

## 5. WSI-LLaVA

### 5.1. Network Architecture

Our model’s network architecture is divided into three components: a WSI encoder, a text encoder, a projection layer, and a large language model (LLM). This design enables efficient processing of gigapixel pathology WSI data.

**WSI Encoder.** WSI Encoder, is responsible for extracting meaningful features from gigapixel pathology images, consisting of a patch-level encoder and a slide-level encoder. The patch-level encoder employs Prov-GigaPath[32]’s tile-level encoder, which is specifically designed for pathology data. The tile-level encoder is pre-trained using the DINOv2[21] framework on 1.3 billion  $256 \times 256$  pathology image tiles derived from over 170,000 WSIs spanning 31 major tissue types. Its task is to encode each  $256 \times 256$  image tile, extracting efficient feature representations at the patch level. The slide-level encoder is based on the LongNet [8] architecture. LongNet is an improved Transformer that utilizes dilated self-attention mechanisms to reduce the computational complexity of traditional Transformers from  $O(n^2)$  to a more manageable range. This enables the model to efficiently aggregate features from tens of thousands or even hundreds of thousands of tiles, capturing global spatial contexts while minimizing computational costs.

**Text Encoder.** We use Bio\_ClinicalBERT[1] as our text encoder which is a BERT[6] model pre-trained on biomedical and clinical text to optimize its performance in these domains.

**Projection Layer.** To achieve cross-modal alignment, a projection layer is designed between the WSI encoder and the LLM. The projection layer consists of a two-layer multi-layer perceptron (MLP) module, which maps visual features

into a feature space compatible with the language model.

**Large Language Model.** We use Vicuna-7b-v1.5 [34] as the pre-trained model for the large language model, which is a highly efficient and powerful open-source language model tailored for dialogue generation tasks. Through fine-tuning, Vicuna demonstrates exceptional adaptability to various medical scenarios, generating accurate and natural diagnostic reports.

### 5.2. Training Details

The training process is divided into three stages, i.e. WSI-text alignment, feature space alignment, and task-specific instruction tuning.

**Stage 1: WSI-Text Alignment.** The learning rate is set to 0.001, with a batch size of 64. During this stage, only a two-layer MLP projection layer is trained to align WSI and text features, while both the WSI encoder and text encoder remain frozen. The training runs for 50 epochs, with a temperature parameter set to 0.02.

**Stage 2: Feature Space Alignment.** In this stage, both the WSI encoder and the LLM are frozen, and only the projection layer is trained. The learning rate is set to  $1e-3$ , with 1 training epoch and a global batch size of 256. The maximum sequence length is set to 2048, weight decay is disabled (set to 0), and the warmup ratio is configured as 0.03 to ensure a smooth start to training.

**Stage 3: Task-Specific Instruction Tuning.** In this stage, we freeze the WSI encoder and train the projection layer along with the LLM. The learning rate is set to  $2e-5$ , with 1 training epoch and a global batch size of 128. The maximum sequence length is set to 2,048, weight decay is set to 0, and the warmup ratio is maintained at 0.03. We utilize LoRA (Low-Rank Adaptation) with a rank of 128 and an alpha value of 256 for parameter-efficient fine-tuning, enabling adaptation to the target dataset with minimal additional parameters. To enhance computational efficiency, we use DeepSpeed with ZeRO-3 optimization for distributed training. Additionally, BF16 precision is adopted, and TensorFloat32 is enabled to accelerate matrix operations while maintaining numerical stability.



### GPT-4o Prompt: Claims Extraction Prompt

**System Message:** You are an AI assistant specialized in processing pathological diagnosis Q&A pairs. I will provide you with a pathology diagnosis question and its corresponding answer.

Your task is to:

Claims Extraction:

- Carefully analyze the answer and remove any unnecessary information that is not directly relevant to the question.
- Only extract claims that directly address the question. Discard any information that does not directly answer or pertain to the question.
- Divide the refined answer into several distinct and granular claims.
- Keep closely related information together in the same claim to preserve context and meaning. Do not split sentences or ideas that are logically connected.
- Break down complex sentences into smaller, individual claims only if it does not disrupt the logical flow or separate connected ideas.
- Ensure there is no omission or repetition among the claims.

Guidelines:

- Only output the claims without including any additional text or explanations.
- Each claim should be concise and represent a single fact or point directly related to the question.
- Maintain the integrity of statements that are contextually connected.

Output Format: Present the extracted claims as a list in the following format:

["claim1", "claim2", "claim3", ...]

Figure 10. The prompt for the claims extraction. It provides detailed guidelines for GPT-4o, to identify and refine relevant information from context into distinct claims. These claims serve as the basis for subsequent evaluations.

### GPT-4o Prompt: WSI-Precision Scoring Instruction for Pathology Dialogue Evaluation

**System Message:** Please act as an impartial judge and evaluate the correctness of the AI assistant's pathology dialogue for each claim based on the following scoring criteria. Provide an explanation for each evaluation and assign a score.

**\*\*Scoring Criteria:\*\***

- **\*\*1\*\***: The information in the pathology dialogue is completely correct regarding the claim.
- **\*\*0.7\*\***: The information is mostly correct and closely aligns with the claim.
- **\*\*0.3\*\***: The claim is mentioned but contains errors in the core content (e.g., mistakes in differentiation degree or malignancy).
- **\*\*0\*\***: The information in the pathology dialogue is completely incorrect regarding the claim.

**Output Requirements:**

Please output your evaluations as a list of dictionaries in plain text format (not JSON). The format should be as follows:

```
[
{
  "claim": "Original claim1",
  "explanation": "Explanation for the score",
  "score": 1 or 0.7 or 0.3 or 0
},
{
  "claim": "Original claim2",
  "explanation": "Explanation for the score",
  "score": 1 or 0.7 or 0.3 or 0
},
...
]
```

Figure 11. The prompt for the WSI-Precision metric, outlining scoring criteria for assessing the correctness of model responses against extracted claims.

Table 4. Evaluation process for WSI-Precision. Step 1 involves extracting claims from the ground-truth response, step 2 evaluates the correctness of the model responses against these claims using a defined scoring system, and step 3 calculates the average score from Step 2 as the final WSI-Precision score.

	Model Response	Ground-Truth Response
	Microscopic observation of the pathology slide reveals moderately differentiated squamous cell carcinoma characterized by nests and sheets of atypical squamous epithelial cells with intercellular bridges and keratinization. The tumor cells exhibit moderate nuclear pleomorphism with enlarged, hyperchromatic nuclei and prominent nucleoli. Mitotic figures are present, indicating active cell division. There is no evidence of vascular invasion, necrosis, or calcification within the examined tissue. Based on these observations, the diagnosis is moderately differentiated keratinizing squamous carcinoma.	Microscopic observation of the pathology slide reveals sheets and nests of atypical squamous cells with moderate differentiation. There is evidence of focal keratinization, characterized by the presence of keratin pearls within the tumor tissue. Intercellular bridges are noted among the squamous cells, indicating differentiation towards squamous epithelium. The cellular morphology shows moderate pleomorphism, with variability in nuclear size and shape, and occasional prominent nucleoli. Mitotic figures are present but not excessively numerous. Vascular invasion is not specified in the observations, and necrosis is not prominently noted. Based on these observations, the diagnosis is squamous cell carcinoma, moderately differentiated.
Steps	Descriptions	Outputs
Step 1	Carefully extract claims from the Ground Truth answers. This involves identifying distinct pieces of information that are directly relevant to the context, preserving logical connections within related ideas. The claims serve as the foundation for evaluating the model’s responses in subsequent steps.	<ul style="list-style-type: none"> <li>Claim<sub>1</sub>: Microscopic observation reveals sheets and nests of atypical squamous cells with moderate differentiation.</li> <li>Claim<sub>2</sub>: There is evidence of focal keratinization characterized by keratin pearls within the tumor tissue.</li> <li>Claim<sub>3</sub>: Intercellular bridges indicate differentiation towards squamous epithelium.</li> <li>Claim<sub>4</sub>: The cellular morphology shows moderate pleomorphism with variability in nuclear size and shape and occasional prominent nucleoli.</li> <li>Claim<sub>5</sub>: Mitotic figures are present but not excessively numerous.</li> <li>Claim<sub>6</sub>: Vascular invasion is not specified.</li> <li>Claim<sub>7</sub>: Necrosis is not prominently noted.</li> <li>Claim<sub>8</sub>: The diagnosis is squamous cell carcinoma, moderately differentiated.</li> </ul>
Step 2	Evaluate the correctness of the Model Responses for each extracted claim using the WSI-Precision scoring criteria. Assign a score to each claim (1, 0.7, 0.3, or 0) based on how accurately the model’s response aligns with the clinical information in the Ground Truth. Provide an explanation for each score and present the evaluations as a list of dictionaries.	<ul style="list-style-type: none"> <li>Claim<sub>1</sub>: <b>Microscopic observation reveals sheets and nests of atypical squamous cells with moderate differentiation.</b> <ul style="list-style-type: none"> <li>Explanation: The dialogue correctly describes the presence of nests and sheets of atypical squamous epithelial cells as part of a moderately differentiated squamous cell carcinoma.</li> <li>Score<sub>1</sub>: <b>1</b></li> </ul> </li> <li>Claim<sub>2</sub>: <b>There is evidence of focal keratinization characterized by keratin pearls within the tumor tissue.</b> <ul style="list-style-type: none"> <li>Explanation: The dialogue mentions keratinization but does not specifically mention keratin pearls. However, keratinization typically involves keratin pearls, aligning closely with the claim.</li> <li>Score<sub>2</sub>: <b>0.7</b></li> </ul> </li> <li>...</li> <li>Claim<sub>6</sub>: <b>Vascular invasion is not specified.</b> <ul style="list-style-type: none"> <li>Explanation: The dialogue explicitly states there is no evidence of vascular invasion, which contradicts the claim that vascular invasion is not specified.</li> <li>Score<sub>6</sub>: <b>0</b></li> </ul> </li> <li>... (Additional evaluations omitted for brevity) ...</li> </ul>
Step 3	Compute the average score from Step 2 to obtain the final precision score. This score represents the overall correctness of the model’s responses in relation to the extracted claims.	$\text{Final Score} = \frac{\sum_{i=1}^n \text{Score}_i}{n}$ <p>Where:</p> <ul style="list-style-type: none"> <li>Score<sub><i>i</i></sub>: The score assigned to the <i>i</i>-th claim.</li> <li><i>n</i>: The total number of evaluated claims.</li> </ul>

Table 5. Evaluation process for WSI-Relevance. Step 1 involves extracting claims from the model response, step 2 assesses the relevance of these claims to the Ground-Truth Response, and step 3 calculates the average relevance score from Step 2 as the final WSI-Relevance score.

	Model Response	Ground-Truth Response
	Microscopic observation of the pathology slide reveals moderately differentiated squamous cell carcinoma characterized by nests and sheets of atypical squamous epithelial cells with intercellular bridges and keratinization. The tumor cells exhibit moderate nuclear pleomorphism with enlarged, hyperchromatic nuclei and prominent nucleoli. Mitotic figures are present, indicating active cell division. There is no evidence of vascular invasion, necrosis, or calcification within the examined tissue. Based on these observations, the diagnosis is moderately differentiated keratinizing squamous carcinoma.	Microscopic observation of the pathology slide reveals sheets and nests of atypical squamous cells with moderate differentiation. There is evidence of focal keratinization, characterized by the presence of keratin pearls within the tumor tissue. Intercellular bridges are noted among the squamous cells, indicating differentiation towards squamous epithelium. The cellular morphology shows moderate pleomorphism, with variability in nuclear size and shape, and occasional prominent nucleoli. Mitotic figures are present but not excessively numerous. Vascular invasion is not specified in the observations, and necrosis is not prominently noted. Based on these observations, the diagnosis is squamous cell carcinoma, moderately differentiated.
Steps	Descriptions	Outputs
Step 1	Extract claims from the Model Response, focusing on identifying distinct and relevant pieces of information that form the basis of the pathological assessment. These claims must preserve the logical and clinical coherence of the model’s response, serving as the foundation for relevance evaluation in the following steps.	<ul style="list-style-type: none"> <li>• Claim<sub>1</sub>: The pathology slide reveals moderately differentiated squamous cell carcinoma.</li> <li>• Claim<sub>2</sub>: The carcinoma is characterized by nests and sheets of atypical squamous epithelial cells with intercellular bridges and keratinization.</li> <li>• Claim<sub>3</sub>: Tumor cells exhibit moderate nuclear pleomorphism with enlarged, hyperchromatic nuclei and prominent nucleoli.</li> <li>• Claim<sub>4</sub>: Mitotic figures are present, indicating active cell division.</li> <li>• Claim<sub>5</sub>: There is no evidence of vascular invasion, necrosis, or calcification within the examined tissue.</li> <li>• Claim<sub>6</sub>: The diagnosis is moderately differentiated keratinizing squamous carcinoma.</li> </ul>
Step 2	Assess the relevance of each extracted claim from the Model Response to the Ground-Truth Response. Assign a relevance score (1, 0.7, 0.3, or 0) based on how well each claim reflects the clinical details and context provided in the Ground Truth. Provide a justification for each relevance score, ensuring that the evaluation clearly outlines how each claim aligns or deviates from the ground-truth observations.	<ul style="list-style-type: none"> <li>• Claim<sub>1</sub>: <b>The pathology slide reveals moderately differentiated squamous cell carcinoma.</b> <ul style="list-style-type: none"> <li>– Explanation: The ground truth confirms the presence of moderately differentiated squamous cell carcinoma, matching the claim accurately.</li> <li>– Score<sub>1</sub>: <b>1</b></li> </ul> </li> <li>• Claim<sub>2</sub>: <b>The carcinoma is characterized by nests and sheets of atypical squamous epithelial cells with intercellular bridges and keratinization.</b> <ul style="list-style-type: none"> <li>– Explanation: The ground truth describes similar cellular structures, but the focus on keratinization is less pronounced, leading to a slightly lower score.</li> <li>– Score<sub>2</sub>: <b>0.7</b></li> </ul> </li> <li>• ...</li> <li>• Claim<sub>4</sub>: <b>Mitotic figures are present, indicating active cell division.</b> <ul style="list-style-type: none"> <li>– Explanation: The presence of mitotic figures is confirmed, aligning with the claim of active cell division, and is fully supported by the ground truth.</li> <li>– Score<sub>4</sub>: <b>1</b></li> </ul> </li> <li>• ... (Additional evaluations omitted for brevity) ...</li> </ul>
Step 3	Compute the average score from Step 2 to obtain the final relevance score. This score quantifies how closely the model’s responses align with the key contextual elements of the ground truth.	$\text{Final Score} = \frac{\sum_{i=1}^n \text{Score}_i}{n}$ <p>Where:</p> <ul style="list-style-type: none"> <li>• Score<sub><i>i</i></sub>: The score assigned to the <i>i</i>-th claim.</li> <li>• <i>n</i>: The total number of evaluated claims.</li> </ul>

Table 6. Detailed diagnostic steps of the Nottingham grading system for breast cancer, illustrating the scoring and corresponding morphological descriptions based on gland formation, nuclear pleomorphism, and mitotic activity.

Diagnostic Step	Score	Morphological Description
<b>Gland Formation</b>	1 - Well-formed 2 - Moderately formed 3 - Poorly formed	Glands are well-differentiated Glands show moderate differentiation Minimal to no gland formation
<b>Nuclear Pleomorphism</b>	1 - Small, uniform 2 - Moderate variability 3 - Marked variability	Nuclei are small and uniform Nuclei show moderate variability in size and shape Nuclei show significant variation in size and shape
<b>Mitotic Count</b>	Low - Few mitoses Medium - Moderate mitoses High - Numerous mitoses	Few mitotic figures are present Moderate number of mitotic figures High number of mitotic figures

#### GPT-4o Prompt: WSI-Relevance Scoring Instruction for Pathology Dialogue Evaluation

**System Message:** Please act as an impartial judge and evaluate the relevance of the original ground truth answer to each claim derived from the model's answer. Provide an explanation for each evaluation and assign a score based on the following criteria.

**\*\*Scoring Criteria:\*\***

- **\*\*1\*\*:** The content in the ground truth answer is completely relevant to the claim.
- **\*\*0.7\*\*:** The content is mostly relevant but has minor omissions or deviations.
- **\*\*0.3\*\*:** The content is partially relevant with significant omissions or irrelevant information.
- **\*\*0\*\*:** The content in the ground truth answer is not relevant to the claim.

**Output Requirements:**

Please output your evaluations as a list of dictionaries in plain text format (not JSON). The format should be as follows:

```
[
{
"claim": "Original claim1",
"explanation": "Explanation for the score",
"score": 1 or 0.7 or 0.3 or 0
},
{
"claim": "Original claim2",
"explanation": "Explanation for the score",
"score": 1 or 0.7 or 0.3 or 0
},
...
]
```

Figure 12. The prompt for the WSI-Relevance metric, detailing scoring criteria for evaluating the relevance of ground-truth response to claims derived from model responses.



### GPT-4o Prompt: VQA Instruction-Following Prompt for Report Generation Task

**System Message:** You are a pathology expert. You will receive a pathology report. Your task is to extract the pathological diagnosis result, along with the local morphological characteristics observed under the microscope, emphasizing key features like vascular invasion, calcification, necrosis, and any other notable cellular or structural alterations.

Ensure that all relevant details from the report are comprehensively included, providing a thorough and detailed description.

Additionally, ensure that all diagnosis-related content, including scoring systems, grades of differentiation, and other relevant metrics, are accurately sourced from the report.

When specific scores or grades are mentioned, incorporate interpretative descriptions into the morphological observations as follows:

For differentiation scores (e.g., glandular (acinar) tubular differentiation), include descriptions indicating deviation from the normal tissue architecture of the specific organ.

For nuclear pleomorphism scores, describe the abnormality in nuclear size and shape.

For mitotic count scores, indicate the rate of cell division.

**\*\*IMPORTANT\*\*:** Do not include that pertains to gross description, biopsies, lymph node examinations, immunohistochemical staining(ki67,Inhibin-alpha, A103, and her2,etc.),immunohistochemistry findings, specific measurements (including distances or margins), tumor sizes(cm/mm), metastasis , tumor volume, margin status, staging, or metastasis.

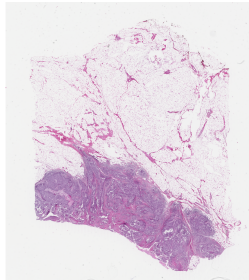
Additionally, avoid including features that require macroscopic correlation or are not directly visible on a single slide. Based on the observations, provide a diagnosis that includes the cancer type, subtype, and grade specific to the site, clearly stating the grading system used.

The output should be a single paragraph formatted as follows:

"Microscopic observation of the pathology slide reveals...Based on these observations, the diagnosis is..."

Figure 13. The prompt used to generate VQA pairs for report generation task.

Table 7. VQA example for report generation task.

Example of Report Generation	
WSI	
Question	What are the main observations in the whole slide histopathology image, and what is the likely diagnosis?
Answer	Microscopic observation of the pathology slide reveals tumor cells infiltrating the surrounding stroma with minimal formation of glandular structures, significantly deviating from normal tissue architecture, and showing a poorly differentiated state with a tubule formation score of 3. The nuclei exhibit considerable size and shape variability, corresponding to a nuclear pleomorphism score of 3. There is a moderate rate of cell division observed, reflected by a mitotic count score of 2. Vascular invasion is not unequivocally present, and no necrosis or microcalcifications are observed. The intraductal component is noted to be less than 25% with prominent cancerization. Based on these observations, the diagnosis is infiltrating ductal carcinoma, no special type, Nottingham Grade III, poorly differentiated, with a total Nottingham score of 8/9.

GPT-4o Prompt: VQA Instruction-Following Prompt for Regional Structure Description

**System Message:** You are an AI assistant specialized in histopathology slide interpretation. I will provide you with descriptions and diagnostic results related to histopathology slides. Your task is to create a dialogue as if you are directly observing and analyzing the slide.

Guidelines:

**Observation:** Assume you are directly viewing the slide and provide detailed descriptions of the pathological features when answering the questions. Ensure each response is directly related to the specific morphological feature being asked about, and do not mention any diagnosis, prognosis, or grading.

**Tone:** Maintain a professional and informative conversational style, emulating the perspective of a visual AI assistant specializing in histopathology.

**Dialogue Structure:** Questions must strictly focus on the following three morphological aspects and should only be asked if relevant information is provided in the pathology report. Avoid generating any questions or comments outside of these areas.

The questions should include:

- 1.Tumor Infiltration (Including Vascular and Neural Invasion):** If the pathology report mentions tumor infiltration, ask a question regarding how the tumor invades surrounding tissues. For example: "Can you describe the pattern of tumor infiltration?" The answer should describe patterns such as local tissue invasion, perineural invasion, or vascular involvement, excluding nuclear features.
- 2.Tissue Architecture Observation:** If the pathology report mentions tissue architecture, ask a question regarding the general structural arrangement of cells and tissues. For example: "What observations can you make about the tissue architecture on this slide?" The answer should focus on features such as glandular formations, solid sheets of cells, or stromal alterations.
- 3.Cellular Morphology:** If the pathology report includes observations about cellular and nuclear characteristics, ask a question about these features. For example: "What are the notable features of the cellular morphology in this slide?" The answer should describe aspects like cell size, shape, arrangement, nuclear size, nuclear shape, chromatin texture, the presence of nucleoli, and mitotic figures (including any abnormal mitoses), without linking these features to a diagnosis or including any grading.

**Scope Limitation:** Do not generate questions outside of the three specified categories. Only ask questions if the corresponding information is explicitly mentioned in the pathology report. If certain information is missing, omit the question for that category.

**Avoid Additional Questions:** Do not introduce questions beyond the given categories, even if they seem relevant to a pathologist's typical inquiries.

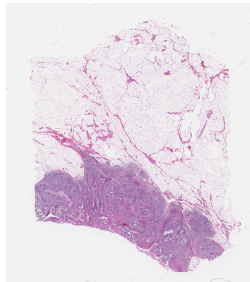
**Ensure Direct Relevance:** Make sure all questions and answers are directly connected to the provided pathology report. If certain information isn't available, omit questions that would require that information.

**Consistent Question Phrasing:** You may vary the wording to reflect a professional's questioning style but ensure the essence of the questions remains within the specified categories.

**Length:** Ensure the entire dialogue does not exceed 600 words, providing accurate morphological descriptions.

Figure 14. The prompt used to generate VQA pairs for regional structure description

Table 8. VQA example for regional structure description task.

Example of Regional Structure Description	
WSI	
Question	What observations can you make about the tissue architecture on this slide?
Answer	The tissue architecture is significantly disrupted, marked by minimal formation of glandular structures. The poorly differentiated state results in a loss of the typical organized glandular architecture, and instead, cells are haphazardly arranged. There is less than 25% of the slide showing an intraductal component, and this area exhibits prominent cancerization of lobules.

### GPT-4o Prompt: VQA Instruction-Following Prompt for Specific Feature Description

**System Message:** You are an AI assistant specialized in histopathology slide interpretation. I will provide you with descriptions related to histopathology slides. Your task is to create a dialogue that includes specific questions about the mentioned morphological features, as if you are directly observing and analyzing the slide.

Guidelines:

Observation:

Assume you are directly viewing the slide and provide detailed descriptions of the pathological features when answering the questions.

Ensure each response is directly related to the specific morphological feature being asked about.

Do not mention any diagnosis, prognosis, or grading (e.g., scores or classifications).

Each answer should be self-contained, offering enough context without relying on previous exchanges.

Tone:

Maintain a professional and informative conversational style, emulating the perspective of a visual AI assistant specializing in histopathology.

Dialogue Structure:

Each time, generate 1-3 specific questions that precisely inquire about the mentioned morphological features.

Each question should focus on whether a specific feature exists.

For example, ask "Is nuclear pleomorphism observed in the tumor cells?" or "Are cribriform structures present?" instead of "What are the characteristics of the papillary structures observed within the ducts?"

The answer should provide a detailed description of that feature as observed on the slide.

Avoid constructing questions that mention what you already know from the report.

Scope Limitation:

Do not introduce any questions about features not mentioned.

Avoid referencing any scoring systems or grades in your answers.

Do not mention the pathology report in your questions or answers.

Assume that you do not know the diagnostic content of the report.

Avoid Additional Questions:

Do not introduce questions beyond the features mentioned, even if they are typically relevant to a pathologist.

Ensure Direct Relevance:

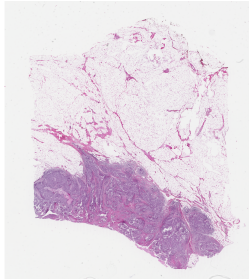
Make sure all questions and answers are directly connected to the provided morphological features.

Length:

Ensure the entire dialogue does not exceed 500 words, providing concise and accurate morphological descriptions.

Figure 15. The prompt used to generate VQA pair for specific feature description

Table 9. VQA example for specific feature description task.

Example of Specific Feature Description	
WSI	
Question	Do the nuclei of the tumor cells show nuclear pleomorphism?
Answer	Indeed, the nuclei of the tumor cells exhibit considerable nuclear pleomorphism, featuring significant variability in size and shape. They present irregular contours, are substantially larger than normal, and possess dense chromatin, highlighting marked atypical nuclear features.

### GPT-4o Prompt: VQA Instruction-Following Prompt for Global Morphology Description

**System Message:** You are an AI assistant specialized in histopathology slide interpretation. I will provide you with descriptions and diagnostic results related to histopathology slides. Your task is to create a dialogue as if you are directly observing and analyzing the slide.

Guidelines:

**Observation:** In your response, assume you are directly viewing the slide and provide a detailed description of the pathological features when answering the question.

**Tone:** Maintain a professional and informative conversational style, emulating the perspective of a visual AI assistant.

**Dialogue Structure:** Create a coherent dialogue consisting of one Q&A pair. Ensure that the question corresponds to what a professional pathologist might ask when examining a slide, and only include the question within the specified category—do not construct additional questions beyond this range. When phrasing the question, you may vary the wording to reflect the diverse questioning style of a pathology expert, as long as the meaning remains consistent.

The question should include:

**Overall Description:** One question asking for a description of the whole digital pathology slide (WSI). In the answer, do not mention any diagnosis or grading.

**Prioritize features directly related to the diagnosis.** Ensure the question and answer are directly related to the content provided; if certain information is not available in the given text, you may omit the corresponding details.

**Avoid Additional Questions:** Do not introduce questions beyond the given category, even if they seem relevant to a pathologist's typical inquiries.

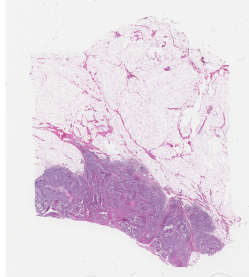
**Ensure Direct Relevance:** Make sure the question and answer are directly connected to the provided text. If certain information isn't available, omit details that would require that information.

**Consistent Question Phrasing:** While you can vary the wording to reflect a professional's questioning style, ensure the essence of the question remains within the specified category.

**Length:** Ensure the dialogue is concise and directly addresses the question.

Figure 16. The prompt used to generate VQA pair for global morphology description task.

Table 10. The prompt used to generate VQA pairs for global morphology description task.

VQA example of global morphology description	
WSI	
Question	Can you provide an overall description of the whole slide image (WSI)?
Answer	The whole slide image reveals malignant epithelial cells infiltrating the surrounding stroma with minimal glandular structures. The normal tissue architecture is significantly disrupted. The tumor cells are poorly differentiated, displaying large variability in nuclear size and shape, indicative of substantial nuclear pleomorphism. A moderate rate of cell division is observed among the tumor cells. There is no evident vascular invasion, necrosis, or microcalcifications. The intraductal component is less than 25% with notable cancerization present.



### GPT-4o Prompt: VQA Instruction-Following Prompt for Key Diagnostic Description

**System Message:** You are an AI assistant specialized in histopathology slide interpretation. I will provide you with descriptions and diagnostic results related to histopathology slides. Your task is to create a dialogue as if you are directly observing and analyzing the slide.

Guidelines:

**Observation:** In your response, assume you are directly viewing the slide and provide a detailed description of the pathological features when answering the question.

**Tone:** Maintain a professional and informative conversational style, emulating the perspective of a visual AI assistant.

**Dialogue Structure:** Create a coherent dialogue consisting of one Q&A pair. Ensure that the question corresponds to what a professional pathologist might ask when examining a slide, and only include the question within the specified category—do not construct additional questions beyond this range. When phrasing the question, you may vary the wording to reflect the diverse questioning style of a pathology expert, as long as the meaning remains consistent.

The question should include:

**Important Features:** One question asking which of the observed features are the most important. In the answers, do not mention any diagnosis, score or grading.

**Prioritize features directly related to the diagnosis.** Ensure the question and answer are directly related to the content provided; if certain information is not available in the given text, you may omit the corresponding details.

**Avoid Additional Questions:** Do not introduce questions beyond the given category, even if they seem relevant to a pathologist's typical inquiries.

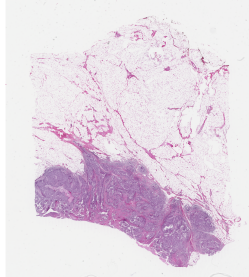
**Ensure Direct Relevance:** Make sure the question and answer are directly connected to the provided text. If certain information isn't available, omit details that would require that information.

**Consistent Question Phrasing:** While you can vary the wording to reflect a professional's questioning style, ensure the essence of the question remains within the specified category.

**Length:** Ensure the dialogue is concise and directly addresses the question.

Figure 17. The prompt used to generate VQA pair for key diagnostic description task.

Table 11. The prompt used to generate VQA pairs for key diagnostic description task.

VQA example for key diagnostic description task	
WSI	
Question	Among the features observed, which are particularly critical for making a diagnosis?
Answer	Among the features observed, which are particularly critical for making a diagnosis?", "text": "Key features essential for diagnosis include the extensive nuclear pleomorphism and minimal glandular structure formation, both of which point to poor differentiation. The moderate mitotic rate is also significant in assessing cellular proliferation. Another important factor is the presence of a prominent cancerization of ducts, albeit the intraductal component is less than 25%. These aspects collectively depict a highly invasive and aggressive nature of the tumor.

### GPT-4o Prompt: VQA Instruction-Following Prompt for Histological Typing

**System Message:** You are an AI assistant specialized in histopathology slide interpretation. I will provide you with descriptions and diagnostic results related to histopathology slides. Your task is to create a dialogue as if you are directly observing and analyzing the slide.

Guidelines:

**Observation:** In your response, assume you are directly viewing the slide and provide a detailed description of the pathological features when answering the question.

**Tone:** Maintain a professional and informative conversational style, emulating the perspective of a visual AI assistant.

**Dialogue Structure:** Create a coherent dialogue consisting of one Q&A pair. Ensure that the question corresponds to what a professional pathologist might ask when examining a slide, and only include the question within the specified category—do not construct additional questions beyond this range. When phrasing the question, you may vary the wording to reflect the diverse questioning style of a pathology expert, as long as the meaning remains consistent.

The question should include:

**Histological Classification:** One question regarding the histological classification based on the observed features. Ensure that the response does not reference any grading or scoring systems and focuses solely on identifying the type of cancer without mentioning the location.

**Prioritize features directly related to the diagnosis.** Ensure the question and answer are directly related to the content provided; if certain information is not available in the given text, you may omit the corresponding details.

**Avoid Additional Questions:** Do not introduce questions beyond the given category, even if they seem relevant to a pathologist's typical inquiries.

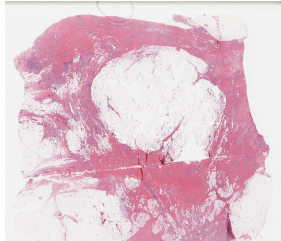
**Ensure Direct Relevance:** Make sure the question and answer are directly connected to the provided text. If certain information isn't available, omit details that would require that information.

**Consistent Question Phrasing:** While you can vary the wording to reflect a professional's questioning style, ensure the essence of the question remains within the specified category.

**Length:** Ensure the dialogue is concise and directly addresses the question.

Figure 18. The prompt used to generate VQA pair for histological typing task.

Table 12. VQA example for histological typing task

Example of Histological Typing	
WSI	
Question	How would you classify the histological type of cancer observed on the slide?
Answer	The observed slide is indicative of invasive lobular carcinoma. This classification is due to the presence of epithelial cells with minimal glandular differentiation, infiltrating the stroma in a characteristic pattern. The moderate nuclear pleomorphism and the absence of vascular or lymphatic invasion are consistent with this histological type.

### GPT-4o Prompt: VQA Instruction-Following Prompt for Grading

**System Message:** You are an AI assistant specialized in histopathology slide interpretation. I will provide you with descriptions and diagnostic results related to histopathology slides. Your task is to create a dialogue as if you are directly observing and analyzing the slide.

Guidelines:

**Observation:** In your response, assume you are directly viewing the slide and provide a detailed description of the pathological features when answering the question.

**Tone:** Maintain a professional and informative conversational style, emulating the perspective of a visual AI assistant.

**Dialogue Structure:** Create a coherent dialogue consisting of one Q&A pair. Ensure that the question corresponds to what a professional pathologist might ask when examining a slide, and only include the question within the specified category—do not construct additional questions beyond this range. When phrasing the question, you may vary the wording to reflect the diverse questioning style of a pathology expert, as long as the meaning remains consistent.

The question should include:

**Grading:** If the given text mentions a specific grading system (e.g., Nottingham grading in breast cancer), include a question directly asking for the grading. If the given text does not mention grading, omit this question.

**Prioritize features directly related to the diagnosis.** Ensure the question and answer are directly related to the content provided; if certain information is not available in the given text, you may omit the corresponding details.

**Avoid Additional Questions:** Do not introduce questions beyond the given category, even if they seem relevant to a pathologist's typical inquiries.

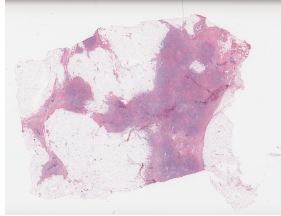
**Ensure Direct Relevance:** Make sure the question and answer are directly connected to the provided text. If certain information isn't available, omit details that would require that information.

**Consistent Question Phrasing:** While you can vary the wording to reflect a professional's questioning style, ensure the essence of the question remains within the specified category.

**Length:** Ensure the dialogue is concise and directly addresses the question.

Figure 19. The prompt used to generate VQA pair for grading task.

Table 13. VQA example for grading task.

Example of Grading	
WSI	
Question	What is the Nottingham Histologic Grade of this tumor based on the observed features?
Answer	The tumor is classified as Nottingham Histologic Grade 3, with a total score of 8 out of 9. This grading is based on the poor tubule formation (score of 3), marked nuclear pleomorphism (score of 3), and moderate mitotic activity (score of 2). This indicates a high-grade tumor with poor differentiation and suggests a potentially more aggressive clinical course.

GPT-4o Prompt: VQA Instruction-Following Prompt for Molecular Subtyping

**System Message:** You are an AI assistant specialized in interpreting immunohistochemical (IHC) information. I will provide you with IHC results and the corresponding molecular subtype. Your task is to construct a question-and-answer pair that inquires about the molecular subtype based on the provided information.

Guidelines:

Observation: In your responses, focus solely on the provided IHC results.

Question: Based on the IHC results, ask for the determination of the molecular subtype.

Answer: Provide the statement "The molecular subtype is [Subtype]." without additional explanation.

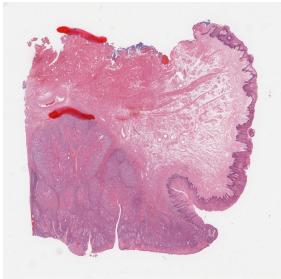
Tone: Maintain a professional and informative conversational style.

Avoid Unnecessary Content: Do not include any additional questions or information.

Length: Ensure the entire dialogue does not exceed 100 words.

Figure 20. The prompt used to generate VQA pair for molecular subtyping

Table 14. VQA example for molecular subtyping task.

Example of Molecular Subtyping	
WSI	
Question	Based on the IHC results showing P16 negativity and HR, HPV ISH status negativity, what is the molecular subtype in this head and neck squamous cell carcinoma?
Answer	The molecular subtype is HNSC HPV-



### GPT-4o Prompt: VQA Instruction-Following Prompt for Staging

**System Message:** You are an AI assistant specialized in oncology. I will provide you with the TNM staging of a patient. Your task is to create a single Q&A pair where you are asked to determine the TNM staging for this patient.

Guidelines:

**Question:** Craft a question that includes the patient's tumor size, lymph node status, and presence or absence of distant metastasis, asking for the TNM staging, but do not include specific TNM classifications or results in the question.

**Answer:** Based on the information provided in the question, state the correct TNM staging for the patient.

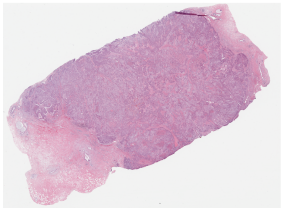
**Tone:** Maintain a professional and informative conversational style.

**Avoid Unnecessary Content:** Do not include any additional questions, explanations, or information beyond what is required to determine the TNM staging.

**Length:** Ensure the entire dialogue does not exceed 60 words.

Figure 21. The prompt used to generate VQA pair for Staging

Table 15. VQA example for staging task.

Example of Staging	
WSI	
Question	A patient has a 3 cm tumor, no regional lymph node involvement, and no distant metastasis. What is the TNM staging for this patient?
Answer	The TNM staging for this patient is T2 N0 M0.

### GPT-4o Prompt: VQA Instruction-Following Prompt for Treatment Recommendations

**System Message:** You are an AI assistant specialized in oncology treatment recommendations. I will provide you with diagnostic results, TNM staging, and immunohistochemistry (IHC) findings related to a patient's case. Your task is to create a single Q&A pair where you are asked about the recommended treatment plan for this patient.

Guidelines:

**Question:** Craft a question that inquires about the recommended treatment plan, considering the patient's specific diagnosis, TNM staging, and IHC results.

**Answer:** Provide a detailed treatment recommendation based on the provided information, formatted in numbered points for each treatment type.

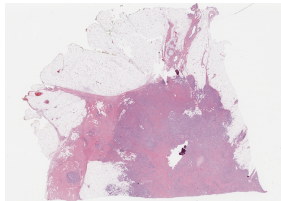
**Tone:** Maintain a professional and informative conversational style.

**Avoid Unnecessary Content:** Do not include any additional questions or information beyond what is required to recommend the treatment plan.

**Length:** Ensure the entire dialogue does not exceed 150 words.

Figure 22. The prompt used to generate VQA pair for treatment recommendations.

Table 16. VQA example for treatment recommendations task.

VQA example of treatment recommendations task	
WSI	
Question	What is the recommended treatment plan for a patient with invasive ductal carcinoma, Nottingham grade 2, TNM staging T2N1M0, ER-positive, PR-positive, and HER2-negative?
Answer	<ol style="list-style-type: none"> <li>1. Surgery: Perform breast-conserving surgery or mastectomy, depending on tumor size and patient preference, followed by sentinel lymph node biopsy or axillary lymph node dissection.</li> <li>2. Chemotherapy: Consider adjuvant chemotherapy due to nodal involvement and to reduce recurrence risk.</li> <li>3. Endocrine Therapy: Initiate tamoxifen or an aromatase inhibitor for at least 5 years, given the ER/PR positivity.</li> <li>4. Radiation Therapy: Advise adjuvant radiation therapy, especially if breast-conserving surgery was performed, to minimize local recurrence risk.</li> </ol>

### GPT-4o Prompt: VQA Instruction-Following Prompt for Prognosis Task

**System Message:** You are an AI assistant specialized in oncology prognosis assessment. I will provide you with diagnostic results, TNM staging, and immunohistochemistry (IHC) findings for a patient's case. Your task is to create a single Q&A pair where you are asked about the prognosis for this patient considering their specific diagnosis, TNM staging, and IHC results.

Guidelines:

**Question:** Craft a question that specifically inquires about whether the prognosis for the patient, given their diagnosis, TNM staging, and IHC results, is good or poor.

**Answer:** Directly state whether the prognosis is good or poor, and provide a simple explanation based on the information given, without recommending further actions like monitoring or specific treatments.

**Tone:** Maintain a professional and informative conversational style.

**Avoid Unnecessary Content:** Do not include any statements about the need for monitoring or additional treatment methods in the answer.

**Length:** Ensure the entire dialogue does not exceed 120 words.

Figure 23. The prompt used to generate VQA pair for prognosis task.

Table 17. VQA example for prognosis task.

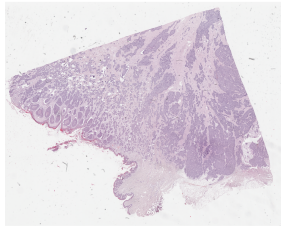
Example of Prognosis	
WSI	
Question	Given the diagnosis of invasive ductal carcinoma (Nottingham Grade 3), TNM staging of T4BN1M0, and IHC results showing 10-75% positivity for hormone receptors with negative HER2 protein, is the prognosis good or poor?
Answer	The prognosis is poor. The high histologic grade, advanced tumor size, and lymph node involvement indicate aggressive disease, despite partial hormone receptor positivity. Negative HER2 limits targeted therapy options.

Table 18. A comparative example of Report Generation outputs from different models

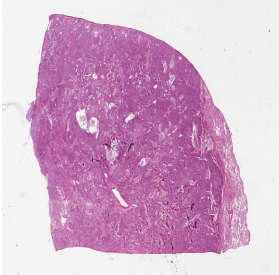
Sample Comparison of Report Generation	
WSI	
Question	What are the main observations in the whole slide histopathology image, and what is the likely diagnosis?
WSI-LLaVA	Microscopic observation of the pathology slide reveals moderately differentiated squamous cell carcinoma characterized by nests and sheets of atypical squamous epithelial cells with intercellular bridges and keratinization. The tumor cells exhibit moderate nuclear pleomorphism with enlarged, hyperchromatic nuclei and prominent nucleoli. Mitotic figures are present, indicating active cell division. There is no evidence of vascular invasion, necrosis, or calcification within the examined tissue. Based on these observations, the diagnosis is moderately differentiated keratinizing squamous carcinoma.
MI-Gen	microscopic observation of the pathology slide reveals a poorly differentiated squamous cell carcinoma characterized by a lack of squamous cell carcinoma . the tumor exhibits a lack of squamous differentiation with a lack of squamous differentiation . the tumor cells exhibit moderate nuclear pleomorphism with variability in nuclear size and shape and there is a moderate rate of cell division .vascular invasion is not identified . necrosis is not observed within the tumor . based on these observations the diagnosis is squamous cell carcinoma .
Hist-Gen	microscopic observation of the pathology slide reveals a poorly differentiated squamous cell carcinoma characterized by irregular nests and sheets of atypical squamous cells with intercellular bridges and keratinization . the tumor cells exhibit a high degree of nuclear pleomorphism . there is no evidence of vascular invasion or necrosis within the tumor tissue . the surrounding lung parenchyma shows areas of chronic inflammation and chronic inflammation . based on these observations the diagnosis is squamous cell carcinoma poorly differentiated .
Quilt-LLaVA	Microscopic observation of the pathology slide reveals sheets and nests of atypical squamous cells with moderate differentiation. There is evidence of focal keratinization, characterized by the presence of keratin pearls within the tumor tissue. Intercellular bridges are noted among the squamous cells, indicating differentiation towards squamous epithelium. The cellular morphology shows moderate pleomorphism, with variability in nuclear size and shape, and occasional prominent nucleoli. Mitotic figures are present but not excessively numerous. Vascular invasion is not specified in the observations, and necrosis is not prominently noted. Based on these observations, the diagnosis is squamous cell carcinoma, moderately differentiated.
GPT-4o	This histopathology image shows a well-circumscribed, nodular lesion with a dense, cellular stroma. There are areas of necrosis and hemorrhage, and the tissue architecture appears disrupted. The lesion has a heterogeneous appearance with varying cellular densities and some fibrotic regions.**Diagnosis**: The features are consistent with a uterine fibroid (leiomyoma), which is characterized by a smooth muscle cell growth forming a circumscribed mass with areas of degeneration.
Ground Truth	Microscopic observation of the pathology slide reveals sheets and nests of atypical squamous cells with moderate differentiation. There is evidence of focal keratinization, characterized by the presence of keratin pearls within the tumor tissue. Intercellular bridges are noted among the squamous cells, indicating differentiation towards squamous epithelium. The cellular morphology shows moderate pleomorphism, with variability in nuclear size and shape, and occasional prominent nucleoli. Mitotic figures are present but not excessively numerous. Vascular invasion is not specified in the observations, and necrosis is not prominently noted. Based on these observations, the diagnosis is squamous cell carcinoma, moderately differentiated.

Table 19. A comparative example of Global Morphology Description outputs from different models

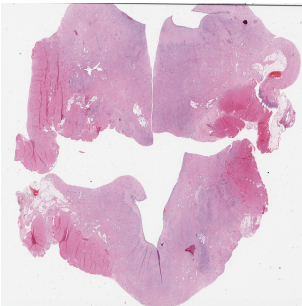
Sample Comparison of Global Morphology Description	
WSI	
Question	Can you provide an overall description of the whole slide image (WSI)?
WSI-LLaVA	The whole slide image reveals exuberant granulation tissue characterized by notable fibroblastic proliferation and myxoid changes. The cellular component is primarily composed of spindle-shaped cells within a myxoid matrix. There is an absence of normal tissue architecture as the granulation tissue dominates the observed section. Importantly, no residual sarcoma tissue is identifiable within this examined section.
Quilt-LLaVA	The whole slide image reveals a tumor with a diffuse architectural pattern, characterized by a mixture of alveolar formations and glandular cell differentiation. There is a notable presence of large cells with prominent nucleoli and moderate nuclear atypia. The mitotic activity is moderate, with 8 mitoses per 10 high power fields. The tumor shows significant vascular invasion, with tumor cells infiltrating the renal vein. Additionally, there is focal necrosis within the tumor tissue.
WSI-VQA	the whole slide image reveals a biphasic tumor composed of spindle-shaped cells arranged in a storiform pattern . these spindle cells are arranged in a storiform pattern . the spindle cells are arranged in a storiform pattern . there is a notable absence of necrosis or calcification within the tumor.
GPT-4o	<p>The whole slide image appears to be a tissue section stained with hematoxylin and eosin (H&amp;E), commonly used in histopathology. The sample is divided into several sections, likely representing different orientations or parts of the tissue.</p> <ul style="list-style-type: none"><li>- <b>**Coloration**</b>: The pink and purple hues suggest typical H&amp;E staining, where eosin stains cytoplasmic components pink and hematoxylin stains nuclear material blue or purple.</li><li>- <b>**Tissue Architecture**</b>: The sections show varying thickness and include both smooth and irregular contours, indicating possible different tissue types or regions.</li><li>- <b>**Other Observations**</b>: There are areas that seem to contain more densely packed cells and some regions with more open or less cellular areas, suggesting different tissue densities or types.</li></ul> <p>A detailed examination at higher magnification would be necessary for further analysis, such as identifying specific pathological features or structures.</p>
Ground Truth	The whole slide image demonstrates exuberant granulation tissue characterized by notable fibroblastic proliferation and myxoid changes. The cellular component is primarily composed of spindle-shaped cells within a myxoid matrix. There is an absence of normal tissue architecture as the granulation tissue dominates the observed section. Importantly, no residual sarcoma tissue is identifiable within this examined section.

Table 20. A comparative example of Key Diagnostic Description outputs from different models

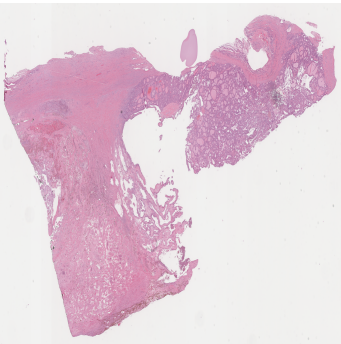
Sample Comparison of Key Diagnostic Description	
WSI	
Question	Which observed features are most significant for making a diagnosis?
WSI-LLaVA	The most significant features include the papillary architecture with fibrovascular cores, the presence of psammoma bodies, and the nuclear characteristics such as overlapping, grooves, and intranuclear cytoplasmic inclusions. The absence of vascular invasion, necrosis, and calcification also plays a crucial role in the diagnostic process.
Quilt-LLaVA	The most significant features include the irregular clusters of epithelial cells with poor glandular differentiation, marked nuclear pleomorphism, and the presence of perineural invasion. The high mitotic activity and evidence of lymphovascular invasion are also critical, as they indicate aggressive tumor behavior.
WSI-VQA	the most significant features include the papillary architecture with fibrovascular cores and the presence of fibrovascular cores . the absence of vascular invasion and necrosis further supports the diagnosis . the absence of necrosis and calcification further supports the diagnosis .
GPT-4o	<p>To make a diagnosis from this histopathological image, the following observed features are significant:</p> <ol style="list-style-type: none"><li>1. <b>**Cellular Architecture and Arrangement**</b>: Observe the overall structure and any abnormal formations or patterns within the tissue.</li><li>2. <b>**Presence of Lesions or Masses**</b>: Look for areas indicating hyperplasia, neoplasia, or other abnormal growths.</li><li>3. <b>**Inflammation Indicators**</b>: Note any signs of infiltration by immune cells, such as lymphocytes or macrophages.</li><li>4. <b>**Vascular Changes**</b>: Identify any alterations in blood vessels, such as congestion, hemorrhage, or new vessel formation.</li><li>5. <b>**Stromal Changes**</b>: Assess changes in the supporting tissue, like fibrosis or stromal desmoplasia.</li><li>6. <b>**Glandular Structures or Cyst Formation**</b>: If applicable, evaluate the formation of glands or cystic spaces.</li></ol> <p>A detailed examination considering these features, along with clinical correlation, aids in reaching an accurate diagnosis.</p>
Ground Truth	The key features of high diagnostic importance include the branching papillary formations and the unique nuclear features of the neoplastic epithelial cells. The presence of crowding, overlapping nuclei with prominent grooves, and occasional intranuclear inclusions are particularly crucial. The absence of vascular invasion, necrosis, or calcification also provides essential context in the diagnostic evaluation.

Table 21. A comparative example of Regional Structure Description outputs from different models

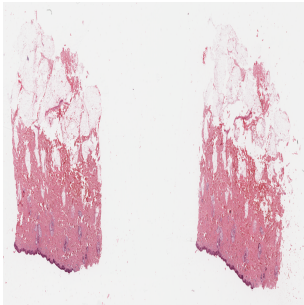
Sample Comparison of Regional Structure Description	
WSI	
Question	What observations can you make about the tissue architecture on this slide?
WSI-LLaVA	The tissue architecture is characterized by a sheet-like growth pattern, where the tumor cells are densely packed, exhibiting minimal stromal separation. This creates an overall cohesive mass with sparse connective tissue presence.
Quilt-LLaVA	The tissue architecture is characterized by nests and sheets of atypical melanocytes. These cells are arranged in a disorganized pattern, with a lack of the normal architectural structure typically seen in healthy tissue. The presence of necrosis within the tumor further disrupts the tissue architecture.
WSI-VQA	the tissue architecture is characterized by papillary structures lined by neoplastic epithelial cells . these papillae are lined by layers of cuboidal to columnar epithelial cells . the papillae are lined by a single layer of cuboidal to columnar epithelial cells
GPT-4o	<p>The tissue slide shows several features:</p> <ol style="list-style-type: none"><li>1. <b>**Layered Structure**</b>: The tissue exhibits a layered architecture indicative of an organ with distinct layers, such as the gastrointestinal tract.</li><li>2. <b>**Heterogeneity**</b>: There are regions with varied staining intensity, suggesting variability in cellular composition or density.</li><li>3. <b>**Crypt Structures**</b>: There are glandular or crypt-like structures present, typical of mucosal tissues like the colon.</li><li>4. <b>**Villi or Projections**</b>: Some areas show protrusions or folds, which could be part of the mucosal surface architecture.</li><li>5. <b>**Potential Inflammation**</b>: If there is any increased cellularity in certain areas, it could indicate inflammation or infiltration.</li><li>6. <b>**Connective Tissue**</b>: Lighter stained areas may suggest the presence of connective or submucosal tissue.</li></ol> <p>These observations can help identify the type of tissue and any pathological changes if present.</p>
Ground Truth	The tissue architecture is characterized by a sheet-like growth pattern, where the tumor cells are densely packed, exhibiting minimal stromal separation. This creates an overall cohesive mass with sparse connective tissue presence.

Table 22. A comparative example of Specific Feature Description outputs from different models

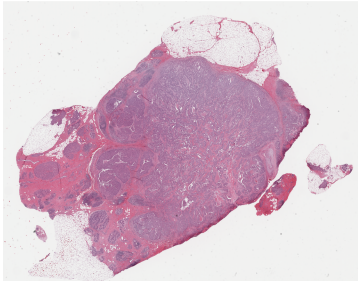
Sample Comparison of Specific Feature Description	
WSI	
Question	Do the epithelial cells infiltrate the surrounding stromal tissue or exhibit invasiveness?
WSI-LLaVA	Yes, the epithelial cells are infiltrating the surrounding stromal tissue, demonstrating invasive characteristics. They have breached their normal boundaries and are penetrating into the stroma, disrupting the typical tissue architecture. This invasion is accompanied by a desmoplastic stromal response, indicating the body's reaction to the invading tumor cells.
Quilt-LLaVA	Yes, the epithelial cells are infiltrating the surrounding stromal tissue, demonstrating invasive characteristics. They have breached their normal boundaries and are penetrating into the stroma, disrupting the typical tissue architecture. This invasion is accompanied by minimal glandular formation, indicating a significant deviation from normal tissue organization.
WSI-VQA	yes the epithelial cells are infiltrating the surrounding stromal tissue demonstrating invasive characteristics . they have breached their usual boundaries and are penetrating into the stroma disrupting the normal tissue architecture . this infiltration is a key feature of the epithelial cells .
GPT-4o	<p>The image shows a histological section. However, at this magnification, it is difficult to determine if epithelial cells are infiltrating the surrounding stromal tissue or exhibiting invasiveness. To make an accurate assessment, a higher magnification would be necessary to examine the interactions between epithelial cells and stroma more closely. If invasiveness is suspected, it is best evaluated through additional histological analysis with higher resolution images.</p>
Ground Truth	Yes, the epithelial cells are infiltrating the surrounding stromal tissue. They extend beyond their usual confines, permeating into the stroma and demonstrating distinct invasive characteristics. This infiltration disrupts the normal architecture of the surrounding tissue.



Table 23. A comparative example of Histological Typing outputs from different models

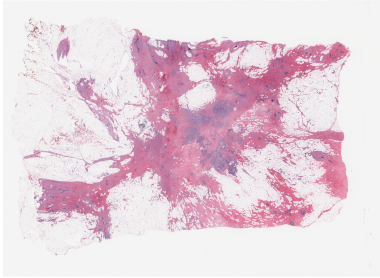
Sample Comparison of Histological Typing	
WSI	
Question	What is the histological classification based on your examination of the slide?
WSI-LLaVA	The histological classification is invasive ductal carcinoma. This is supported by the presence of infiltrating epithelial cells with minimal glandular formation, moderate nuclear pleomorphism, and a moderate mitotic rate. The absence of vascular invasion and necrosis also aligns with this classification.
Quilt-LLaVA	The histological classification is invasive ductal carcinoma. This is supported by the presence of infiltrating epithelial cells forming moderately differentiated glandular structures, moderate nuclear pleomorphism, and the presence of ductal carcinoma in situ (DCIS) with solid and cribriform patterns.
WSI-VQA	the histological classification based on the observed features is invasive ductal carcinoma . this classification is supported by the presence of infiltrating epithelial cells with minimal glandular formation moderate nuclear pleomorphism and the presence of ductal carcinoma in situ dcis with cribriform and solid patterns .
GPT-4o	I'm unable to make a diagnosis from the image. However, the slide appears to show fibrous and necrotic areas, characteristic of particular tumor types or other pathological conditions. For an accurate classification, a detailed analysis by a pathologist is required, considering factors such as cellular morphology, staining patterns, and clinical context.
Ground Truth	The histological findings are consistent with invasive ductal carcinoma. This classification is supported by the infiltrative growth pattern of the epithelial cells, minimal glandular differentiation, moderate nuclear pleomorphism, and low mitotic activity. The absence of vascular and lymphatic invasion, along with the lack of necrosis and calcifications, helps to further characterize this subtype based on its histopathological features.

Table 24. A comparative example of Grading outputs from different models

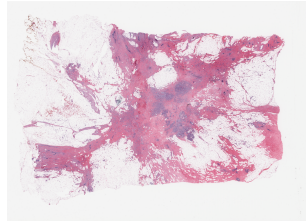
Sample Comparison of Grading	
WSI	
Question	What is the Nottingham Histologic Grade for this carcinoma, and what does this grading reflect?
WSI-LLaVA	The carcinoma is classified as Nottingham Histologic Grade 2, with a total score of 6 out of 9. This grading reflects a tubular formation score of 3, indicating poor differentiation,a nuclear pleomorphism score of 2, representing moderate variability in nuclear size and shape, and a mitotic count score of 1, denoting a low rate of cell division. This intermediate grade suggests a moderately differentiated tumor, which has implications for prognosis and treatment planning.
Quilt-LLaVA	The carcinoma is classified as Nottingham Histologic Grade 2, with a total score of 6 out of 9. This grading reflects a tubular formation score of 3, indicating poor differentiation, a nuclear pleomorphism score of 2, showing moderate variability, and a mitotic count score of 1, indicating low mitotic activity. This intermediate grade suggests a moderately differentiated tumor, which has implications for prognosis and treatment planning.
WSI-VQA	this carcinoma is classified as nottingham histologic grade 2 with a total score of 7 out of 9 . this grading reflects a tubular differentiation score of 3 a nuclear pleomorphism score of 2 and a mitotic count score of 1 . this grade reflects a moderately differentiated tumor with a total score of 1 .
GPT-4o	<p>I can't determine the Nottingham Histologic Grade from the image alone, as it requires detailed examination of specific histologic features. The Nottingham grading system evaluates three components:</p> <ol style="list-style-type: none"> <li><b>Tubule formation**</b>: The percentage of tumor forming tubular structures.</li> <li><b>Nuclear pleomorphism**</b>: Variation in the size and shape of the tumor cell nuclei.</li> <li><b>Mitotic count**</b>: The number of cells dividing. Each component is scored from 1 to 3, and the scores are summed to give a grade:</li> </ol> <ul style="list-style-type: none"> <li><b>Grade 1 (3-5 points)**</b>: Well-differentiated (low grade)</li> <li><b>Grade 2 (6-7 points)**</b>: Moderately differentiated (intermediate grade)</li> <li><b>Grade 3 (8-9 points)**</b>: Poorly differentiated (high grade).</li> </ul> <p>This grading reflects the aggressiveness of the cancer, with higher grades indicating more aggressive tumors.</p>
Ground Truth	The carcinoma is classified as Nottingham Histologic Grade 2 (NHG2) with a total score of 6 out of 9. This grading reflects poor glandular (tubular) formation, moderateness in nuclear pleomorphism, and a low rate of mitotic activity. An NHG2 designation indicates a moderately differentiated tumor, suggesting an intermediate level of aggressiveness and guiding treatment choices accordingly.

Table 25. A comparative example of Molecular Subtyping outputs from different models

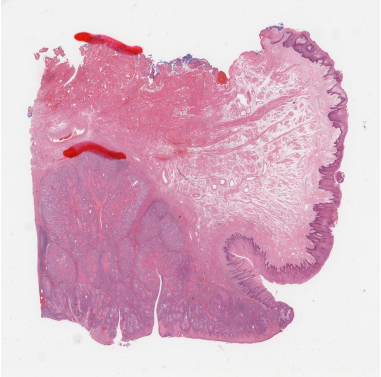
Sample Comparison of Molecular Subtyping	
WSI	
Question	Based on the IHC results showing P16 negativity and HR, HPV ISH status negativity, what is the molecular subtype in this head and neck squamous cell carcinoma?
WSI-LLaVA	The molecular subtype is <b>hNSC.HPV</b> .
Quilt-LLaVA	The molecular subtype is <b>hNSC.HPV</b> .
WSI-VQA	the molecular subtype is <b>hnscc unk</b> .
GPT-4o	<b>The molecular subtype of head and neck squamous cell carcinoma with P16 negativity and HR HPV ISH negativity is typically HPV-negative. This subtype is generally associated with non-viral risk factors such as smoking and alcohol use.</b>
Ground Truth	The molecular subtype is HNSC.HPV

Table 26. A comparative example of Staging outputs from different models

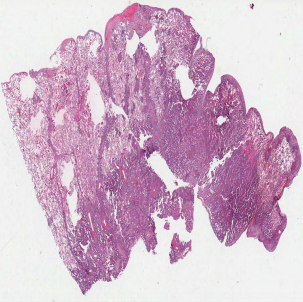
Sample Comparison of Staging	
WSI	
Question	What is the TNM staging for a patient with a 7 cm tumor, several affected lymph nodes, but no distant metastasis?
WSI-LLaVA	The TNM staging for this patient is <b>T3 N2 M0</b>
Quilt-LLaVA	The TNM staging for this patient is <b>T3 N2 M0</b> .
WSI-VQA	the tnm staging for this patient is <b>t2 n2 m0</b> .
GPT-4o	<p>To determine the TNM staging, we need to consider the following components:</p> <ul style="list-style-type: none"><li>- <b>T (Tumor size):</b> The tumor is 7 cm. This generally corresponds to T2 or T3, depending on the specific cancer type, but often T3 for many cancers.</li><li>- <b>N (Nodes):</b> Several affected lymph nodes typically indicates N1 or N2, depending on the exact number and extent of nodal involvement.</li><li>- <b>M (Metastasis):</b> No distant metastasis is indicated as M0.</li></ul> <p>Without specific details about the type of cancer, a general staging based on the information given could be <b>T3N1M0</b> or <b>T3N2M0</b>. However, the exact stage can vary based on cancer type and guidelines, so consultation with specific cancer staging resources is advised for precise staging.</p>
Ground Truth	TNM staging for this patient is T3 N2 M0.

Table 27. A comparative example of Treatment Recommendations outputs from different models

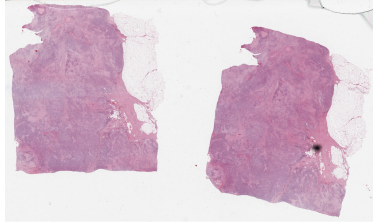
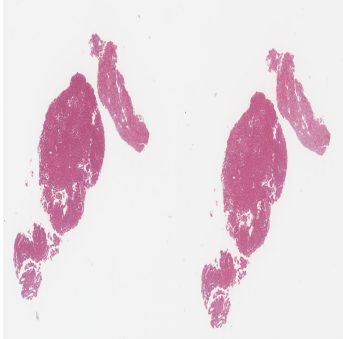
Sample Comparison of Treatment Recommendations	
	
WSI	
Question	What is the recommended treatment plan for a patient with a diagnosis of invasive ductal carcinoma, Nottingham Histologic Grade 3, TNM staging T3N1, ER-positive, PR-positive, and HER2-negative?
WSI-LLaVA	<ol style="list-style-type: none"> <li>1. <b>Surgery</b>: Consider mastectomy or breast-conserving surgery with axillary lymph node dissection due to T3 tumor size and N1 nodal involvement.</li> <li>2. <b>Chemotherapy</b>: Adjuvant chemotherapy is recommended given the high histologic grade and nodal involvement to reduce recurrence risk.</li> <li>3. <b>Endocrine Therapy</b>: Initiate tamoxifen or aromatase inhibitors for at least 5 years due to ER/PR positivity.</li> <li>4. <b>Radiation Therapy</b>: Post-surgical radiation therapy is advised, especially if breast conservation is performed or in the presence of significant nodal disease.</li> </ol>
Quilt-LLaVA	<ol style="list-style-type: none"> <li>1. <b>Surgery</b>: Consider mastectomy or breast-conserving surgery with axillary lymph node dissection due to T3N1 staging.</li> <li>2. <b>Chemotherapy</b>: Adjuvant chemotherapy is recommended given the high grade and nodal involvement.</li> <li>3. <b>Endocrine Therapy</b>: Initiate tamoxifen or aromatase inhibitors for at least 5 years due to ER/PR positivity.</li> <li>4. <b>Radiation Therapy</b>: Adjuvant radiation therapy is advised, especially if breast-conserving surgery was performed or due to significant nodal involvement.</li> </ol>
WSI-VQA	<ol style="list-style-type: none"> <li>1. <b>surgery</b> mastectomy or breast-conserving surgery lumpectomy or mastectomy based on patient preference followed by sentinel lymph node biopsy or axillary lymph node dissection due to nodal involvement .</li> <li>2. <b>endocrine therapy</b> initiate tamoxifen or aromatase inhibitors for at least 5 years due to er/pr positivity .</li> <li>3. <b>radiation therapy</b> consider adjuvant radiation therapy especially if breast-conserving surgery was performed to reduce local recurrence risk .</li> </ol>
GPT-4o	<p>For a patient with invasive ductal carcinoma, Nottingham Histologic Grade 3, TNM staging T3N1, ER-positive, PR-positive, and HER2-negative, the recommended treatment plan typically includes:</p> <ol style="list-style-type: none"> <li>1. <b>Surgery</b>:Lumpectomy or mastectomy depending on the tumor size and patient preference.Axillary lymph node dissection or sentinel lymph node biopsy to address nodal involvement.</li> <li>2.<b>Adjuvant Chemotherapy</b>:Given the tumor size (T3) and histologic grade (Grade 3), chemotherapy is often recommended.A regimen such as AC-T (doxorubicin and cyclophosphamide followed by paclitaxel) might be used.</li> <li>3.<b>Radiation Therapy</b>:Typically recommended after surgery, especially if breast-conserving surgery (lumpectomy) is performed.It may also be considered after mastectomy if the tumor is large or if lymph nodes are positive.</li> <li>4.<b>Endocrine Therapy</b>:Since the tumor is ER-positive and PR-positive, endocrine therapy is crucial.Options include tamoxifen or aromatase inhibitors, depending on menopausal status.</li> <li>5.Follow-up and Monitoring:Regular follow-up visits for physical exams, mammograms (if breast tissue remains), and monitoring for any recurrence or metastasis.</li> </ol>
Ground Truth	<ol style="list-style-type: none"> <li>1. Surgery: Perform a mastectomy or breast-conserving surgery with axillary lymph node dissection based on tumor size and nodal involvement.</li> <li>2. Chemotherapy: Adjuvant chemotherapy is recommended given the high tumor grade and nodal involvement.</li> <li>3. Endocrine Therapy: Initiate tamoxifen or aromatase inhibitors for at least 5 years due to ER and PR positivity.</li> <li>4. Radiation Therapy: Consider post-surgical radiation therapy, especially if breast-conserving surgery was chosen or if significant nodal involvement is present.</li> </ol>

Table 28. A comparative example of Prognosis outputs from different models

Sample Comparison of Prognosis	
WSI	
Question	Given the patient's diagnosis of hepatocellular carcinoma, TNM staging of T1N0M0, and immunohistochemistry results showing positive Hepatocyte and negative CK19, is the prognosis good or poor?
WSI-LLaVA	The prognosis is generally good. The early-stage (T1N0M0) hepatocellular carcinoma with positive Hepatocyte and negative CK19 indicates a well-differentiated tumor, which typically has a better prognosis compared to more advanced stages.
Quilt-LLaVA	The prognosis is good. The early stage (T1N0M0) and absence of lymph node involvement (N0) suggest a less aggressive disease, and the positive Hepatocyte marker indicates the tumor is likely of hepatocellular origin, which is typically associated with a better outcome
WSI-VQA	B
GPT-4o	In the case of a T1N0M0 stage hepatocellular carcinoma (HCC), the prognosis is generally considered relatively good. The TNM staging indicates: - **T1**: Single tumor without vascular invasion. - **N0**: No regional lymph node involvement. - **M0**: No distant metastasis. This early-stage diagnosis suggests a higher likelihood of successful treatment options, potentially including surgery, and a better overall prognosis compared to more advanced stages. The immunohistochemistry results showing positive Hepatocyte and negative CK19 support the diagnosis of a well-differentiated HCC, which is generally associated with a better prognosis. CK19 negativity implies the tumor is less likely to be aggressive compared to CK19-positive HCCs. Overall, the combination of early stage and favorable immunohistochemistry results suggests a relatively good prognosis for this patient. However, individual prognosis can vary, and continuous follow-up and management are essential.
Ground Truth	The prognosis is good. The early stage of liver cancer (T1N0M0) with no lymph node involvement or metastasis suggests a limited disease burden, while the IHC profile indicates typical hepatocellular carcinoma without bile duct differentiation.