

IBISAgent: Reinforcing Pixel-Level Visual Reasoning in MLLMs for Universal Biomedical Object Referring and Segmentation

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Abstract

Recent research on medical MLLMs has gradually shifted its focus from image-level understanding to fine-grained, pixel-level comprehension. Although segmentation serves as the foundation for pixel-level understanding, existing approaches face two major challenges. First, they introduce implicit segmentation tokens and require simultaneous fine-tuning of both the MLLM and external pixel decoders, which increases the risk of catastrophic forgetting and limits generalization to out-of-domain scenarios. Second, most methods rely on single-pass reasoning and lack the capability to iteratively refine segmentation results, leading to suboptimal performance. To overcome these limitations, we propose IBISAgent—a novel agentic MLLM that reformulates segmentation as a vision-centric, multi-step decision-making process. IBISAgent enables MLLMs to generate interleaved reasoning and text-based click actions, invoke segmentation tools, and produce high-quality masks without architectural modifications. By iteratively performing multi-step visual reasoning on masked image features, IBIS-Agent naturally supports mask refinement and promotes the development of pixel-level visual reasoning capabilities. We further design a two-stage training framework consisting of cold-start supervised fine-tuning and agentic reinforcement learning with tailored, fine-grained rewards, enhancing the model’s robustness in complex medical referring and reasoning segmentation tasks. Extensive experiments demonstrate that IBISAgent consistently outperforms both closed-source and open-source SOTA methods. All datasets, code, and trained models will be released publicly.

1. Introduction

Multimodal large language models (MLLMs) has yielded notable advancements in developing powerful medical AI

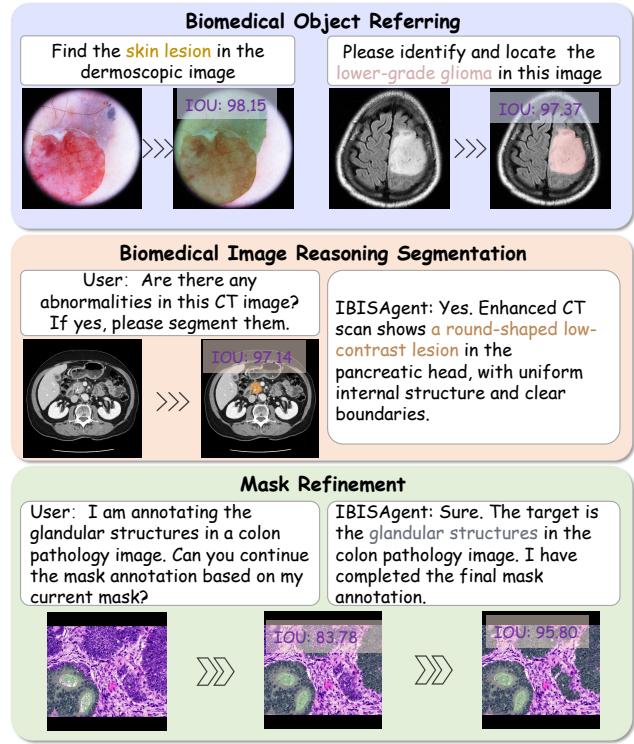


Figure 1. IBISAgent flexibly supports a wide range of fine-grained biomedical image understanding tasks, including referring and reasoning segmentation. It also handles a novel mask-refinement task that assists annotators in completing partially labeled masks.

assistants [4, 21, 33, 43]. These models now achieve high scores on exam-style medical question-answering benchmarks [8, 16, 19, 29]. However, daily clinical diagnosis is far more complex than a single structured question-and-answer interaction, since holistic medical image analysis comprises multiple subtasks, such as segmentation and detection of biomedical objects [46]. Prevailing medical MLLMs focus on visual question answering (VQA) and are largely confined to image-level understanding tasks, thus

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failing to achieve fine-grained pixel-level comprehension.

Recently, increasing efforts have been devoted to equipping MLLMs with pixel-level reasoning segmentation capabilities [3, 18, 23, 32, 45]. These models typically introduce additional task-specific segmentation tokens (*e.g.*, <SEG>), which are decoded through external pixel decoders to generate segmentation masks. Building on this foundation, many studies [1, 13, 38, 41] have adopted similar strategies to adapt MLLMs for medical image segmentation. Despite their effectiveness, the segmentation capabilities of existing medical MLLMs are still limited. Their dependence on joint fine-tuning of the MLLM and external pixel decoders heightens the risk of *catastrophic forgetting*, resulting in strong in-domain performance but weak cross-domain generalization. Moreover, the introduction of implicit segmentation tokens disrupts the MLLM’s natural text output space, thereby weakening its reasoning ability and failing to reflect the model’s intrinsic pixel-level understanding [35].

These limitations motivate a re-examination of how to better elicit pixel-level visual reasoning in MLLMs for biomedical image segmentation (BIS). Unlike natural images, biomedical images often exhibit subtle and complex visual semantics, such as faint lesion cues and nuanced pathological patterns. A single forward pass for segmentation is often inadequate. In contrast, human experts typically perform segmentation in a multi-step, interactive manner. For instance, annotators iteratively refine masks through positive and negative clicks using interactive segmentation tools [17, 26, 30]. It is natural to ask whether current MLLMs can observe an image multiple times, re-evaluate their intermediate decisions, and adapt to feedback to perform self-evolving segmentation—thereby emulating the strategies and interactive behaviors of human annotators through the use of segmentation tools.

Therefore, we propose IBISAgent, a novel agentic MLLM that reformulates segmentation as a multi-step Markov Decision Process. IBISAgent decouples pixel-level visual grounding and mask prediction. It iteratively generates interleaved reasoning and text-based click commands, invokes segmentation tools, and refines the current segmentation based on evolving visual features. Compared with previous medical MLLMs that rely on implicit tokens and additional pixel decoders, IBISAgent preserves the LLM’s inherent internal language representations and extends segmentation beyond mere pixel prediction to encompass fine-grained visual reasoning and action planning. This design facilitates vision-centric, multi-step decision-making and enables genuine reasoning to support advanced tasks such as automatic mask refinement (Fig. 1). Moreover, by treating segmentation models as plug-and-play tools controllable through language, IBISAgent enhances flexibility and extensibility by eliminating rigidly defined input–output templates (*e.g.*, “It’s <SEG>.”), thereby facilitating the im-

plementation of a unified framework across diverse tasks.

To develop IBISAgent, we first employ an automated iterative click-simulation algorithm to transform existing BIS datasets into high-quality annotation trajectories. Then, we construct a high-quality dataset comprising 640K samples, each annotated with step-wise reasoning traces, click action trajectories, and corresponding masks. We further propose a two-stage training protocol. First, we perform cold-start supervised fine-tuning (SFT) to enable IBISAgent to learn visual reasoning and plan click actions according to user instructions. we employ reinforcement learning (RL) with novel fine-grained rewards—particularly, a region-based click placement reward and a progressive segmentation improvement reward—to further enhance decision-making, allowing the model to autonomously discover efficient and advanced action policies rather than merely imitating the click trajectories learned during the SFT stage.

We conduct a comprehensive evaluation on multiple benchmarks, spanning both in-domain and zero-shot scenarios, to rigorously assess the performance of IBISAgent. Results show that our model exhibits strong pixel-level visual reasoning abilities and significantly exceeds the SOTA MLLMs. Our contributions can be summarized as follows:

- We present IBISAgent, a novel agentic framework that equips MLLMs with fine-grained pixel-level visual reasoning, enabling high-quality segmentation without architectural modifications or implicit tokens.
- We construct a comprehensive dataset and introduce effective training strategies—cold-start SFT and RL with tailored fine-grained rewards—to foster strong decision-making and advanced action planning.
- We conduct extensive held-in and held-out experiments to evaluate IBISAgent, and the results verify its superiority on biomedical object referring and segmentation tasks.

2. Related Work

Pixel-Level Understanding in Medical MLLMs. Recent advancements [12, 40, 41] in medical MLLMs have increasingly focused on enhancing the models’ fine-grained, pixel-level understanding to enable accurate detection and segmentation of biomedical structures. Inspired by the pioneering general-domain model LISA [18], which introduced a “reasoning segmentation” task to enable models to parse complex, implicit text queries and generate corresponding masks, numerous recent studies [12, 14, 39, 40] have adapted and extended this paradigm to the medical domain to address its unique challenges. These LISA-style MLLMs follow an innovative “embedding-as-mask” paradigm, in which the hidden-state embeddings of a special <SEG> token are projected by the LLM and subsequently decoded into segmentation masks via a vision decoder. While promising, these methods require MLLMs to learn task-specific implicit tokens and undergo additional

joint fine-tuning with a segmentation decoder. This process disrupts the MLLM’s original text output space and increases the risk of catastrophic forgetting, thereby compromising semantic generalization by deviating from language-based outputs. Moreover, existing methods are limited to single-turn reasoning and grounding, lacking an inherent mechanism for autonomous, self-evolving, multi-step refinement of mask predictions. These challenges represent the key issues our work aims to address.

MLLMs with Segmentation Tools. Recent studies [11, 20, 24, 25] have explored activating the intrinsic pixel-level understanding capabilities of MLLMs via RL, enabling the models to generate bounding boxes or point prompts that precisely localize target regions. These spatial coordinates are subsequently passed to SAM as prompts to generate the corresponding segmentation masks. However, these methods are constrained to single-turn reasoning and grounding. In complex real-world scenarios, MLLMs often struggle to precisely localize target regions in a single step. In contrast, we reformulate segmentation as a multi-step Markov Decision Process, enabling the MLLM to perform iterative mask refinement and exhibit self-reflective behavior—capabilities absent in prior work. This formulation effectively mitigates error accumulation and substantially improves performance. Furthermore, during the RL process, we design step-wise rewards that provide segmentation-quality-guided feedback at each iteration, further enhancing the agent’s stability and generalization ability.

3. Method

IBISAgent is a unified multimodal agent capable of pixel-space reasoning for biomedical image segmentation and mask refinement by adaptively generating spatial prompts and invoking segmentation tools. The ability is inherited from the model’s native capability of visual grounding and action planning, and further incentivized and enhanced via end-to-end SFT (Sec. 3.2) and RL training (Sec. 3.3).

3.1. Architecture Overview.

As illustrated in Fig. 2, given a user question Q and an input image I , the agent generates a multi-step, interleaved reasoning path P to derive the final answer. Unlike the predominant textual reasoning paradigm, this pixel-space reasoning path P can be represented as an T -step chain: $P = \{(r_t, a_t, o_t)\}_{t=1}^T$, where each step comprises textual thinking r_t , an action a_t which refers to spatial click operations, and the resulting segmentation observation o_t generated based on a_t . This iterative thought-action-observation loop continues until the model reaches a conclusive answer or when predefined limits on context length or interaction turns are reached. The core components are detailed below:

- **Textual Thinking:** The internal reasoning process used by the policy model to select the next action, conditioned on

the interaction history and the current observation.

- **Action:** The action space comprises two options: (1) click operations and (2) emitting a final answer. For click operations, each action is parameterized by three components: Target, which specifies the class name of the current segmentation objective; Attribute $\in \{+1, -1\}$, which indicates whether the click is positive or negative; and Coordinate_2d $\in [0, 1]^2$: represents the relative position of the point within the image, scaled to the $[0, 1]$ range for both x and y axes. Note that our method supports performing click operations on multiple targets at once. That is, in the action, it can contain multiple triples consisting of Target, Attribute, and Coordinate_2d. For clarity, in the following exposition, we focus on the single-target setting as a representative example to describe the method.
- **Observation:** The observation produced by executing a_t in the environment. Concretely, it corresponds to the segmentation mask generated by a segmentation tool (e.g., MedSAM2 [27]) given the inputs of the click prompts in a_t , the previous step’s output mask M_{t-1} as a spatial prior, and the original image. The initial observation o_0 is an empty mask, whereas the final observation represents the optimal target mask. This observation is appended to the interaction history and fed back to the model.

Rollout Formulation. Our objective is to train a policy π_θ that emulates the annotation behavior of human experts using an interactive segmentation tool. The policy iteratively generates textual reasoning with a series of positive and negative click points conditioned on the current image I and the evolving mask M , progressively refining the segmentation to achieve a high-quality result. At each step t , the policy is defined as:

$$r_{t+1}, a_{t+1} \sim \pi_\theta(\cdot | I, Q, P_{<t}). \quad (1)$$

We instruct the model to mark its textual thinking, action, and final answers in the output using the special tokens `<think>`, `<action>`, and `<answer>`. When the model output includes `<action>`, we automatically parse the action into a format compatible with the interactive segmentation model. Subsequently, all previous actions $a_{0:t}$, the current mask M_t , and the original image I are fed into the interactive segmentation model F_{seg} , which generates the updated mask M_{t+1} . Furthermore, we overlay M_{t+1} as a semi-transparent mask on the original image I to create a new composite image o_{t+1} . This image o_{t+1} are then inserted into the `<obs>` field and appended to the ongoing trajectory, serving as the input for the MLLM in next step, allowing the model to simultaneously perceive information about M_{t+1} and I in a single frame. This iterative reasoning process continues until the model determines that the segmentation has reached satisfactory quality. It then outputs a designated end token in `<action>` and generates the fi-

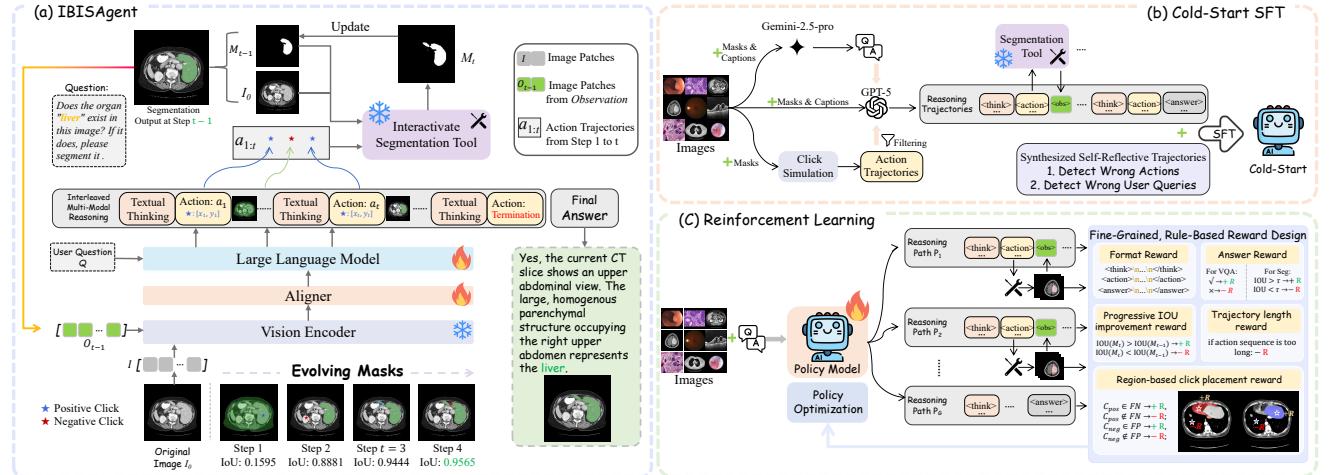


Figure 2. **Overview of IBISAgent.** (a) Overall architecture of the agent; (b) illustration of the cold-start SFT training process; and (c) illustration of the RL training process.

nal $\langle \text{answer} \rangle$. The system and user prompts are provided in Appendix E. Based on this formulation, IBISAgent supports flexible usage scenarios, including both from-scratch segmentation and refinement of pre-existing masks.

3.2. Cold-Start Supervised Fine-Tuning

We aim to cultivate a novel pixel-space reasoning paradigm within IBISAgent. Pure prompting, however, is insufficient to endow multimodal agents with the precision and robustness required to reliably perform iterative visual operations in real-world medical scenarios. To establish a strong foundation for subsequent reinforcement learning, we first initialize IBISAgent’s fine-grained pixel understanding and mask-refinement capability through supervised fine-tuning (SFT) on a cold-start dataset $\mathcal{D}_{\text{cold}}$, which provides ground-truth reasoning and click-annotation trajectories. In the following, we detail the procedures for data curation and instruction tuning employed in our framework.

Collect Seed Datasets. Existing biomedical segmentation datasets contain only final masks, without trajectories that capture the step-by-step annotation process. Collecting such data by re-hiring human annotators would incur substantial cost and require significant time investments. This motivates us to explore whether trajectory supervision can be automatically derived from existing mask annotations using a rule-based procedure. To this end, we utilize the large-scale BiomedParseData [46], containing 3.4 million image–mask–label tuples that cover 82 biomedical object types across 9 imaging modalities. The dataset provides diverse, high-quality masks that supply rich pixel-level details for fine-grained analysis and serve as reliable supervision for synthesizing click-based annotation trajectories.

Trajectory Generation. Inspired by prior research on interactive segmentation, we adopt the click-simulation strategy F_{cs} proposed in [42]. Given the current mask M_t

and the GT mask M_{gt} , F_{cs} outputs the next click action $a_{t+1} = F_{\text{cs}}(M_t, M_{\text{gt}})$. Specifically, this function computes the false positive and false negative regions between the current mask M_t and the GT mask M_{gt} , placing the next click action at the center of the error region based on the size and position of these regions. Based on F_{sim} , we can simulate high-quality trajectories $[M_0, a_0, M_1, a_1, \dots, M_T, a_T]$. The full trajectory generation algorithm and an illustrative example are presented in the Appendix B.1.

Question, Answer, and Reasoning Generation. We first filter the data based on trajectory quality by removing (1) overly long trajectories and (2) those whose final mask Dice score falls below a predefined threshold. For the remaining samples, we prompt Gemini-2.5-Pro [6] to generate question–answer pairs conditioned on each image, its GT mask, and the corresponding mask description. This process produces fine-grained queries that explicitly focus on grounding and segmenting the specified mask regions. The question set Q includes diverse query types, ranging from those that explicitly specify the segmentation target to those that require the model to first reason over the image and adaptively identify the target region on its own. The prompts for QA generation and examples are provided in Appendix B.2. We further use GPT-5 [28] to synthesize reasoning for each click action, conditioning on the QA, the correct next action, and pixel-level TP/FN information of the current mask. All generated reasoning traces are post-filtered for format and correctness by human annotations. More details are provided in Appendix B.3.

Reflective Behavior Synthesis. In complex scenarios, if the model cannot backtrack or undo previous actions, an inaccurate decision at any step may propagate and negatively impact subsequent predictions, ultimately degrading the final segmentation quality. To enhance robustness, we syn-

thesize additional samples with self-reflection trajectories, covering two types of error correction: (1) Self-correction, where the agent detects a wrong action, reverts to the previous state, and re-reasons over the interaction history to produce the correct action; and (2) User inconsistency correction, where, in mask-refinement scenarios, if the segmentation target described in the instruction does not align with the initial mask, the agent first discards the erroneous mask and re-segments according to the user instruction.

Cold-Start Training Objective. Through systematic curation, we obtain a dataset $\mathcal{D}_{\text{cold}}$ containing 456K samples, including both gold-standard and error-induced self-correction trajectories for cold-start SFT. The training objective is to minimize the average negative log-likelihood over all reasoning and action tokens. We employ the standard SFT loss for training. Specifically, we apply loss masks to tokens corresponding to segmentation outputs from executed actions as well as to designated erroneous actions within the self-correction trajectories. Masking the erroneous actions prevents the policy from learning to execute the incorrect actions. Our SFT strategy endows the model with strong pixel-level reasoning and self-reflection abilities, providing a solid foundation for subsequent RL.

3.3. Agentic Reinforcement Learning

We further optimize IBISAgent through RL with carefully designed rewards, enabling it to adaptively discover new action strategies and achieve higher-level decision-making, thereby moving beyond the constraints of mimicking the action trajectories learned during SFT.

Dataset Curation. Unlike $\mathcal{D}_{\text{cold}}$, the RL training data includes only images, GT masks, and QA pairs, without click trajectories or reasoning trace annotations. This design encourages the model to autonomously explore and strengthen its pixel-level reasoning ability during RL, thereby achieving stronger generalization beyond supervised imitation.

Specifically, we randomly sample image–mask pairs from BioMedParse that are not included in $\mathcal{D}_{\text{cold}}$. Following the same QA generation procedure as in the SFT stage, we obtain 562K VQA instances. In addition, we incorporate widely used biomedical VQA datasets that do not require fine-grained pixel-level reasoning or segmentation. This hybrid data composition enables IBISAgent to selectively activate pixel-space reasoning only when necessary. In total, 886K VQA samples are used for RL training, forming the dataset \mathcal{D}_{rl} . More details of \mathcal{D}_{rl} are in the Appendix A.2.

Reward Design. Unlike prior works [11, 24, 25, 44] that rely on overly simplified, outcome-only reward designs, we introduce a novel, fine-grained, rule-based reward framework that delivers dense feedback throughout the reasoning process. This enables the model to develop more efficient and effective decision-making strategies. Formally, the reward framework consists of the following components:

- Format reward $\mathcal{S}_{\text{format}}$, which evaluates the structural validity of the model’s output R . It checks whether all required special tokens appear in the correct order and whether the `<action>` fields can be successfully parsed according to the predefined schema.

- Final-answer reward \mathcal{S}_{ans} , which encompasses multiple task types. For close-ended QA questions, we simply check the exact match between the predicted and answers. For segmentation task, we compute the IoU between the predicted masks and GT masks and assign piecewise rewards based on predefined IoU thresholds.

- **Region-based click placement reward** $\mathcal{S}_{\text{click}}$ is defined as a bonus granted only when the model produces a reasonable click action. Specifically, given the model-predicted click a_t , we use the segmentation tool to generate the corresponding mask M_t and compute the false-positive (FP) and false-negative (FN) regions between M_t and the GT mask M_{gt} . A positive click is expected to fall within an FN region, while a negative click should lie within an FP region. Rewards and penalties are assigned accordingly, encouraging the model to place clicks in semantically meaningful locations rather than arbitrarily.

- **Progressive segmentation improvement reward** $\mathcal{S}_{\text{pseg}}$. This reward enforces that each action a_t leads to a segmentation improvement over the previous step. In other words, the mask produced after executing a_t must achieve a higher quality than the mask at step $t - 1$. This mechanism encourages the agent to consistently refine the segmentation rather than performing redundant actions or oscillating among repetitive operations. Concretely, we compute the IoU of the generated mask at each step t ; if the score surpasses that of the mask from the previous action a_{t-1} , the agent receives a reward; otherwise, no reward is given.

- **Trajectory length reward** \mathcal{S}_{len} . If the action sequence to complete segmentation is shorter than a predefined threshold, a reward is given; otherwise, penalties increasing with trajectory length are applied to encourage efficiency.

The final reward \mathcal{S} is derived as: $\mathcal{S} = \frac{1}{5}(\mathcal{S}_{\text{ans}} + \mathcal{S}_{\text{format}} + \mathcal{S}_{\text{click}} + \mathcal{S}_{\text{pseg}} + \mathcal{S}_{\text{len}})$. Formal equations for each reward component are provided in Appendix C. Our fine-grained reward scheme better reflects the complexity of iterative segmentation, guiding the model to produce actions that are both spatially valid and semantically accurate.

Optimization. Based on the rollout formulation and rewards defined above, we optimize the policy using GRPO [7] without the KL penalty term [9] on dataset \mathcal{D}_{rl} :

$$\mathcal{L}_{\text{RL}} = \mathbb{E}_{\substack{(I, Q, A) \sim \mathcal{D}_{\text{rl}} \\ \{P_i\}_{i=1}^G \sim \pi_{\theta_{\text{old}}}(\cdot | I, Q)}} \left(-\frac{1}{G} \sum_{i=1}^G \frac{1}{N_i} \sum_{t=1}^{T_i} \min(\pi_{\theta_{i,t}} \mathcal{A}_i, \right. \\ \left. \text{clip}(\pi_{\theta_{i,t}}, 1 - \epsilon, 1 + \epsilon) \mathcal{A}_i) \right), \quad (2)$$

$$\pi_{\theta_{i,t}} = \frac{\pi_{\theta}(r_{i,t}, a_{i,t} | I, Q, P_{i,<t})}{\pi_{\theta_{\text{old}}}(r_{i,t}, a_{i,t} | I, Q, P_{i,<t})}. \quad (3)$$

Benchmarks	Methods	General-Purpose MLLMs with Segmentation Capability				Medical MLLMs with Segmentation Capability				Ours
		LISA [18]	LISA++ [45]	SAM4MLLM [5]	VisionReasoner [25]	MedPLIB [13]	Citrus-V [40]	UniBiomed [41]	MMedAgent [20]	
In-domain testset D_{test}										
IOU \uparrow		9.44 (20.46)	9.49 (20.76)	15.85 (27.84)	16.11 (29.11)	22.29	30.61	50.74	36.13	85.58
DSC \uparrow		14.11 (25.73)	14.30 (25.94)	21.16 (33.04)	22.05 (35.50)	27.35	37.63	58.31	42.85	92.21
F1-score \uparrow		20.18 (32.15)	20.75 (32.34)	32.53 (42.75)	34.78 (46.72)	38.94	53.75	69.22	56.64	96.39
Out-of-domain testset MeCOVQA-G+										
IOU \uparrow		10.07 (15.24)	9.87 (15.01)	16.99 (21.19)	18.27 (24.46)	33.36	46.54	24.88	26.54	80.63
DSC \uparrow		15.44 (21.30)	14.70 (21.26)	21.85 (26.35)	25.08 (30.24)	41.19	52.65	31.74	33.81	89.27
F1-score \uparrow		21.69 (28.04)	21.25 (27.96)	32.94 (38.57)	37.83 (42.08)	53.47	69.84	43.63	44.17	95.24
Held-out in-house testset										
IOU \uparrow		5.23 (9.12)	5.46 (9.45)	8.28 (14.00)	10.10 (17.66)	20.12	32.08	35.62	27.39	72.09
DSC \uparrow		9.58 (14.33)	9.69 (14.80)	13.59 (18.04)	15.88 (24.57)	27.80	38.63	41.55	34.26	83.78
F1-score \uparrow		13.03 (17.15)	13.17 (17.72)	19.07 (25.26)	22.49 (30.07)	39.42	50.76	54.97	45.88	91.76

Table 1. Comparison of segmentation performance on both in-domain and out-of-domain benchmarks. LISA [18], LISA++ [45], VisionReasoner [25], and SAM4MLLM [5] are re-implemented using their official codebases. We evaluate two settings: (1) directly loading their publicly released model weights (shown in blue); and (2) further fine-tuning these models on our SFT and RL training datasets, which include the same images, masks, and QA pairs used for IBISAgent (shown in “()”), ensuring fair comparison. MedPLIB [13], Citrus-V [40], MMedAgent [20], and UniBiomed [41] are also re-implemented following their official repositories. For these models, we directly load the released weights without additional fine-tuning, as they were pretrained on large-scale public datasets that partially overlap with ours.

Here, G is the number of rollout reasoning paths; $P_i = \{(r_{i,t}, a_{i,t}, o_{i,t})\}_{t=1}^{T_i}$ denotes the i -th reasoning path; N_i is the total length of P_i excluding observation tokens; \mathcal{S}_i is the reward of P_i ; and π_θ and $\pi_{\theta_{\text{old}}}$ represent the current and old policy distributions, respectively. The normalized score $\mathcal{A}_i = [\mathcal{S}_i - \text{mean}(\{\mathcal{S}_j\}_{j=1}^G)]/\text{std}(\{\mathcal{S}_j\}_{j=1}^G)$, reflects the relative quality of each reasoning path within the rollout group, enabling the model to distinguish between learnable and poor reasoning trajectories. Through RL training, the agent learns to adaptively reason over pixel features and plan click actions when necessary, achieving superior autonomous interactive segmentation.

4. Experiment

4.1. Experimental Setup

Evaluation Benchmarks. For segmentation performance evaluation, we conduct experiments on three datasets: (1) In-domain test set D_{test} . We randomly sample 3K image–mask pairs from the BiomedParseData [46] test split across 9 imaging modalities. (2) Out-of-domain benchmark. We adopt the MeCOVQA-G+ [12, 40] test set, which includes 3K samples across 5 imaging modalities. This benchmark pairs biomedical images with natural-language queries that explicitly request segmentation of specific anatomical structures or lesions. (3) Held-out in-house dataset. Since many foundation models and MLLMs are trained on large-scale public datasets, training–testing overlap may vary across prior works, and the public benchmarks in (1) and (2) may contain samples seen during pre-training. To ensure fair evaluation and avoid unintentional data leakage, we additionally evaluate on a private held-out dataset collected from three medical centers, comprising 1K CT, MRI, and pathology images across seven can-

cer types. For VQA performance evaluation, we use four widely adopted medical VQA benchmarks: PathVQA [8], SLAKE [22], VQA-RAD [19], and OmniMedVQA [10]. Further benchmark details are provided in Appendix A.3.

Metrics. For the segmentation task, we report mIOU and Dice score for mask segmentation, and F1 Score for mask-to-entity correspondence accuracy. For the VQA task, we evaluate the accuracy of the model’s responses.

Implementation Details. We implement IBISAgent based on Qwen2.5-VL-7B [2]. MedSAM2 [27] is used as the interactive segmentation tool. The training is conducted on a cluster of 16 NVIDIA A100 GPUs. For the cold-start SFT stage, we optimize the model with a learning rate of 1×10^{-5} for 10 epochs. The total batch size is 256. The subsequent RL optimization is implemented using the VERL [34] framework, where we set the training batch size to 256 and generate 4 candidate reasoning paths per question, up to a maximum of 20 times of actions. We use a constant learning rate of 1×10^{-6} and set the maximum context length to 32K tokens. RL training runs for 12 epochs.

4.2. Comparison with Previous SOTA Methods

Segmentation Performance. We compare IBISAgent against two groups of baselines in Tab. 1: (1) General-purpose MLLMs with segmentation capability, including LISA-7B [18], LISA++ 7B [45], SAM4MLLM-8B [5], and VisionReasoner-7B [25] (using SAM2 [30]). (2) Medical MLLMs that support segmentation, including MedPLIB-7B [13], Citrus-V 8B [40], UniBiomed-1B [41], and MMedAgent-7B [20] (using MedSAM [26]).

Compared with general-domain MLLMs, IBISAgent achieves substantially higher performance across all benchmarks. Since these models were trained solely on datasets containing natural images, we further fine-tune them us-



Figure 3. Qualitative Analysis. We present the responses and segmentation outputs on a reasoning–segmentation example. Existing MLLMs exhibit incorrect reasoning and low-quality segmentation, highlighting their misaligned fine-grained vision–language understanding. In contrast, **IBISAgent** delivers substantially improved reasoning quality and segmentation performance.

Method	UniBiomed [41]	MedPLIB [13]	Citrus-V [40]	MMedAgent [20]	IBISAgent
Efficiency Inference Time (s)	5.82	3.14	8.25	10.42	28.70

Table 2. Computational efficiency comparison. All experiments are conducted on the same A100 GPU.

ing our cold-start SFT and RL datasets—which include the same images, masks, and QA pairs used for training IBISAgent—to ensure fairness. Even after this additional fine-tuning, IBISAgent still significantly outperforms these models, demonstrating that its superiority does not simply arise from the use of a specialized dataset. Instead, the improvements primarily stem from our novel and effective design, which emulates the annotation process of human experts, enabling multi-round reasoning and refinement. This domain-specific modification, tailored for medical imaging, ultimately yields markedly better segmentation results.

Compared with existing medical-specific MLLMs, IBIS-Agent achieves substantially superior segmentation performance. On average, it surpasses these models by at least 35.13% in IoU, 37.58% in DSC, and 29.79% in F1 score. Notably, Citrus-V [40] and UniBiomed [41] were trained on datasets far larger than ours; nevertheless, our method consistently outperforms them, further confirming that the improvements arise from the effectiveness of our proposed technical components rather than from the use of a specialized dataset. In particular, MMedAgent [20] is also a tool-augmented MLLM that employs MedSAM [26] for segmentation. IBISAgent still markedly outperforms this model, demonstrating that its advantages do not merely arise from the integration of segmentation tools, but from more accurate grounding and iterative reasoning-based segmentation mask refinement.

Methods	MeCOVQA-G+			In-House Testset		
	IoU ↑	DSC ↑	F1 ↑	IoU ↑	DSC ↑	F1 ↑
GPT-4o [15] + MedSAM2 [27]	11.75	17.39	22.42	7.23	10.40	15.16
LLaVA-Med [21] + MedSAM2 [27]	24.54	31.38	35.70	20.03	26.94	37.75
HuatuoGPT-Vision [41] + MedSAM2 [27]	35.86	43.41	54.79	30.25	36.72	52.28
Lingshu [43] + MedSAM2 [27]	39.63	47.18	60.31	31.19	37.55	54.02
Chiron [37] + MedSAM2 [27]	39.58	47.16	60.25	30.75	36.90	53.37
IBISAgent	80.63	89.27	95.24	72.09	83.78	91.76

Table 3. Comparison of IBISAgent with tool-augmented MLLM agents. Except for the closed-source models, all competing methods in this table are implemented using their official open-source code and model weights, followed by further fine-tuning on our $\mathcal{D}_{\text{cold}}$ and \mathcal{D}_{rl} datasets to ensure a fair comparison.

Qualitative Analysis. As shown in Fig. 3, we present qualitative results that further demonstrate the merits of IBISAgent. For a case requiring reasoning to identify a liver tumor, the powerful closed-source GPT-4o [15] outputs seemingly correct textual reasoning but produces an incorrect localization bounding box. This indicates that the model fails to align textual reasoning with visual features—it may be hallucinating plausible answers rather than truly understanding the medical image, ultimately leading to incorrect localization. MedPLIB [13] provides coarse localization that roughly captures the lesion region but suffers from false-positive predictions. Moreover, its language output is highly constrained—when performing segmentation, the model rigidly outputs only the token “<SEG>”, losing the rich language generation capability originally inherent to large language models. UniBiomed [41] produces incorrect textual reasoning and responses, describing objects that do not exist in the image and generating low-quality segmentation masks. This observation reinforces our motivation: current methods that rely on implicit “<SEG>” tokens for segmentation disrupt the MLLM’s native text output space, compromising both its language capability and semantic generalization. Moreover, these approaches exhibit fundamentally limited pixel-level visual reasoning, preventing the model from truly understanding fine-grained visual features. In contrast, IBISAgent not only generates correct and coherent textual reasoning but also adaptively produces high-quality masks through step-by-step, precise pixel grounding. This capability arises from our design that decouples reasoning from segmentation, thereby preserving the MLLM’s inherent language reasoning ability while simultaneously enabling adaptive, multi-round refinement.

Efficiency Comparison. We randomly sampled 1,000 cases (30%) from the out-of-domain testset MeCOVQA-G+ [12, 40] to measure the average time required by different models to process each sample. The results are reported in Tab. 2. Because IBISAgent performs multi-round mask refinement, its per-case inference time is longer than that of existing MLLMs. Fundamentally, such multi-step interactions between the agent and the environment are intended to trade additional computation time for improved perfor-

mance—an inherent limitation of multi-round agent systems. Nevertheless, the inference overhead of IBISAgent remains within an acceptable range, especially in light of the substantial performance gains it delivers.

4.3. Ablation Studies

IBISAgent vs. Prompting-based MLLM Agents. To validate the effectiveness of formulating segmentation as an interleaved fine-grained visual reasoning and action planning Markov decision process, we design several baseline agent workflows that directly predict bounding boxes or points using MLLMs, followed by segmentation with MedSAM2 [27]. We then compare IBISAgent with these agent systems to evaluate the advantages of our iterative, multi-round, reasoning-driven formulation. Specifically, we construct different agent systems using GPT-4o [15], LLaVA-Med [21], HuatuoGPT-Vision [4], Lingshu [43], and Chiron [37]. The results are shown in Tab. 3. IBISAgent consistently outperforms all competing agent systems, demonstrating that our method effectively activates the model’s intrinsic pixel-level reasoning ability, enabling advanced segmentation performance that cannot be achieved through simple workflow-style tool calling.

Effectiveness of Training Strategies. To evaluate the effectiveness of our training framework, we compare IBIS-Agent with several Qwen2.5-VL-7B-based variants: (1) \mathcal{M}_{base} , a prompt-driven baseline equipped with MedSAM2 [27]; (2) \mathcal{M}_{cold} , trained solely with cold-start SFT; (3) $\mathcal{M}_{cold+reflect}$, trained with cold-start SFT augmented by synthesized self-reflective trajectories; (4) \mathcal{M}_{rl} , trained exclusively with RL; and (5) $\mathcal{M}_{cold+rl}$. The results in Table 4 demonstrate the effectiveness of our training strategies. The prompt-only approach is neither adaptable nor robust, whereas progressively incorporating our proposed training stages yields substantial improvements over the base model, highlighting the necessity of each component. The RL stage provides the largest performance gain, indicating that RL’s exploration-exploitation dynamics and reward feedback are crucial for acquiring context-aware decision-making policies and enabling genuine vision-centric multi-step reasoning. Furthermore, by integrating all training strategies, IBISAgent surpasses all baselines, further supporting our motivation for developing a versatile training framework that strengthens the model’s pixel-level visual reasoning capabilities.

Significance of Different Reward Signals. We demonstrate the effectiveness of the proposed Region-based Click Placement Reward \mathcal{S}_{click} , Progressive Segmentation Improvement Reward \mathcal{S}_{pseg} , and Trajectory Length Reward \mathcal{S}_{len} using the ablation results in Tab. 5. We begin by removing all three reward signals to establish a baseline that relies solely on the standard format reward and final answer reward (shown in the gray row). We then progres-

Method	Training Strategies			In-House Testset		
	SFT	Self-Reflection	RL	IoU \uparrow	DSC \uparrow	F1 \uparrow
<i>prompt-driven \mathcal{M}_{base}</i>					11.77	16.83
\mathcal{M}_{cold}	✓			53.42	62.01	68.61
$\mathcal{M}_{cold+reflect}$	✓	✓		57.16	67.73	74.52
\mathcal{M}_{rl}			✓	62.77	71.29	77.50
$\mathcal{M}_{cold+rl}$	✓		✓	68.92	78.08	85.44
IBISAgent	✓	✓	✓	72.09	83.78	91.76

Table 4. Ablation study on our training strategies. Checkmarks (✓) indicate which strategies are applied.

Reward Signals	MeCOVQA-G+				In-House Testset						
	\mathcal{S}_{click}	\mathcal{S}_{pseg}	\mathcal{S}_{len}	IoU \uparrow	DSC \uparrow	F1 \uparrow	$T_{avg} \downarrow$	IoU \uparrow	DSC \uparrow	F1 \uparrow	$T_{avg} \downarrow$
				73.77	82.62	88.53	11.29	68.96	79.17	87.06	13.44
✓				76.60	85.77	91.23	10.61	70.45	81.23	89.30	12.74
	✓			77.64	86.85	92.31	8.59	70.62	81.40	89.56	10.07
		✓		74.19	82.88	89.05	5.94	69.03	79.65	87.48	7.22
✓	✓			80.61	89.19	95.24	8.12	72.05	83.74	91.71	9.68
✓		✓		77.73	86.88	92.34	5.03	70.75	81.63	89.78	6.49
✓	✓	✓		79.37	88.25	93.97	4.26	71.16	82.28	90.55	5.43
✓	✓	✓	✓	80.63	89.27	95.24	3.67	72.09	83.78	91.76	4.89

Table 5. Ablation study on reward design. The gray row indicates the baseline that excludes all segmentation-tailored rewards and uses only the standard format and answer rewards.

sively incorporate different combinations of our proposed reward signals to examine their impact on segmentation performance. We also report the average predicted trajectory length (steps) to comprehensively evaluate how these rewards influence both segmentation quality and interaction efficiency. Each reward contributes substantially to the overall performance. The rewards \mathcal{S}_{click} and \mathcal{S}_{pseg} provide the greatest improvements in mask quality, as they ensure accurate click localization and encourage each interaction step to make a positive contribution to the segmentation outcome. Meanwhile, \mathcal{S}_{pseg} and \mathcal{S}_{len} improve interaction efficiency by discouraging redundant or uninformative clicks and preventing unnecessarily long trajectories, enabling the model to learn when to stop. By integrating all reward components, IBISAgent achieves an optimal balance between segmentation performance and interaction efficiency.

5. Conclusion

In this paper, we present IBISAgent, a novel MLLM-based agent capable of pixel-level visual reasoning for unified biomedical object referring and segmentation. IBISAgent reformulates segmentation as a multi-step Markov Decision Process and enhances MLLMs’ pixel-level understanding without introducing additional model components. We develop IBISAgent through a two-stage training protocol and design fine-grained rewards that incentivize continuous self-improvement reasoning. Additionally, we introduce a large-scale high-quality dataset with thinking and action trajectories. Through comprehensive empirical evaluation,

we demonstrate the competitive performance of IBISAgent across diverse segmentation tasks. Our study paves the way for future exploration of vision-centric, multi-step decision-making agents for holistic medical image analysis.

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IBISAgent: Reinforcing Pixel-Level Visual Reasoning in MLLMs for Universal Biomedical Object Referring and Segmentation

Supplementary Material

A. Dataset Details

A.1. Dataset for SFT

Our dataset \mathcal{D}_{cold} for cold-start Supervised Fine-Tuning (SFT) is a large-scale, high-quality collection of textual reasoning and action trajectories for interactive segmentation. It comprises a total of 47,146 individual samples (e.g., slices or images), which collectively contain 456,795 visual question-answer (VQA) pairs that capture a wide range of diverse scenarios. The dataset is meticulously curated by filtering segmentation trajectories to ensure high fidelity, achieving an overall average Intersection over Union (IoU) of 94.27 (median: 95.07) and an average Dice score of 0.9703 (median: 97.47). This high level of accuracy confirms the quality of the segmentation ground truths generated by the trajectories. Furthermore, the average trajectory length per sample is 8.69 steps, indicating a rich capture of the multi-step refinement processes required for complex segmentation tasks.

A.1.1. Modality Diversity

The dataset is characterized by its extensive diversity, covering 9 distinct medical imaging modalities. This broad range ensures that models trained on this data can generalize across various imaging types, from common modalities like CT and MRI to more specialized ones like Pathology and OCT. A detailed breakdown of the dataset composition by modality is presented in Tab. 6.

A.1.2. Task Diversity

In addition to modality diversity, the dataset spans 38 distinct segmentation tasks. These tasks are derived from a combination of the Medical Segmentation Decathlon (MSD) dataset [36], covering both organs (e.g., ‘liver’, ‘heart’) and tumors (e.g., ‘brain tumor’), and various other specialized public biomedical datasets (e.g., ‘ACDC’, ‘LIDC-IDRI’, ‘GlaS’) derived from BioMedParse [46]. This task diversity exposes the model to a wide array of anatomical structures, pathologies, and image characteristics. The detailed statistics for each task group are provided in Sec. E.

A.2. Dataset for RL

A.2.1. Pixel-Level Reasoning Corpus for RL

In addition to the cold-start SFT dataset, we curated a large-scale, high-quality corpus specifically for the RL stage. As detailed in Sec. 3.3, this corpus is also sampled from BioMedParse [46] including some samples used in \mathcal{D}_{cold} . It

contains only the images, ground-truth masks, and QA pairs that require identifying fine-grained visual cues and localizing the specified mask region, thereby compelling the agent to autonomously explore and learn effective action policies.

This RL corpus comprises a total of 60,826 samples, which collectively contain 564,385 QA pairs. Similar to the SFT dataset, this corpus is highly diverse, spanning 8 medical imaging modalities and 39 distinct segmentation tasks. Detailed statistical breakdowns by modality and task group are provided in Fig. 4a and Fig. 14a, respectively.

A.2.2. Commonly-Used Medical VQA Datasets.

During RL training, we jointly use common medical VQA datasets and our curated pixel-level reasoning corpus. This hybrid training strategy preserves the model’s visual understanding and question-answering abilities, enabling the policy to selectively invoke pixel-space reasoning only when necessary. Ablation studies (as shown in the main paper) confirm that this data configuration is both reasonable and effective. Tab. 7 reports the number of VQA pairs in the medical VQA datasets used in our training.

A.3. Testing Benchmarks

A.3.1. In-domain test set \mathcal{D}_{test}

To comprehensively evaluate the model’s generalization capabilities and robustness in pixel-level reasoning, we constructed a diverse test set \mathcal{D}_{test} that is strictly disjoint from the training corpora (\mathcal{D}_{cold} and the \mathcal{D}_{rl} corpus). This dataset is designed to assess performance across a wide spectrum of medical imaging modalities and challenging segmentation scenarios.

The test set comprises a total of 9,902 samples, containing 156,289 VQA pairs. Unlike the training sets, which emphasize breadth by covering a wide variety of tasks, the test set focuses on more complex and challenging scenarios. Specifically, the test set places greater emphasis on fine-grained visual feature recognition—such as identifying tiny structures, intricate abnormalities, lesions, and tumors—to ensure that the benchmark rigorously evaluates the model’s ability to handle challenging targets. Consequently, the test set spans 32 distinct task groups.

In terms of modality, \mathcal{D}_{test} covers 8 major medical imaging types: CT, MRI, X-Ray, Ultrasound, Pathology, Endoscopy, Dermoscopy, and Fundus. This distribution ensures that the evaluation reflects real-world clinical diversity. The statistical distributions of samples and QA pairs by modality and by specific dataset are visualized in Fig. 4b

Table 6. Statistical overview of the **SFT** dataset \mathcal{D}_{cold} , categorized by imaging modality. Detailed breakdown by task group is shown in Sec. E.

Modality	Samples	Total QAs	Avg. Length	Avg. IoU	Median IoU	Avg. DSC	Median DSC
CT	22,504	209,291	8.30	0.9462	0.9519	0.9722	0.9753
Dermoscopy	1,302	13,086	9.05	0.9348	0.9338	0.9662	0.9658
Endoscope	2,431	17,434	6.17	0.9548	0.9609	0.9768	0.9800
Fundus	472	4,850	9.28	0.8834	0.8772	0.9378	0.9346
MRI	7,453	82,616	10.08	0.9404	0.9457	0.9691	0.9721
OCT	205	1,850	8.02	0.9116	0.9074	0.9537	0.9515
Pathology	1,195	11,765	8.85	0.9081	0.9243	0.9501	0.9607
Ultrasound	3,499	36,972	9.57	0.9341	0.9360	0.9659	0.9669
X-Ray	8,085	78,931	8.76	0.9460	0.9542	0.9721	0.9766
Total	47,146	456,795	8.69	0.9427	0.9507	0.9703	0.9747

and Fig. 14b, respectively.

Table 7. The distribution of commonly-used medical VQA datasets used in RL stage. “HuatuoV_A” and “HuatuoV_I” refer to the Huatuo_PubMedVision_Alignment and Huatuo_PubMedVision_InstructionTuning VQA datasets, respectively.

Dataset	VQA Number
HuatuoV_A	128000
HuatuoV_I	128000
PMC_VQA	32000
VQA_RAD	8000
SLAKE	9000
PATH_VQA	19000

A.3.2. Out-of-domain test set MeCOVQA-G+

Datasets for training and evaluating text-segmentation alignment in the medical domain are extremely scarce. One of the few publicly available resources is MeCoVQA-G, which was recently introduced alongside the MedPlib paper [13]. MeCoVQA-G is a large-scale, pixel-level VQA subset of the MeCoVQA family, constructed by pairing biomedical images with natural-language questions that explicitly ask the model to segment a given anatomical structure or lesion. Each sample contains a 2D image slice, a templated question targeting a specific anatomical class, and the corresponding binary segmentation mask as the ground-truth answer. The released split is 100K training pairs and 2,344 test pairs.

MeCOVQA-G+ [40] is a thoroughly re-annotated and expanded edition of the MeCoVQA-G [13]. MeCOVQA-G+ increases both the scale and modality diversity of its predecessor, delivering a more reliable and comprehensive benchmark for medical text-to-segmentation tasks. MeCOVQA-G+ comprises 3,157 carefully curated

text–segmentation pairs. The samples span a wide range of modalities, including X-ray, CT, MRI, ultrasound, and endoscopy. Each image has been meticulously reviewed by a team of medical experts to ensure the accuracy of the segmentation masks.

A.3.3. Held-out in-house test set

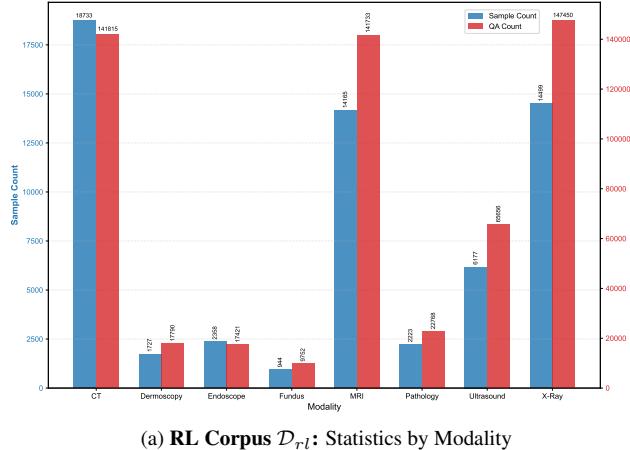
For testing, in addition to our in-domain test set \mathcal{D}_{test} , we use a completely held-out in-house dataset comprising 1k CT, MRI, and histopathology images across 7 cancer types for zero-shot evaluation. In this held-out set, CT images include 100 liver tumor cases, 100 gallbladder tumor cases, 100 pancreatic cancer cases, and 100 kidney tumor cases. MRI images include 100 colon tumor cases and 100 brain cancer cases. Histopathology images include 400 breast cancer cases. For each case, human annotators construct a VQA pair along with a corresponding reasoning trajectory.

B. More Implementation Details

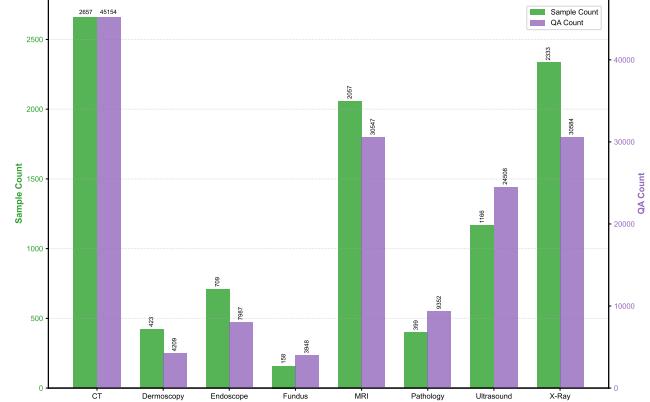
B.1. Trajectory Generation

To train our model for multi-step medical image segmentation, we require a dataset of expert-like interaction trajectories. We employed an automated algorithm to generate these trajectories by simulating the sequential refinement process an expert annotator would perform, leveraging the click simulation strategy proposed in [42]. The algorithm iteratively interacts with a pre-trained interactive segmentation model (specifically MedSAM2 [27]), intelligently placing clicks to correct errors in the current prediction until it closely matches the ground truth.

The core of this method is a deterministic, greedy strategy for selecting the next interaction point, augmented by a **mask prompting mechanism** to ensure stability. At each step t , we strictly utilize the low-resolution mask logits from the previous step, denoted as $M_{logits}^{(t-1)}$, alongside the cumu-



(a) **RL Corpus \mathcal{D}_{rl} :** Statistics by Modality



(b) **In-domain Test Set \mathcal{D}_{test} :** Statistics by Modality

Figure 4. Modality distribution. (a) The RL corpus \mathcal{D}_{rl} (training stage) contains 60,826 samples and 564,385 QAs across 8 modalities. (b) The In-domain Test set \mathcal{D}_{test} comprises 9,902 samples and 156,289 QAs covering the same 8 modalities. The dual-axis plots show the sample count (left axis) and total QA pairs (right axis) for each category.

lative click history H_t . This simulates a realistic annotation workflow where the annotator refines an existing mask rather than starting from scratch at each interaction.

First, we identify the error regions in the current prediction $M_p^{(t)}$. The False Negative (FN) region, M_{fn} , represents the target area missed by the model, while the False Positive (FP) region, M_{fp} , represents areas incorrectly included in the prediction:

$$M_{fn} = M_{gt} \setminus M_p^{(t)}, \quad M_{fp} = M_p^{(t)} \setminus M_{gt} \quad (4)$$

To emulate human behavior prioritizing large error regions, we compute the Euclidean distance transform for both error masks, denoted as D_{fn} and D_{fp} . The algorithm selects the next click $a_t = (c_t, l_t)$ by targeting the pixel with the maximum distance value (i.e., the center of the largest error region):

$$(c_t, l_t) = \begin{cases} (\arg \max D_{fn}, 1) & \text{if } \max(D_{fn}) \geq \max(D_{fp}) \\ (\arg \max D_{fp}, 0) & \text{otherwise.} \end{cases} \quad (5)$$

Crucially, the update rule for the segmentation model \mathcal{S} incorporates both the updated history and the dense mask prompt from the previous iteration:

$$M_p^{(t+1)}, M_{logits}^{(t+1)} = \mathcal{S}(I, H_t \cup \{a_t\}, M_{logits}^{(t)}) \quad (6)$$

where $M_{logits}^{(0)}$ is initialized as None. This iterative process continues until the IoU exceeds a threshold τ_{iou} or the maximum step count T_{max} is reached. The implementation logic is detailed in Algorithm 1. An example process is depicted as Fig. 5.

B.2. QA Generation

To train IBISAgent to understand diverse user intents and perform pixel-level tasks, we constructed a comprehensive instruction dataset. We utilized Gemini-2.5-Pro to generate a rich set of visual question-answering (VQA) pairs and instructions.

Hallucination Prevention via Fact-Based Generation. A critical challenge in generating medical instructions is preventing the LLM from hallucinating non-existent anatomical features or pathologies. To mitigate this, we strictly conditioned the generation process on ground-truth evidence. Specifically, we provided Gemini-2.5-Pro with the raw image, the ground-truth mask, and a verified caption of the biomedical object. The model was explicitly instructed to generate prompts **only** based on these visible facts, ensuring that every instruction (e.g., “Segment the left lung”) corresponds to an object actually present in the image.

Hierarchical Instruction Categories. We designed a taxonomical prompt library to cover different phases of the segmentation process, as illustrated in Fig. 6:

- **Initialization Prompts.** These prompts initiate the segmentation task from scratch. To mimic real-world user behavior, we categorized them into 7 broad types, ranging from *Direct Commands* to *Goal-Oriented* statements.
- **Specialized Query Templates.** We applied a 70/30 split between standard imperative prompts and **Interrogative Queries** to enhance the model’s flexibility. For the latter, we designed 5 specific sub-templates to mimic clinical uncertainty:

- Conditional Logic: “Is there a {object_name}? If so, please segment it.”
- Compound Requests: “Can you find and segment the {object_name}?”

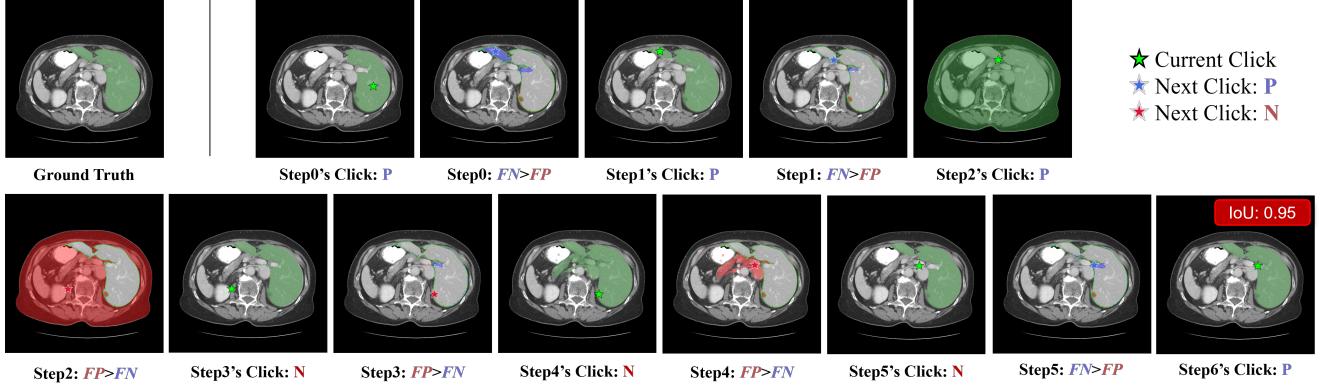


Figure 5. **An illustrative example of the automated trajectory generation process for liver segmentation.** The algorithm progressively refines the predicted mask through iterative interactions.

For each iteration (e.g., Step 0), two visualization panels are presented: (1) The **first image** displays the *current segmentation state*, showing the predicted mask (green translucent overlay) generated by the current click (marked by a green star). (2) The **second image** illustrates the *error analysis* against the Ground Truth (delineated by a **green outline**). The differences are visualized as blue translucent regions for False Negatives (FN, under-segmentation) and red translucent regions for False Positives (FP, over-segmentation). The star in this panel indicates the calculated **next action** based on the largest error region: a **blue star** denotes a Positive Click (P) to correct under-segmentation, while a **red star** denotes a Negative Click (N) to correct over-segmentation.

- (iii) *Clinical Protocol Tone*: “I need to verify the presence of a {object_name}...”
- (iv) *Indirect/Conversational*: “I’m wondering if there’s a {object_name}...”
- (v) *Concise Checks*: “Visible {object_name}? Please provide segmentation.”
- **Refinement Prompts.** We categorized them into 6 types. These prompts are used during the iterative interaction steps. They focus on fine-grained adjustments, such as *Requesting Next Steps* (e.g., “What is the next step?”), *Error Correction* (e.g., “The mask extends beyond the boundary”), and *Verification* (e.g., “Is this segmentation complete?”).

Diverse Assistant Response Generation. To ensure that the agent’s output is naturalistic and varied rather than robotic, we also constructed a template library for the **Assistant’s final responses**. These are categorized into 5 styles: *Direct & Concise* (“Segmentation complete.”), *Confident Affirmation* (“The object has been successfully segmented.”), *Object-Referencing* (“The {object_name} is fully segmented.”), *Question-Answering* (“Yes, the object was found...”), and *Conversational* (“All done!”). This diversity prevents the model from overfitting to a single termination phrase.

During data construction, we dynamically fill all user and assistant templates with the specific anatomical target name (e.g., “left ventricle”) and imaging modality (e.g., “MRI”), ensuring high relevance and grammatical correctness.

B.3. Reasoning Generation for Our SFT Dataset

A cornerstone of our SFT dataset is the high-quality, step-by-step reasoning (<think> . . . </think>) that accompanies each agent action. Generating this data presents a significant challenge: our agent (M1) operates from a limited, first-person perspective (seeing only the current segmentation mask), but the optimal reasoning for its next action (e.g., “correcting an over-segmentation”) requires an “oracle” or “ground-truth” perspective (knowing the precise False Positive and False Negative regions).

To solve this, we employed a “Teacher-Student” (or “Oracle-Agent”) generation pipeline. We utilized the powerful **GPT-5** model as the “Teacher” (M2) to synthesize reasoning traces for our “Student” (M1).

Our core innovation lies in a sophisticated prompt strategy that leverages the advanced role-playing capabilities of GPT-5 to bridge the information gap between the Oracle and the Agent.

1. **Persona and Perspective Simulation.** The system prompt instructs M2 to adopt the persona of an “expert radiologist.” Critically, it commands M2 to generate reasoning strictly from the limited perspective of the junior agent. The prompt explicitly states: “*This agent ONLY SEES ONE THING: a single, combined green mask... Write as if you are genuinely deducing the next step from only the visible image.*” This forces the teacher model to reverse-engineer the logic: instead of simply stating the error (which it knows), it must explain **why** the visual features (e.g., texture differences, anatomical landmarks) suggest an error exists.

2. **Privileged Information.** While M2 writes from the

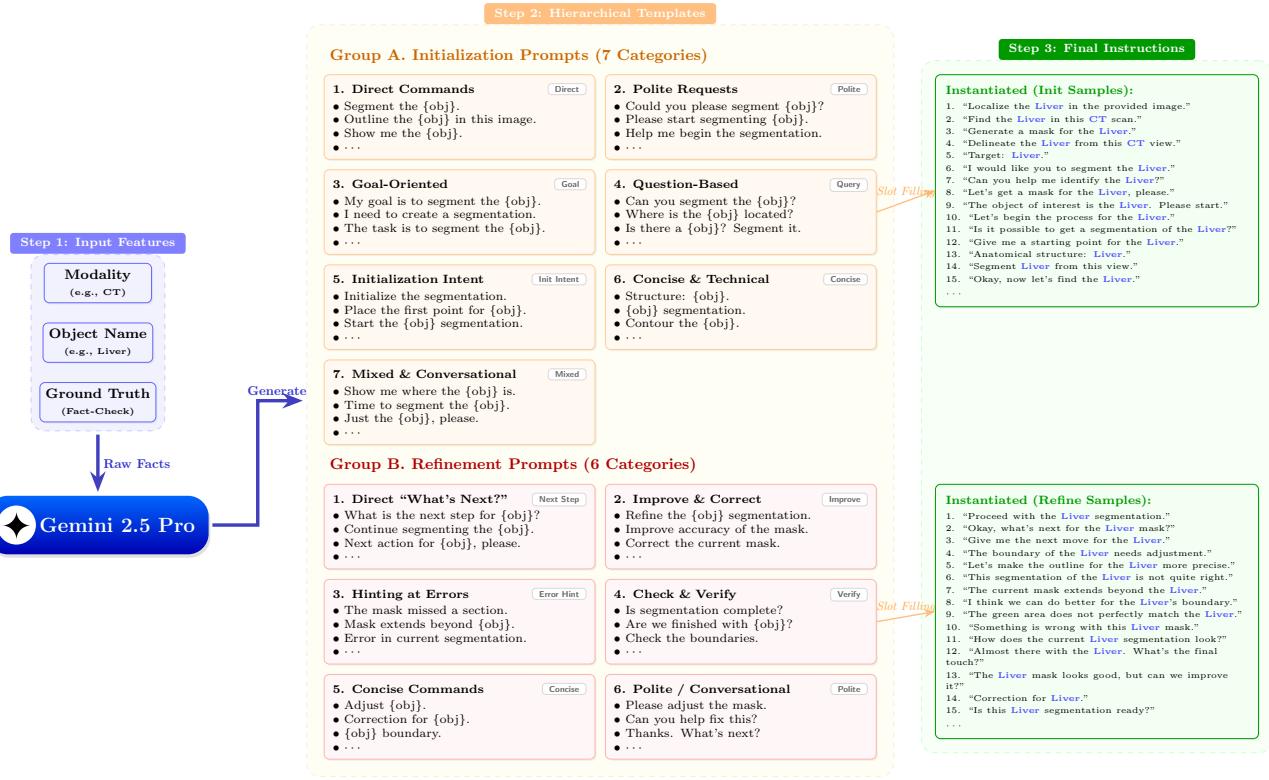


Figure 6. **The hierarchical prompt generation pipeline.** To ensure both diversity and factual accuracy, we leverage **Gemini 2.5 Pro** to synthesize a comprehensive instruction library. Conditioned on ground-truth input features (Step 1), the model dynamically generates a taxonomical prompt set (Step 2) divided into **Group A: Initialization Prompts** (7 categories, covering imperative to conversational tones) and **Group B: Refinement Prompts** (6 categories, focusing on iterative corrections). These templates are then instantiated into final instructions (Step 3), creating a rich dataset (50 items per group) that covers diverse user intents while strictly adhering to visual facts.

agent’s perspective, it views a privileged “oracle” image. As shown in Fig. 7 (Left), this image explicitly visualizes segmentation errors: a **Green Mask** for True Positives, a **Red Mask** for False Positives (over-segmentation), and a **Blue Mask** for False Negatives (under-segmentation). It also indicates the “correct” next action (Positive/Negative point).

3. Preventing Information Leakage. A primary risk in this pipeline is “prompt leakage,” where the teacher accidentally reveals its privileged knowledge (e.g., mentioning “the red mask”). Thanks to the superior instruction-following capability of GPT-5 compared to smaller models, we effectively mitigated this using a robust set of **Forbidden Concepts**. The system prompt strictly prohibits the output from containing terms like ‘Red’, ‘Blue’, ‘Cross’, ‘TP’, ‘FP’, ‘FN’, or ‘Ground Truth’.

As shown in Fig. 8, this approach generates dense, anatomically grounded reasoning traces without requiring manual templates for every scenario (like we did before using smaller models).

C. Reward Functions

The reasoning-format reward. The reasoning-format reward S_{format} evaluates the structural validity of R by verifying that the model’s output includes all required special tokens in the prescribed order. Specifically, the model should enclose its chain-of-thought between `<think>` and `</think>` tags, place the tool-call choices and parameters between `<tool_call>` and `</tool_call>` tags, and place the final answer between `<answer>` and `</answer>` tags. Outputs that adhere to this structure receive a positive reward.

$$S_{format} = \begin{cases} 1, & \text{if all required fields appear} \\ & \text{and are in the correct order,} \\ 0, & \text{otherwise.} \end{cases} \quad (7)$$

The final-answer reward. The final-answer reward S_{ans} encompasses multiple task types, thereby providing the agent with diverse feedback. For **multiple-choice questions**, we simply check the exact match between the pre-

Algorithm 1: Pseudo-code for Trajectory Generation

```

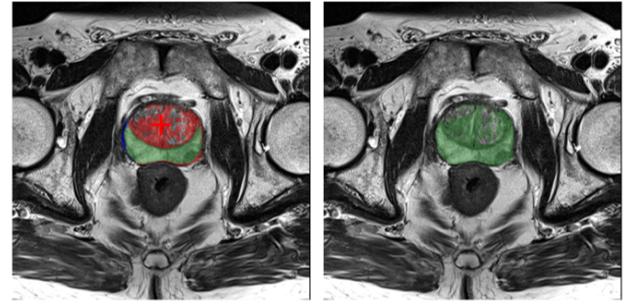
1 def generate_trajectory(image, gt_mask, model,
2                         max_steps=20, iou_thresh=0.95):
3     pred_mask = np.zeros_like(gt_mask)
4     low_res_logits = None
5     history = []
6
7     for step in range(max_steps):
8         # Check Stop Condition
9         iou = calculate_iou(pred_mask, gt_mask)
10        if iou >= iou_thresh:
11            break
12
13        # Identify Error Regions (FN & FP) and
14        # Find Click
15        fn_mask = (gt_mask == 1) & (pred_mask ==
16        0)
17        fp_mask = (gt_mask == 0) & (pred_mask ==
18        1)
19
20        fn_dist = cv2.distanceTransform(fn_mask.
21            astype(np.uint8), ...)
22        fp_dist = cv2.distanceTransform(fp_mask.
23            astype(np.uint8), ...)
24
25        if np.max(fn_dist) >= np.max(fp_dist):
26            coords = np.unravel_index(np.argmax(
27                fn_dist), fn_dist.shape)
28            history.append((coords, 1))
29        else:
30            coords = np.unravel_index(np.argmax(
31                fp_dist), fp_dist.shape)
32            history.append((coords, 0))
33
34        # Update Prediction using Points AND
35        # Previous Mask Logits
36        points = [p[0] for p in history]
37        labels = [p[1] for p in history]
38
39        pred_masks, scores, logits = model.
40        predict(
41            point_coords=points,
42            point_labels=labels,
43            mask_input=low_res_logits
44        )
45
46        # Select best mask and update logits for
47        # next iteration
48        best_idx = np.argmax(scores)
49        pred_mask = pred_masks[best_idx]
50        low_res_logits = logits[best_idx]
51
52    return history, pred_mask

```

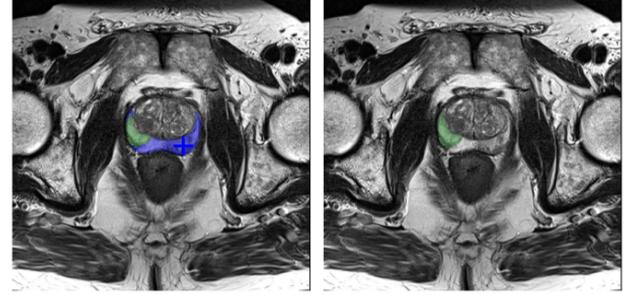
dicted answer and the ground truth:

$$S_{\text{ans}}(A, \hat{A}) = \mathbb{I}(A = \hat{A}). \quad (8)$$

Here, A denotes the ground-truth answer and \hat{A} is the predicted answer obtained by rule-based parsing of the model's final output. The indicator \mathbb{I} is defined to be 1 if $A = \hat{A}$ and



(a) A Negative Click example for Prostate segmentation. The M2 (oracle) view (Left) shows the False Positive (FP, red) region. The M1 (agent) view (Right) only sees the combined green mask.



(b) A Positive Click example for Prostate segmentation. The M2 (oracle) view (Left) shows the False Negative (FN, blue) region. The M1 (agent) view (Right) only sees the incomplete green mask.

Figure 7. Comparison of the “Oracle” view (for M2) and the “Agent” view (for M1) used in SFT reasoning generation.
Notably, this agent-visible mask (green) is the sum of the oracle’s True Positive (green) and False Positive (red) areas. M1 must learn to infer the expert’s corrective reasoning from this limited perspective.

0 otherwise.

For **segmentation** tasks, in contrast to earlier reward designs, we use MedSAM2 as external reward providers. Given either click points predicted by the MLLM, we query MedSAM2 to obtain a segmentation mask. We then compute the IOU between this mask and the ground-truth mask and assign piecewise rewards as follows:

$$S_{\text{ans}} = \begin{cases} 3, & \text{IoU} > 0.80, \\ 2, & 0.70 < \text{IoU} \leq 0.80, \\ 1, & 0.50 < \text{IoU} \leq 0.70, \\ 0, & \text{otherwise.} \end{cases} \quad (9)$$

This segmentation reward supplies strong positive feedback only when the predicted region closely matches the ground truth, while at lower IoU levels it provides guidance that encourages gradual improvement.

Region-based click placement reward. A core innovation of our framework is that we introduce explicit spatial constraints into the reward signal. Unlike generic RL agents that may learn to click arbitrarily to trigger tool usage, we

SYSTEM PROMPT (Persona & Constraints)

You are an expert radiologist. Your task is to examine a user's prompt, a ground-truth image, and a given correct action, and then generate a single, high-quality `<think>` block with the detailed, analytical reasoning that justifies that specific action, all from the perspective of a segmentation agent.

1. Your Core Task and Persona

Your must adopt the persona of an agent that only sees the medical image and a plain green mask (if present). You will be secretly shown a ground-truth image to guide your reasoning, but you must never reveal this secret knowledge.

- **Secret Knowledge (Teacher View):**
Green/Red/Blue Masks: Indicate correctly, over-, and under-segmented areas.
Blue/Red Crosses (+/-): Indicate the correct location for a Positive/Negative point.

• **Agent's View (Your Persona):**
Sees only a uniform green mask which is the sum of the correct (Green) and over-segmented (Red) areas.

2. Reasoning Instructions for Each Scenario

Your `<think>` block must reverse-engineer the correct action from the agent's limited perspective, using your expert anatomical knowledge.

(1) **Prefinalization (No Mask):**

You see a Blue Cross (+). Justify why this location is an ideal starting point. Analyze its anatomical position (e.g., center of the target, clear texture, away from ambiguous borders).

(2) **For Refinement (Under-segmentation):**

You see a Blue Mask (missed area) and a Blue Cross (+). The agent sees an incomplete mask. Your reasoning must identify the

missing anatomical part and explain why a positive point is needed there.

Example logic: "The current mask covers the main body of the liver, but it's missing the superior lobe. To complete the segmentation, I must add a point to this unmasked region."

(3) **For Refinement (Over-segmentation):**

You see a Red Mask (extra area) and a Red Cross (+). The agent sees a mask that is too large. Your reasoning must identify which adjacent structure has been incorrectly included and explain why a negative point is necessary.

Example logic: "The mask for the right kidney appears to have bled into the adjacent psoas muscle. To correct this, I will place a negative point on the incorrectly included muscle tissue."

(4) **For Termination (No Errors):**

You see no errors masks or crosses. The agent sees a green mask. Your reasoning must be a step-by-step evaluation of the mask boundaries against known anatomical landmarks. Conclude that the segmentation is highly accurate and optimally aligned. You should reason that any remaining minor imperfections are clinically insignificant and cannot be substantially improved with another single point, thus justifying termination.

3. Mandatory Rules

(1) **FORBIDDEN CONCEPTS:** Your output inside `<think>` MUST NOT contain any of the following words or refer to their concepts: Red, Blue, Cross, TP, FP, FN, Ground Truth, Teacher, Junior, Correct. Adherence is critical.

(2) **MAINTAIN PERSONA:** Write as if you are genuinely deducing the next step from only the visible image and the plain green mask. Never reveal your access to the secret knowledge.

(3) **STRICT FORMAT:** Your entire response must be only the `<think>...</think>` block and its content. No other text, tags, or formatting.

(4) **EXPERT QUALITY:** Provide a detailed, step-by-step thought process that reflects deep anatomical understanding. Avoid short, superficial statements.

USER PROMPT (Context Injection)

Here is the context for the current segmentation step.

--- USER INSTRUCTION ---

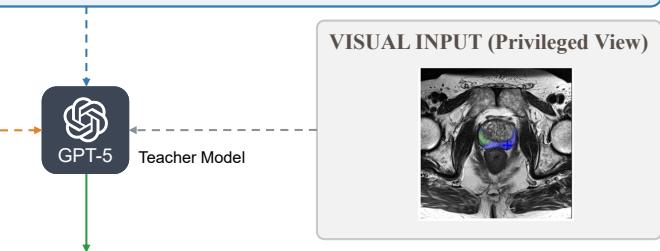
The mask for the prostate has missed a section.

--- CORRECT ACTION ---

Positive Click (0.5325, 0.6794)

--- YOUR TASK ---

Based on the provided ground-truth image, generate the detailed `<think>` block that justifies the specified correct action from the perspective of the segmentation agent.



GENERATED THINKING (Student Logic)

The current mask identifies the central gland of the prostate but fails to cover the peripheral zone on the right lateral side. Examining the T2-weighted intensity, the unmasked region shares the same hyperintense texture as the segmented area, bounded by the clear hypointense line of the prostatic capsule which lies further out. The current boundary stops prematurely before reaching this anatomical landmark, resulting in an under-segmentation of the organ. To complete the segmentation, a positive point should be placed in this missed lateral region to expand the mask outward until it aligns with the true anatomical capsule.

Figure 8. The prompt engineering pipeline for synthesizing pixel-level reasoning traces. To bridge the gap between ground-truth knowledge and the agent's limited perspective, we employ a Teacher-Student strategy using GPT-5. The pipeline integrates three key components: (1) a System Prompt that establishes an expert persona and enforces strict constraints; (2) the User Context containing the target instruction and correct action; and (3) the Privileged Oracle View where error regions are explicitly visualized. The model is tasked with “reverse-engineering” the reasoning, producing vision-based justifications for the corrective action without revealing its access to the privileged information.

enforce semantically valid interactions through S_{click} . This reward serves as a dense supervision signal, ensuring that the agent’s actions are grounded in the anatomical reality of the image.

Let $a_t = (c_t, p_t)$ denote the action at step t , where $c_t \in \mathbb{R}^2$ is the spatial coordinate and $p_t \in \{+1, -1\}$ indicates a positive or negative click type. Let M_{t-1} be the segmentation mask from the previous step (with M_0 initialized as an empty mask). We define the eligible error regions for interaction based on the ground truth mask M_{gt} :

$$\Omega_{\text{FN}} = M_{gt} \setminus M_{t-1}, \quad \Omega_{\text{FP}} = M_{t-1} \setminus M_{gt} \quad (10)$$

A click is considered valid if a positive point falls within the under-segmented region (Ω_{FN}) or a negative point falls within the over-segmented region (Ω_{FP}). The reward function is formalized as:

$$S_{\text{click}}(a_t) = \begin{cases} r_{\text{click}}, & \text{if } p_t = +1 \wedge c_t \in \Omega_{\text{FN}}, \\ r_{\text{click}}, & \text{if } p_t = -1 \wedge c_t \in \Omega_{\text{FP}}, \\ -\lambda_{\text{miss}}, & \text{otherwise.} \end{cases} \quad (11)$$

where $r_{\text{click}} = 1$ is a positive bonus for spatially accurate clicks, and $\lambda_{\text{miss}} = 1$ is a penalty for invalid clicks. This

reward effectively guides the policy to minimize the symmetric difference between the predicted and ground-truth masks step-by-step.

Progressive segmentation improvement reward. To prevent the agent from engaging in redundant operations or oscillating between states without improving the result, we incorporate a progressive improvement reward S_{pseg} . This component evaluates the marginal contribution of each action to the overall segmentation quality.

Let $\text{IoU}(M, M_{gt})$ denote the Intersection-over-Union between a mask M and the ground truth. We calculate the quality gain ΔQ_t after executing action a_t :

$$\Delta Q_t = \text{IoU}(M_t, M_{gt}) - \text{IoU}(M_{t-1}, M_{gt}). \quad (12)$$

The reward is assigned only if the action yields a strictly positive gain:

$$S_{\text{pseg}} = \mathbb{I}(\Delta Q_t > 0) \quad (13)$$

This incentivizes the agent to strictly ascend the gradient of segmentation quality.

Trajectory length reward. Efficiency is a critical metric for clinical assistants. To encourage the model to achieve

Methods	VQA-RAD	PathVQA	SLAKE	AVG.
GPT-4o [15]	64.9	58.1	70.9	64.6
LLaVA-Med-7B [21]	53.1	44.2	47.5	48.3
HuatuoGPT-Vision-34B [4]	62.0	51.3	69.5	60.9
Lingshu [43]	66.1	68.7	78.0	70.9
Chiron [37]	72.7	68.9	77.3	73.0
IBISAgent	73.4	69.2	83.5	75.4

Table 8. Comparison of IBISAgent with existing MLLMs on different VQA benchmarks.

high-quality segmentation with the minimum number of interactions, we introduce a trajectory length reward S_{len} . Let T be the total number of steps taken in a reasoning path, and T_{opt} be a predefined optimal threshold. The reward is defined as:

$$S_{\text{len}} = \begin{cases} r_{\text{eff}}, & \text{if } T \leq T_{\text{opt}}, \\ -\gamma \cdot (T - T_{\text{opt}}), & \text{if } T > T_{\text{opt}}. \end{cases} \quad (14)$$

where $r_{\text{eff}} = 1$ is a bonus for efficient completion, and $\gamma = 0.2$ is a decay factor that applies a linear penalty for each additional step beyond the threshold. This formulation balances the trade-off between exhaustive refinement and interaction efficiency.

D. More Experiments

D.1. VQA Performance.

We also conducted experiments demonstrating that pixel-level reasoning not only improves segmentation performance but also enhances the model’s VQA capabilities. The results of evaluation across three medical VQA benchmarks are summarized in Tab. 8. IBISAgent outperforms both open-source and proprietary MLLMs. IBISAgent outperforms both open-source and proprietary MLLMs. Notably, compared with existing medical MLLMs trained on large-scale VQA datasets, IBISAgent achieves at least a 2.4% improvement in average accuracy. This further validates our motivation that enhancing MLLMs’ understanding of fine-grained medical image features fundamentally improves their medical image analysis capabilities. Pixel-level exploration of localized regions closely mirrors the way clinicians interpret and reason about medical images, and our work effectively stimulates and strengthens this critical capability in MLLMs.

D.2. Impact of Segmentation Tool Types

We further examine the effect of replacing the interactive segmentation tool used by IBISAgent. Specifically, we substitute the default MedSAM 2 [27] with alternative tools, including MedSAM [26], SAM [17], and SAM 2 [31], and compare the resulting performance, as shown in Tab. 9. We find that IBISAgent remains highly robust to the choice of

Methods	MeCOVQA-G+			In-House Test set		
	IoU ↑	DSC ↑	F1 ↑	IoU ↑	DSC ↑	F1 ↑
IBISAgent (SAM)	79.95	88.74	94.83	71.82	83.19	90.98
IBISAgent (SAM 2)	80.32	89.01	95.08	71.93	83.40	91.36
IBISAgent (MedSAM)	80.29	89.00	95.03	71.91	83.37	91.32
IBISAgent (MedSAM 2)	80.63	89.27	95.24	72.09	83.78	91.76

Table 9. Ablation study on segmentation tool types.

interactive segmentation tool, exhibiting only minor differences in final segmentation accuracy across these replacements. This robustness arises from IBISAgent’s ability to generate precise click-point locations and perform multi-round refinement, which jointly help maintain segmentation quality and ensure strong test-time stability. These results indicate that IBISAgent can effectively adapt to a wide range of interactive segmentation tools, rather than relying solely on MedSAM 2.

D.3. The Performance of the Segmentation Tools

We also report the standalone performance of the segmentation tools on the test sets as a reference, further highlighting the superiority of our method. Tab. 10 presents the results. In this comparison, we evaluate segmentation performance both with and without GT bounding-box prompts. Because MedSAM and MedSAM 2 support only visual prompts, their results in the “w/o bbox” setting are marked as \times . From Tab. 10, we observe that IBISAgent consistently achieves the highest performance across both segmentation modes. These findings indicate that IBISAgent exhibits strong generalization in text-driven segmentation and, when using GT bbox as the first step, delivers segmentation quality that consistently surpasses the competing tools such as MedSAM, MedSAM 2, and BiomedParse.

Overall, these results further validate the advantages of IBISAgent. Under our formulation, the agent performs precise pixel-level visual reasoning to accurately localize target regions and iteratively refine masks, enabling segmentation performance that exceeds the inherent upper bound of the underlying segmentation tools themselves.

D.4. More Case Studies

We provide additional qualitative comparisons to further prove the robustness of IBISAgent in different anatomical regions. As illustrated in Fig. 9 and Fig. 10, we present two challenging scenarios including a low-contrast pancreatic tumor and an irregular lung tumor, respectively. Consistent with our observations in Sec. 4.2, existing MLLMs frequently suffer from severe hallucinations, incorrect grounding, or missed diagnoses when discerning subtle pathological cues. In contrast, IBISAgent successfully initiates correct segmentation and employs its unique reasoning-driven refinement mechanism to correct errors—such as retracting

Models	In-domain test set				MeCOVQA-G+				In-House Test set			
	w/o bbox		with bbox		w/o bbox		with bbox		w/o bbox		with bbox	
	IOU	DSC	IOU	DSC	IOU	DSC	IOU	DSC	IOU	DSC	IOU	DSC
SAM 2 [26]	×	×	80.30	85.61	×	×	65.12	75.54	×	×	51.08	56.65
MedSAM [26]	×	×	79.73	85.44	×	×	60.32	71.74	×	×	49.50	53.28
MedSAM2 [27]	×	×	82.07	87.28	×	×	71.30	81.12	×	×	59.24	64.49
BiomedParse [46]	83.03	87.19	84.28	89.67	37.68	45.39	67.41	78.36	27.48	34.23	55.87	60.68
IBISAgent	85.58	92.21	86.37	92.48	80.63	89.27	81.56	90.11	72.09	83.78	72.96	84.83

Table 10. Comparison with interactive segmentation tools. Best and second-best results are shown in **bold** and underline, respectively. \times means that the model does not support text instruction following.

masks from adjacent healthy tissues—ultimately achieving high-quality segmentation and accurate diagnostic descriptions.

We also present additional segmentation results in Fig. 11, showcasing IBISAgent’s multi-round segmentation trajectories on various biomedical images and illustrating its iterative refinement process across different segmentation tasks.

D.5. How IBISAgent Corrects Errors

In Fig. 12, we present several representative examples that illustrate how IBISAgent corrects different types of errors, further demonstrating its robustness. We consider three typical scenarios. (1) Deceptive or incorrect instructions: When the user provides misleading or erroneous instructions describing a nonexistent target, IBISAgent correctly recognizes that the specified object is not present in the image and refrains from producing an incorrect mask, highlighting its genuine understanding of fine-grained visual cues. (2) Inconsistent initial masks: During mask refinement, if the user supplies an initial mask that does not match the described segmentation target, IBISAgent detects the inconsistency, corrects the erroneous mask, and generates the appropriate segmentation result. (3) Backtracking to undo incorrect decisions: During multi-round mask refinement, IBISAgent has access to the full interaction history, enabling it to assess whether the current segmentation trajectory is reasonable. When an incorrect action leads to a sub-optimal mask, the agent can automatically backtrack, undo the erroneous decision, and re-plan its click sequence. This ability largely stems from our use of Reflective Behavior Synthesis during SFT, which provides synthetic examples of such behavior and strengthens the agent’s robustness.

E. System and User Prompts

The detailed system prompt and user prompt used by IBIS-Agent are shown as Fig. 13.

F. Future Works

IBISAgent endows MLLMs with powerful pixel-level visual reasoning capabilities. Together with our novel behavioral formulation and training framework, IBISAgent substantially pushes the boundary of MLLM-based biomedical image reasoning and segmentation. Nevertheless, several open challenges remain. First, the current agent operates primarily in 2D settings; extending IBISAgent to 3D scenarios—or even developing a unified 2D–3D MLLM agent—represents a highly promising research direction. Second, further improvements in the efficiency of multi-step agentic interaction will be essential to reduce computational overhead.

Existing MLLMs

GPT-4o

CT image showing a soft-tissue mass near the uncinate process/head of the pancreas.

Question: Does this CT image show any abnormalities? If there is any, please isolate the abnormal area and provide a description of the anomaly.

Answer: Yes, The CT scan shows the presence of a round-shaped low-contrast pancreatic lesion.

MedPLIB

The CT image does not show any abnormalities.

UniBiomed

<p> millimetric calcific foci. </p> [SEG]</end>

IBISAgent

VS

Interactive Segmentation Tool

Iteration 1

<think> Within the pancreatic parenchyma, there is a focal area of hypoattenuation relative to the surrounding gland, suggesting a lesion consistent with a possible tumor. Since no segmentation has yet been initiated, the ideal approach is to begin by placing a positive point in the region that most clearly represents the lesion. The indicated position lies centrally within this low-attenuation focus,</think>

<action>{"Target": "pancreatic tumor", "Attribute": "1", "Coordinate 2d": "[0.4648, 0.4023]"}</action>

IOU: 86.68

Iteration 2

<think> The current segmentation includes a structure that largely corresponds to the pancreatic tumor, but the mask appears to extend slightly beyond the true tumor margin into adjacent soft tissue. The boundary on the left side of the mask lacks a clear interface, suggesting that the segmentation has accidentally encompassed non-tumorous tissue. To refine the delineation, a corrective action should focus on reducing this over-extended region. Placing a negative point in this region will help the model retract the mask from the adjacent tissue and better conform to the true tumor boundary,....</think>

<action>{"Target": "pancreatic tumor", "Attribute": "-1", "Coordinate 2d": "[0.4277, 0.4355]"}</action>

IOU: 97.14

Iteration 3

<think> Given the smooth, anatomically consistent margins and the absence of clear areas for refinement, any further adjustment would be unlikely to enhance the delineation meaningfully. Therefore, the segmentation is both accurate and complete, justifying termination at this stage.</think>

<action>Termination</action>

<answer>Enhanced CT scan shows a round-shaped low-contrast lesion in the pancreatic head, with clear boundaries.</answer>

Accurate spatial understanding and High-quality masks !

Figure 9. Qualitative comparison on the pancreatic tumor case. Existing MLLMs fail to provide reliable analysis: GPT-4o identifies the wrong location, MedPLIB misses the diagnosis entirely, and UniBiomed hallucinates unrelated calcific foci with an incorrect mask. Conversely, IBISAgent accurately identifies the low-contrast lesion and performs multi-step refinement to distinguish the tumor from the surrounding pancreatic parenchyma, achieving an IoU of 97.14%.

Existing MLLMs

GPT-4o
There is a heterogeneous soft-tissue mass in the right lung, predominantly involving the right lower lobe.

MedPLIB
No. Wrong answer Missed diagnosis

Citrus-V
The CT image does not show any abnormalities. No lesions or masses are visible in the lung fields, and the mediastinal structures appear normal.

UniBiomed
<p> lung pathology. </p> [SEG]<|end|>

IBISAgent  

Iteration 1
<think> The current image shows an axial chest CT at the level of the upper lobes. The task is to delineate the lung tumor. At this stage, there is no segmentation mask yet, so an initial point must be placed to start the delineation. The ideal location for that point is the central portion of the visible mass within the right lung field, where there is a clear contrast between the solid lesion and surrounding aerated lung tissue. Placing the point here ensures that the algorithm captures the lesion's true boundaries evenly in all directions. The chosen position lies well within the densest, most homogeneous part of the tumor, away from ill-defined peripheral borders and vascular structures, providing a robust seed for accurate segmentation of the lung tumor region. </think>
<action> {“Target”: “lung tumor”, “Attribute”: “1”, “Coordinate 2d”: “[0.5957, 0.5215]”} </action>

Iteration 2
<think> The current mask extends beyond the true tumor boundaries, encroaching into the adjacent mediastinal region where normal soft tissue structures such as vessels and mediastinal fat are visible. This area lies anterior and slightly medial to the actual tumor mass, which presents as a denser, more heterogeneous lesion within the parenchyma of the right lung. To refine the segmentation, a negative point should be placed in this region to retract the mask margin away from the mediastinum and restore confinement to the pulmonary parenchyma. </think>
<action> {“Target”: “lung tumor”, “Attribute”: “-1”, “Coordinate 2d”: “[0.5469, 0.4102]”} </action>

Iteration 3
<think> The current mask captures the central portion of a pulmonary lesion within the right lung field, but it extends slightly beyond the true tumor boundary into an adjacent area of normal aerated parenchyma... To correct this, a negative point should be placed within that erroneously included area to retract the mask boundary back to the actual tumor edge, ensuring... while excluding surrounding healthy lung. </think>
<action> {“Target”: “lung tumor”, “Attribute”: “-1”, “Coordinate 2d”: “[0.5645, 0.4531]”} </action>

Iteration 4
<think> The current segmentation of the lung tumor appears slightly excessive, extending beyond the true lesion boundary into the adjacent aerated parenchyma of the right upper lobe. To refine the segmentation, a corrective point should be placed over this region with normal parenchymal appearance, helping the model retract the boundary and exclude the non-tumorous tissue while preserving the actual lesion. </think>
<action> {“Target”: “lung tumor”, “Attribute”: “-1”, “Coordinate 2d”: “[0.6250, 0.4961]”} </action>

Iteration 5
<think> The current segmentation accurately encompasses the solid pulmonary lesion within the right upper lobe, capturing its core density and margins consistent with the mass seen on the CT slice. </think>
<action> Termination </action>
<answer> There is an irregular mixed-density lung tumor located in the upper lobe of the right lung. The lesion exhibits rough, spiculated margins, and lobulation is visible along its edges. </answer> Accurate spatial understanding and High-quality masks !

IOU: 8.13 IOU: 71.19 IOU: 93.34 IOU: 95.76

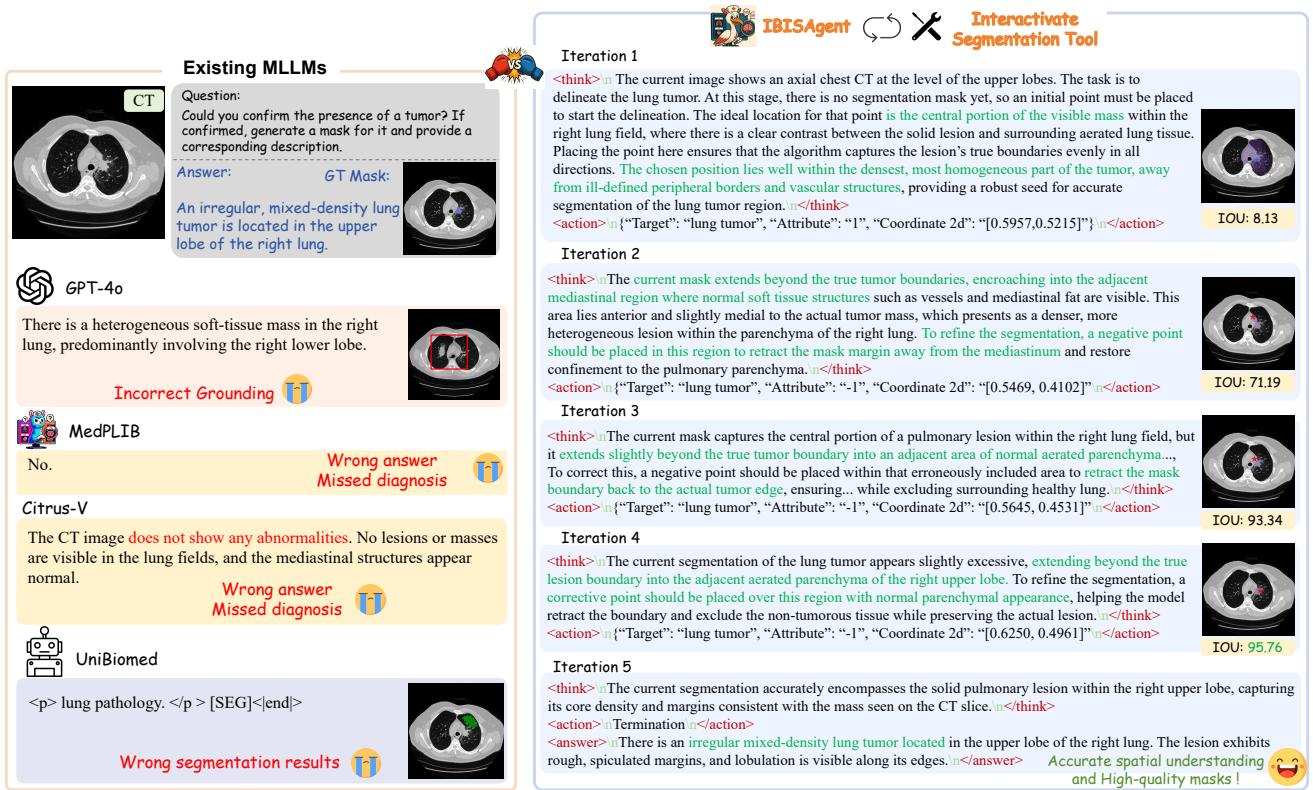


Figure 10. **Qualitative comparison on the lung tumor case.** While baseline models fail to detect the abnormality and GPT-4o mislocalizes the lesion, IBISAgent demonstrates superior pixel-level reasoning. Through five iterations, the agent detects the irregular mass and progressively corrects over-segmentation errors in the mediastinal and parenchymal regions, resulting in a 95.76% IoU.

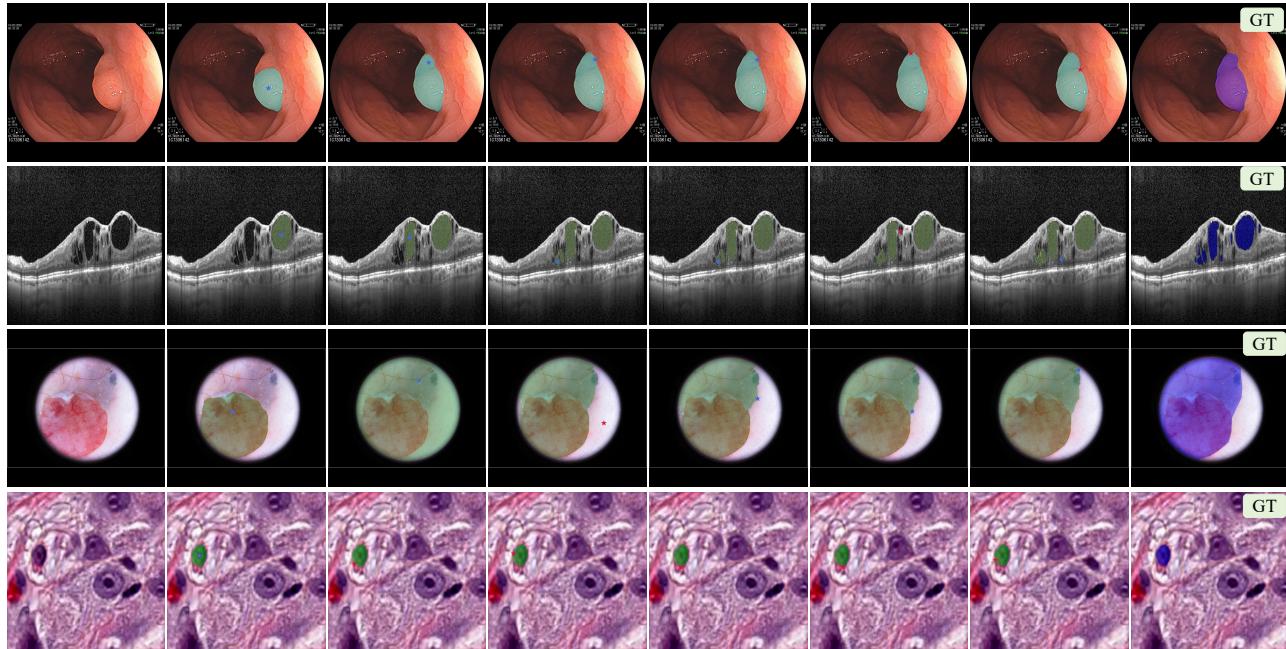
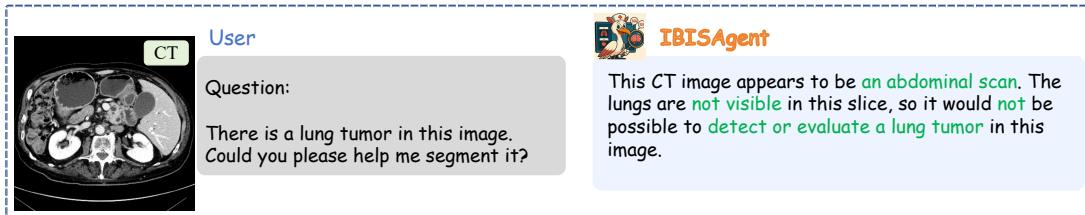
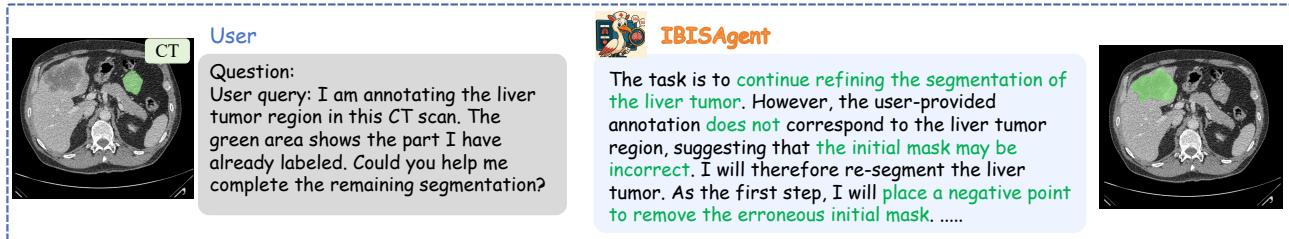


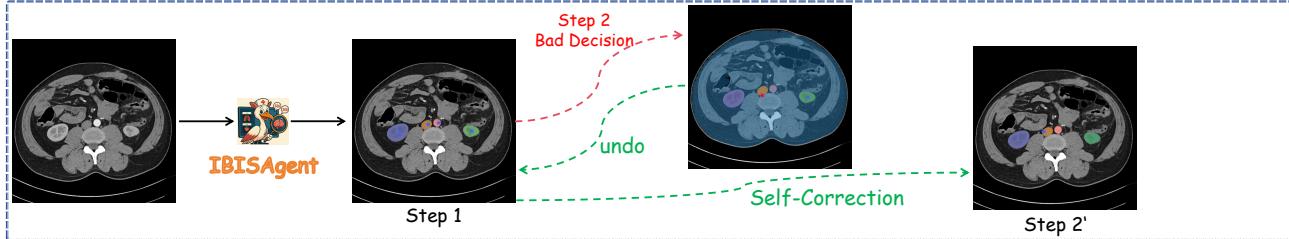
Figure 11. Visualization of IBISAgent’s multi-round segmentation trajectories on various biomedical images, illustrating its iterative refinement process across different segmentation tasks.



(1) How IBISAgent Handles Deceptive or Incorrect Instructions 😊



(2) How IBISAgent Handles Incorrect User-Provided Annotation 😊



(3) An Instance of IBISAgent's Self-Correction Behavior 😊

Figure 12. Illustrations of how IBISAgent corrects different types of errors. (1) An example showing IBISAgent’s response when the user provides deceptive or incorrect instructions describing a nonexistent target. (2) A case where the initial mask provided by the user does not match the described segmentation target, and how IBISAgent reacts accordingly. (3) An example demonstrating IBISAgent’s ability to backtrack and undo an incorrect decision, followed by re-planning and selecting new click points.

SYSTEM PROMPT

You are a precise and expert medical segmentation agent. Your mission is to accurately segment a target object in a medical image through a series of interactive point placements. You will be given an image and an instruction. You must carefully analyze the image state.

- If there is **no mask**, it is an **initialization** step. Your goal is to place a Positive Point on a clear, representative part of the target object.
- If a **semi-transparent green mask** is present, it is a **refinement** step. Your goal is to improve its accuracy. Place a Positive Point on a region of the target that the mask has missed, or a Negative Point on an area the mask has incorrectly included.

Your response must strictly follow this structure: first, your detailed reasoning within **<think>** tags, and then your single, decisive move within **<action>** tags. The only valid actions are **Positive Point (x, y)**, **Negative Point (x, y)**, or **Terminate**. All coordinates (x, y) must be normalized to a 0.0–1.0 scale and formatted to four decimal places, for example: Positive Point (0.5000, 0.2500). Only use Terminate when the mask perfectly aligns with the target boundary. If you Terminate, you must also append a final, concise summary in an **<answer>** tag.

USER PROMPT

Initialization Prompts

- My goal is to segment the {obj}.
- Place the first point for {obj}.
- Where is the {obj} located?
- Where is the {obj} located in this image?
- Is it possible to get a segmentation of the {obj}?
- What would the segmentation for the {obj} look like?
- Visible {obj}? Please provide its segmentation.
- ...

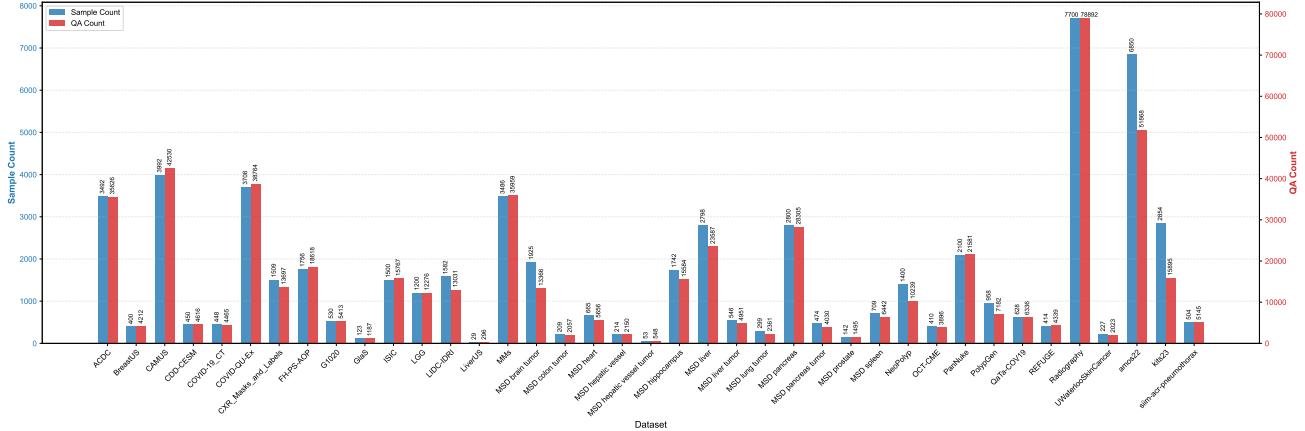
Refinement Prompts

- Can you help me fix this segmentation of the {obj}?
- Let's keep working on this {obj}.
- Thanks. Now, what's the next refinement for the {obj}?
- The {obj} mask looks good, but can we improve it?
- Almost there with the {obj}. What's the final touch?
- The segmentation of the {obj} is ongoing. Please provide the next step.
- ...

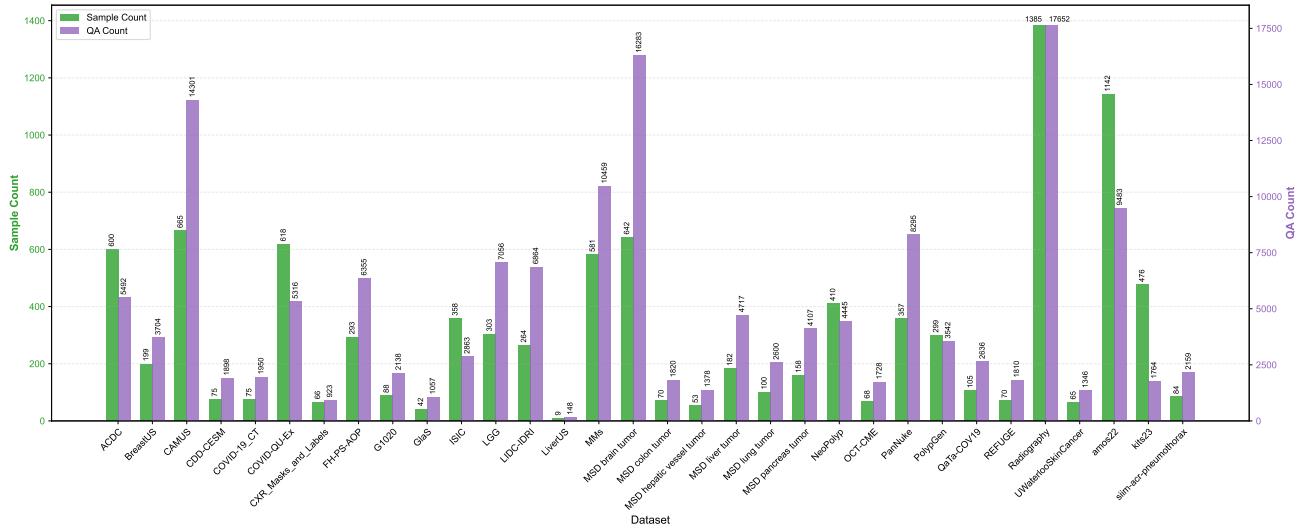
Figure 13. The system and user prompt used in IBISAgent.

Table 11. Detailed statistics for the 38 task groups within our SFT dataset \mathcal{D}_{cold} .

Dataset (Group)	Samples	Avg. Length	Total QAs	Avg. IoU	Median IoU	Avg. DSC	Median DSC
ACDC	1,746	8.60	16,769	0.9453	0.9459	0.9718	0.9722
BreastUS	596	9.17	6,062	0.9351	0.9347	0.9664	0.9662
CAMUS	1,996	9.66	21,278	0.9405	0.9388	0.9693	0.9684
COVID-19_CT	224	9.08	2,258	0.8863	0.8826	0.9394	0.9376
COVID-QU_Ex	1,854	8.82	18,207	0.9584	0.9586	0.9787	0.9789
CXR_Masks_and_Labels	1,509	8.08	13,697	0.9470	0.9504	0.9727	0.9746
FH-PS-AOP	878	9.63	9,336	0.9203	0.9180	0.9584	0.9572
G1020	265	9.26	2,718	0.8834	0.8767	0.9377	0.9343
GlaS	123	8.65	1,187	0.7368	0.7336	0.8422	0.8463
ISIC	1,075	9.29	11,063	0.9331	0.9315	0.9653	0.9645
LGG	910	9.05	9,148	0.9341	0.9345	0.9658	0.9662
LIDC-IDRI	791	7.11	6,416	0.9254	0.9230	0.9612	0.9599
LiverUS	29	9.21	296	0.8940	0.9188	0.9428	0.9577
MMs	1,743	8.88	17,220	0.9484	0.9479	0.9735	0.9732
NeoPolyp	1,473	5.96	10,252	0.9561	0.9611	0.9775	0.9802
OCT-CME	205	8.02	1,850	0.9116	0.9074	0.9537	0.9515
PanNuke	1,072	8.87	10,578	0.9278	0.9267	0.9625	0.9620
PolypGen	958	6.50	7,182	0.9529	0.9603	0.9758	0.9797
QaTa-COV19	314	9.22	3,208	0.9049	0.8996	0.9500	0.9472
REFUGE	207	9.30	2,132	0.8833	0.8776	0.9379	0.9348
Radiography	4,156	8.93	41,254	0.9480	0.9524	0.9732	0.9756
UWaterlooSkinCancer	227	7.91	2,023	0.9430	0.9455	0.9706	0.9720
amos22	3,425	4.86	20,055	0.9640	0.9686	0.9816	0.9840
MSD brain tumor	1,925	5.94	13,366	0.9499	0.9490	0.9743	0.9738
MSD colon tumor	209	8.84	2,057	0.9138	0.9116	0.9549	0.9538
MSD heart	812	15.59	13,473	0.9095	0.9144	0.9524	0.9553
MSD hepatic vessel	306	18.47	5,959	0.8453	0.8405	0.9158	0.9133
MSD hepatic vessel tumor	53	9.34	548	0.7469	0.7495	0.8543	0.8568
MSD hippocampus	319	19.91	6,669	0.9358	0.9231	0.9665	0.9600
kits23	1,427	1.91	4,153	0.9712	0.9698	0.9854	0.9847
MSD liver	10,034	6.95	79,816	0.9549	0.9532	0.9769	0.9760
MSD liver tumor	546	8.07	4,951	0.9313	0.9287	0.9643	0.9630
MSD lung tumor	299	6.90	2,361	0.9352	0.9347	0.9664	0.9663
MSD pancreas	3,586	17.70	67,072	0.9240	0.9234	0.9604	0.9602
MSD pancreas tumor	474	7.50	4,030	0.9320	0.9314	0.9647	0.9645
MSD prostate	204	19.16	4,113	0.8664	0.8601	0.9279	0.9248
siim-acr-pneumothorax	252	9.18	2,565	0.8658	0.8593	0.9278	0.9243
MSD spleen	924	11.42	11,473	0.9458	0.9507	0.9721	0.9747
Total	47,146	8.69	456,795	0.9427	0.9507	0.9703	0.9747



(a) **RL Corpus \mathcal{D}_{rl} :** Detailed statistics across 39 task groups (datasets).



(b) **In-domain Test Set \mathcal{D}_{test} :** Detailed statistics across 32 task groups (datasets).

Figure 14. **Detailed breakdown by sub-dataset.** This figure illustrates the diversity of our data. **(a)** The RL corpus \mathcal{D}_{rl} includes 39 distinct datasets. **(b)** The In-domain Test set \mathcal{D}_{test} covers 32 datasets. Note the dual-axis scale for Sample Count (left) and QA Count (right).