

Appendix A

APPENDIX*A.0.1 Use Case of QUILT-LLAVA*

QUILT-LLAVA is designed to assist pathologists and medical professionals by offering insights that can complement their expertise and enhance decision-making. With its ability to reason beyond immediate context, QUILT-LLAVA proves especially helpful in complex diagnostic scenarios. Additionally, its Iterative Abductive Reasoning-based Q/A data makes it an invaluable educational tool, providing hints and fostering critical thinking rather than delivering direct answers. This feature is particularly beneficial for pathology students and junior pathologists, supporting their learning and skill development. An illustrative example is shown in Fig. [A.2](#).

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

Table A.2: VQA datasets statistics. For PathVQA, we report the evaluation set statistics. PMC-Subset is the histopathology subset retrieved from PMC-VQA.

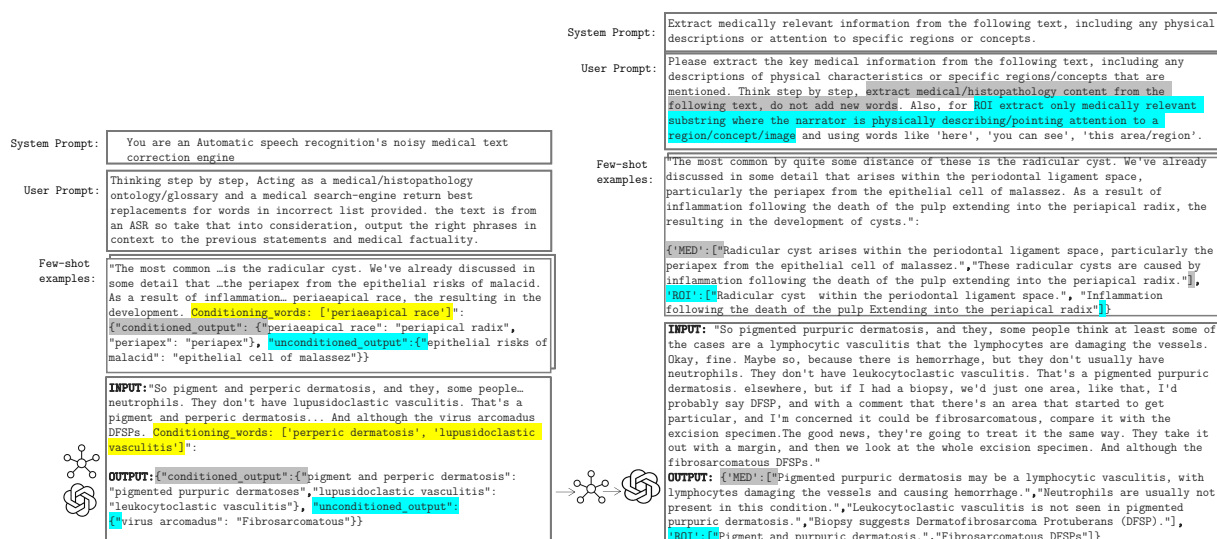
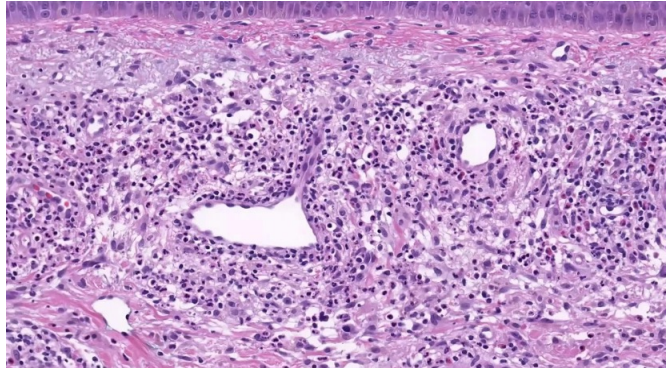


Figure A.1: Using few-shot examples, the LLM is prompted to perform two key tasks. First, it refines noisy ASR text by identifying and correcting errors within the context, with corrections marked in gray and additional issues flagged in blue. Second, it extracts relevant information, distinguishing medical (MED) text in blue and ROI text in gray.



User: Can you provide a concise description of the histopathology image shown?



Quilt-LLaVA: Upon examination of the histopathology image, it is evident that there is a significant presence of lymphocytes. These cells are densely packed and exhibit a high degree of pleomorphism, indicating a possible pathological condition. The lymphocytes are irregular in shape and size, with some displaying enlarged nuclei and prominent nucleoli. In addition to the lymphocytes, there is also a noticeable presence of eosinophils. These cells are characterized by their bright pink cytoplasm and bilobed nuclei. The eosinophils are scattered throughout the tissue, suggesting an ongoing immune response. The overall cellular architecture appears disrupted, with the normal tissue architecture replaced by a dense infiltrate of lymphocytes and eosinophils. This could be indicative of an inflammatory or immune-mediated process. Further diagnostic tests may be required to confirm the exact nature of this pathological condition.



User: The presence of scattered neutrophils throughout the tissue could suggest an acute inflammatory response. Could this be due to a skin condition such as a bug bite or a ruptured cyst?



Quilt-LLaVA: Your observation about the presence of neutrophils is correct, indicating an acute inflammatory response. However, the context of this inflammation is crucial. It's not just any skin condition, but a specific one. Hint: Consider the location of this inflammation. What conditions might cause an acute inflammatory response in this specific area? Also, think about the significance of the neutrophils being scattered throughout the tissue. What does this suggest about the nature of the inflammation?

Figure A.2: An example illustrating where the QUILT-LLaVA is used as an educational tool, providing clues to student pathologists to help them train.



Description

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

Conversation

User: Can you describe the main features visible in this histopathology image?

Assistant: The image primarily showcases a lobule, which is a small rounded glandular formation typically found in breast tissue. This lobule exhibits a classic benign structure with two distinct layers. The outer layer is composed of myoepithelial cells, identifiable by a single row of outer nuclei. The inner layer, on the other hand, consists of luminal cells, marked by another row of nuclei. The space between these cells forms the lumen. This bilayered appearance is a characteristic feature of benign breast parenchyma.

User: Where is this lobular architecture located within the image?

Assistant: The lobular architecture is prominently displayed in the central region of the image, extending towards the upper right quadrant. The bilayered structure of the lobule, with its myoepithelial and luminal cells, is clearly visible in this area.

User: What does this bilayered appearance indicate about the condition of the breast tissue?

Assistant: The bilayered appearance, with distinct myoepithelial and luminal cell layers, is indicative of benign breast parenchyma. This means that the breast tissue appears to be healthy and non-cancerous. However, it's important to note that a definitive diagnosis would require a comprehensive clinical evaluation and possibly additional tests.

Detailed Description

User: In a few words, what does the histopathology image depict?

Assistant: In the central to lower right portion of the histopathology image, there is a clear depiction of a lobule, a characteristic structure in benign breast parenchyma. This lobule is composed of small, rounded glandular formations, demonstrating a classic bilayered appearance. The outer layer of the lobule is made up of myoepithelial cells, which can be identified by a single row of nuclei. Adjacent to this, there is an inner layer composed of luminal cells, also identifiable by a single row of nuclei. The space between these luminal cells forms the lumen. This bilayered structure, with its distinct outer myoepithelial layer and inner luminal cell layer surrounding the lumen, is a hallmark of benign breast tissue. The lobular architecture is well-preserved and clearly visible in this region of the image, further supporting the benign nature of the tissue.

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



Description

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



Diagnosis

Invasive Ductal Carcinoma



Supporting Facts

1. Irregular, infiltrative blue areas in the breast tissue.
2. Presence of irregular, angulated glands infiltrating into the fibrous and fatty stroma.
3. Comparison of benign lobule and malignant invasive breast gland showing irregularity and distortion in latter.
4. Nuclear pleomorphism with variation in size and shape
5. Presence of prominent nucleoli.
6. Frequent mitotic figures indicating rapid growth.
7. Increased nuclear cytoplasmic ratios.
8. Poorly formed, irregular glands on low power view.
9. Infiltrative growth pattern where the glands invade into the surrounding stroma.

Complex Medical Reasoning

User: Can we make a diagnosis based on this single patch of histopathology image?

Assistant: The patch under examination reveals a lobule with a typical bilayered structure. This structure consists of an outer myoepithelial layer and an inner luminal cell layer, surrounding a central lumen. The presence of these two distinct layers of cells and the well-preserved lobular architecture are characteristic features of benign breast parenchyma.

The myoepithelial cells, represented by the outer row of nuclei, play a crucial role in maintaining the integrity of the breast tissue. They act as a natural barrier against potential invasion of cancer cells into the surrounding stroma. The luminal cells, represented by the inner row of nuclei, are the ones that usually undergo malignant transformation in most breast cancers.

However, in this patch, the lobule appears to maintain its normal architecture without any signs of distortion or irregularity. There are no visible signs of nuclear pleomorphism, which would indicate variation in size and shape of the nuclei, a common feature in malignancies. Also, there are no evident mitotic figures, which would suggest rapid cell division and growth, another hallmark of cancer. Based on these observations, this patch seems to represent benign breast tissue. However, it's important to note that this conclusion is based solely on this single patch. Breast cancer, such as invasive ductal carcinoma, often presents as irregular, infiltrative areas in the breast tissue, with angulated glands infiltrating into the fibrous and fatty stroma. These features are not evident in this patch, but they could be present in other areas of the tissue.

Therefore, while this patch appears benign, a definitive diagnosis would require a comprehensive examination of the whole slide image. This would allow for the identification of any areas of irregularity or distortion, increased nuclear cytoplasmic ratios, or poorly formed glands that might suggest an invasive growth pattern. Additionally, correlation with clinical information and possibly additional immunohistochemical studies would be necessary to confirm the diagnosis.

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



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Iterative Abductive Reasoning

User: I see a lobule with small rounded glandular formations, exhibiting a bilayered appearance with an outer myoepithelial layer and an inner luminal cell layer. Could this be indicative of benign breast parenchyma?

Assistant: Your observation of the bilayered appearance of the lobule is correct and it is indeed indicative of benign breast parenchyma. However, it's important to remember that the presence of benign structures doesn't rule out the possibility of malignancy elsewhere.

Hint: While you've correctly identified benign structures, consider looking for signs of irregularity or distortion in the glandular formations. Also, pay attention to the nuclear characteristics. Are there any signs of nuclear pleomorphism or prominent nucleoli? These could be indicative of a more sinister process.

User: I notice some irregularity and distortion in the glandular formations. There also seems to be nuclear pleomorphism and prominent nucleoli. Could this suggest the presence of a malignant process, possibly breast carcinoma?

Assistant: Your observations are indeed suggestive of a malignant process. The presence of nuclear pleomorphism and prominent nucleoli are key features of malignancy. However, the specific type of breast carcinoma might still be unclear. **Hint:** Consider the growth pattern of the glands. Are they infiltrating into the surrounding stroma? Also, look for signs of rapid growth, such as frequent mitotic figures. These features could help you narrow down the type of breast carcinoma.

User: I see the glands infiltrating into the surrounding stroma and frequent mitotic figures. Could this suggest an invasive ductal carcinoma of the breast?

Assistant: CORRECT!!! Your observations and deductions are spot on. The presence of glands infiltrating into the surrounding stroma and frequent mitotic figures are indeed indicative of an invasive process, specifically invasive ductal carcinoma of the breast. **Hint:** None needed. You've made the correct diagnosis based on the evidence available.

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