Enhancing Pancreatic Cancer Staging with Large Language Models: The Role of Retrieval-Augmented Generation

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ABSTRACT

Purpose

Retrieval-augmented generation (RAG) is an emerging technology to enhance the functionality and reliability of large language models (LLMs) by retrieving relevant information from reliable external knowledge (REK). RAG has gained increasing interest in radiology, and we previously reported the utility of NotebookLM, an LLM with RAG (RAG-LLM), for lung cancer staging. However, since the comparator LLM differed from NotebookLM's internal model, it remained unclear whether NotebookLM's advantage stemmed from RAG techniques or inherent differences in LLM performance. To better isolate the impact of RAG and to assess its utility across different cancers, this study compared the performance of NotebookLM and its internal LLM, Gemini 2.0 Flash, in a pancreatic cancer staging experiment.

Materials and methods

A paper summarizing Japan's current pancreatic cancer staging guidelines was used as REK. We compared the performance of three groups—REK+/RAG+ (NotebookLM with REK), REK+/RAG- (Gemini 2.0 Flash with REK), and REK-/RAG- (Gemini 2.0 Flash without REK)—in staging 100 fictional pancreatic cancer cases based on CT findings. Staging criteria included TNM classification, local invasion factors, and resectability classification. In the REK+/RAG+ group, retrieval accuracy was quantified based on the sufficiency of retrieved REK excerpts.

Results

REK+/RAG+ achieved a staging accuracy of 70 %, outperforming REK+/RAG- (38 %) and REK-/RAG- (35 %). For TNM classification, REK+/RAG+ attained 80 % accuracy, exceeding that of REK+/RAG- (55 %) and REK-/RAG- (50 %). Additionally, REK+/RAG+ explicitly presented retrieved REK excerpts as the basis for its classifications, achieving a retrieval accuracy of 92 %.

Conclusion

NotebookLM, a RAG-LLM, outperformed its internal LLM, Gemini 2.0 Flash, in a pancreatic cancer staging experiment, suggesting that RAG may improve the staging accuracy of LLMs. Furthermore, NotebookLM effectively retrieved relevant REK excerpts, providing transparency for radiologists to verify response reliability and highlighting the potential of RAG-LLMs in supporting clinical diagnosis and classification.

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Fig. 1. An overview of the experimental process. Radiologists from our team generated CT findings for 100 fictional pancreatic cancer patients. NotebookLM with REK (REK+/RAG+), Gemini 2.0 Flash with REK (REK+/RAG-), and Gemini 2.0 Flash without REK (REK-/RAG-) conducted cancer staging based on the CT findings in response to Tasks 1–5 (see Table 2). In the REK+/RAG+ group, retrieved excerpts from REK were available alongside the classifications. The REK was uploaded to the NotebookLM web system for RAG processing. In the REK+/RAG- group, the REK was manually entered into the prompt field before providing Tasks 1–5. *REK*=reliable external knowledge, *RAG*=retrieval-augmented generation

KEYWORDS

Large language model (LLM), Retrieval-augmented generation (RAG), Reliable external knowledge (REK), NotebookLM, Gemini 2.0 Flash, Pancreatic cancer staging

1 INTRODUCTION

Large language models (LLMs) have recently attracted attention in radiology, particularly for their potential to assist in image diagnosis and classification. However, their clinical application remains challenging, partly due to the risk of generating incorrect responses or providing answers unsupported by reliable evidence [1]. One strategy to address these challenges is retrieval-augmented generation (RAG), which enhances the accuracy and reliability of LLM-generated responses by retrieving relevant information from reliable external knowledge (REK) and incorporating it into the model's prompt [2, 3]. Research on LLMs with RAG (RAG-LLMs) in radiology is still in its early stages, and their effectiveness, particularly in image interpretation and classification, remains largely unexplored [4, 5].

In a previous study, we evaluated the utility of NotebookLM (https://notebooklm.google), a RAG-LLM developed by Google, for lung cancer staging. We provided it with the latest Japanese lung cancer staging guidelines at the time as REK and tasked it with staging 100 fictional lung cancer cases based on CT findings. NotebookLM exhibited higher classification accuracy compared to GPT-4 Omni (GPT-40). Furthermore, NotebookLM referenced the provided REK content with greater accuracy [6]. These findings highlight NotebookLM's potential in cancer staging; however, its utility beyond lung cancer remains unclear. Moreover, a key limitation of this study was that the LLM used in NotebookLM at the time, Gemini 1.5 Pro, differed from the compared LLM, GPT-40, meaning the comparison was not purely based on the presence or absence of RAG techniques.

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T factor	T0	Tis	T1a	T1	1b	T1c	T2	T3	T4	
Number of patients	2	8	4	6	6	8	4	57	11	_
N factor	N0	N1a	N1	b						
Number of patients	58	22	20							
M factor	M0	M1	_							
Number of patients	67	33								
Local invasion factors	CH	ו D	J1 S	51 1	RP1	PV	1 A	.1	PL1	001
Number of patients	7	4	4 6	52	64	47	3	4	7	16
Resectability classification	R	BR	UR							
Number of patients	42	16	42							

Table 1. Breakdown of staging components for the 100 fictional pancreatic cancer patients.

//gemini.google.com/app), the LLM currently integrated into NotebookLM, we aimed to more purely assess the impact of RAG techniques while minimizing the influence of differences in the underlying language model.

2 MATERIALS AND METHODS

An overview of the experimental process is schematically summarized in Fig. 1. As shown in this figure, we compared the accuracy of cancer staging across three groups: REK+/RAG+ (NotebookLM with REK), REK+/RAG- (Gemini 2.0 Flash with REK), and REK-/RAG- (Gemini 2.0 Flash without REK). In the REK+/RAG+ group, retrieved excerpts from REK were available alongside the classification results. Therefore, we evaluated the specific content of these excerpts and assessed their relevance and appropriateness.

Data preparation

Two radiologists from our team generated CT findings for 100 fictional pancreatic cancer patients, along with staging components (TNM classification, local invasion factors, and resectability classification) based on the latest pancreatic cancer staging guidelines in Japan—the eighth edition of the Japanese classification of pancreatic carcinoma [7]. The CT findings and staging components were subsequently reviewed and confirmed by four additional radiologists and one gastroenterologist. A breakdown of the staging components for the 100 fictional pancreatic cancer patients is provided in Table 1. All the CT findings with staging components are available in Supplementary file 1[†]. Below is an example from the dataset, presenting the first of the 100 cases:

Case 1 CT findings: A nodular pancreatic cancer measuring 20 mm is observed in the body of the pancreas. No local invasion factors are noted. Lymph node metastases are identified in two nodes at station 10 and two nodes at station 11d. No other metastases are observed. Case 1 staging components: T factor: T1c; N factor: N1b; M factor: M0; Local invasion factors: CH0, DU0, S0, RP0, PV0, A0, PL0, OO0; Resectability classification: R.

Preparation of REK and user input

We attempted to use an open-access paper [7], which summarizes the current pancreatic cancer staging guidelines in Japan, as REK for NotebookLM and Gemini 2.0 Flash. However, since the full

[†]Supplementary files 1 to 6 can be found in the ancillary files uploaded with this paper on arXiv.

Task 1	Diagnose the local invasion factors of pancreatic cancer (CH, DU, S, RP, PV, A, PL, OO)
	and respond in the format: e.g., "CH0, DU1, S1, RP1, PV0, A0, PL0, OO1".
Task 2	Based on the answer to Task 1, determine the T classification of pancreatic cancer (T0,
	Tis, T1a, T1b, T1c, T2, T3, T4).
Task 3	Determine the N classification of pancreatic cancer (N0, N1a, N1b) based on the defined
	criteria for regional lymph nodes. Note that Metastasis to non-regional lymph nodes is
	classified under M classification, not N classification.
Task 4	Determine the M classification of pancreatic cancer (M0, M1).
Task 5	Based on the answer to Task 4, determine the resectability classification of pancreatic
	cancer (R, BR, UR). Respond with BR if the classification is BR-PV or BR-A, and UR if it
	is UR-LA or UR-M. If both BR and UR apply, respond with UR.

Table 2. User input for LLMs to perform pancreatic cancer staging.

text of the paper (5418 words, covering Chapters 1 to 8, including figure captions and tables) could not be entered into the prompt field at once, we adopted REK consisting of 4376 words from the paper (Chapters 1 to 6), omitting the final two chapters that were not relevant to staging.

To enable the LLM to perform pancreatic cancer staging, we provided Tasks 1–5, shown in Table 2, as user input in the prompt field, followed by the CT findings for each case. In the REK+/RAG+ group, we uploaded the REK to the NotebookLM web system for RAG processing. In the REK+/RAG- group, we manually entered the REK into the prompt field before providing Tasks 1–5. In the REK-/RAG-group, we entered a prompt instructing adherence to the Japanese Classification of Pancreatic Carcinoma, Eighth Edition by the Japan Pancreas Society before providing Tasks 1–5.

Evaluation

Cancer staging was defined as accurate if all staging components—TNM classification, local invasion factors, and resectability classification—were correctly determined. Staging accuracy was compared across the three groups: REK+/RAG+, REK+/RAG-, and REK-/RAG-. Additionally, the classification accuracy of each staging component was evaluated and compared across these groups. The TNM classification was considered correct only when all T, N, and M factors were accurately classified.

In the REK+/RAG+ group, retrieved excerpts from REK via NotebookLM were available for reference. Therefore, we examined these excerpts for each case and evaluated retrieval accuracy. Retrieval was considered accurate if the excerpts contained sufficient information to correctly classify all of the staging components.

The LLM's answers for each case in the three groups (REK+/RAG+, REK+/RAG-, and REK-/RAG-), along with the retrieved excerpts in the REK+/RAG+ group, are provided in Supplementary file 2^{\dagger} . Additionally, the case-wise accuracy of each staging component across the three groups is presented in Supplementary file 3^{\dagger} , while the case-wise retrieval accuracy in the REK+/RAG+ group is provided in Supplementary file 4^{\dagger} .

3 RESULTS

In the experiment using 100 fictional pancreatic cancer cases, NotebookLM with REK (REK+/RAG+) achieved a staging accuracy of 70 %, whereas Gemini 2.0 Flash with REK (REK+/RAG-) and without REK (REK-/RAG-) showed lower accuracies of 38 % and 35 %, respectively (Fig. 2). For TNM classification, NotebookLM with REK achieved an accuracy of 80 %, outperforming Gemini 2.0 Flash with REK (55 %) and without REK (50 %), with a notable advantage in T and N factors (Fig. 3). A similar

[†]Supplementary files 1 to 6 can be found in the ancillary files uploaded with this paper on arXiv.



Fig. 2. Staging performance of NotebookLM with REK, Gemini 2.0 Flash with REK, and Gemini 2.0 Flash without REK in the experiment using 100 fictional pancreatic cancer cases. Staging was considered accurate if all the staging components—TNM classification, local invasion factors, and resectability classification—were correctly determined. For NotebookLM, retrieval accuracy was also evaluated. Retrieval was considered accurate if the retrieved excerpts from REK contained sufficient information to enable accurate cancer staging. *REK*=reliable external knowledge

trend was seen in the classification accuracy of local invasion factors; however, NotebookLM's advantage in resectability classification was not distinct (Fig. 4).

Unlike Gemini 2.0 Flash with and without REK, NotebookLM presented retrieved excerpts from REK as the basis for its classifications, achieving a retrieval accuracy of 92 % (Fig. 2). For example, Fig. 5 shows the experimental results for Case 98. While Gemini 2.0 Flash with and without REK output only the classification results, which were incorrect, NotebookLM explicitly provided the retrieved REK excerpts as the basis for its correct answers (a subset of the retrieved excerpts is shown in Supplementary file 5^{\dagger}). Fig. 6 shows the results of Case 48, an example where NotebookLM's retrieval was accurate but its staging was inaccurate. Although sufficient information for correctly determining resectability was retrieved from REK (Supplementary file 6^{\dagger}), the model misclassified resectability based on a description that mistakenly identified the splenic vein (a part of the portal venous system, but not the portal vein (PV) itself) as the PV (Fig. 6). There were a few cases (eight in total) in which retrieval from REK was inaccurate. For example, in Case 59, the retrieved excerpts lacked information on "Resectable: R," which was necessary for accurate resectability classification (Supplementary file 2^{\dagger}). Note that the retrieved excerpts for Case 98, Case 48, and Case 59 contain 678, 838, and 981 words, respectively, accounting for approximately 16 %, 19 %, and 22 % of the entire REK (4376 words). These counts, along with those for other cases, can be verified in Supplementary file 2^{\dagger} .

4 DISCUSSION

Several previous studies have tried pancreatic cancer staging from radiology reports using LLMs. Bhayana R. et al. evaluated GPT-3.5 and GPT-4 in generating synoptic radiology reports and assessing tumor resectability for pancreatic ductal adenocarcinoma. Their study found that GPT-4 produced near-perfect synoptic reports, and chain-of-thought prompting improved its accuracy in classifying resectability. However, the model still made some clinically significant misinterpretations that could affect decision-making, so the authors argue that LLM-based applications should be used only as aids under supervised settings [8]. Suzuki K. et al. assessed GPT-4's capability in TNM classification of pancreatic cancer using Japanese radiology reports, and the authors concluded

[†]Supplementary files 1 to 6 can be found in the ancillary files uploaded with this paper on arXiv.



Fig. 3. TNM classification performance of NotebookLM with REK, Gemini 2.0 Flash with REK, and Gemini 2.0 Flash without REK in the experiment using 100 fictional pancreatic cancer cases. The TNM classification was deemed correct only if all T, N, and M factors were accurately identified. Additionally, the classification accuracy for each T, N, and M factor was compared across the three groups. *REK*=reliable external knowledge



Fig. 4. The performance of NotebookLM with REK, Gemini 2.0 Flash with REK, and Gemini 2.0 Flash without REK in determining local invasion factors and resectability classification in the experiment using 100 fictional pancreatic cancer cases. *REK*=reliable external knowledge

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Case 98 CT findings:

An infiltrative pancreatic cancer measuring 41 mm is observed in the tail of the pancreas. Serosal invasion and retropancreatic tissue invasion are noted. Stenosis of the splenic artery is observed, suggesting invasion. Invasion into the left adrenal gland is also noted. No other local invasion factors are identified. Lymph node metastases are observed in three nodes at station 16b. No other metastases are observed.

Correct answer: Task 1: CH0, DU0, S1, RP1, PV0, A1, PL0, OO1 Task 2: T3 Task 3: N0 Task 4: M1 Task 5: UR

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Output by:

NotebookLM with REK

 Based on the image findings and the provided information from the sources, here's a breakdown of the tasks: Task 1: Diagnose the local invasion factors of pancreatic cancer The image findings indicate the following: Serosal invasion is present. Retropancreatic tissue invasion is present. Invasion into the left adrenal gland is present. Stenosis of the splenic artery is observed, suggesting arterial system invasion ①. Therefore, based on the definitions in the source ①②③. CH0, DU0, S1, RP1, PV0, A1, PL0, O01 Task 2: Determine the T classification of pancreatic cancer The tumor is located in the tail of the pancreas and measures 41 mm. The tumor extends beyond the pancreas but does not involve the CA or SMA ②. According to the JPS eighth edition, T3 is defined as a tumor that extends beyond the pancreas but does not involve the CA or SMA. Therefore, based on the information, the classification is T3. 	Correct
 Lymph node metastases are observed in three nodes at station 16b. Lymph node metastasis outside the regional nodes should be recorded as M1 ④. According to Table 2, for a tumor in the tail of the pancreas, regional lymph nodes include 8a, 9, 10, 11p, 11d, and 18 ⑤. Lymph node 16b is around the abdominal aorta b ⑥. Since the metastasis is in station 16b, which is not a regional lymph node for the tail of the pancreas, it should not be considered for N classification ⑤⑦. Therefore, the N classification is N0, meaning no regional lymph node metastasis ⑧. Task 4: Determine the M classification of pancreatic cancer Lymph node metastases are observed in three nodes at station 16b ④. Lymph node metastasis, including nonregional node metastasis, is present, the classification is UR-M (tumor with distant metastasis) ⑨. Therefore, the resectability classification is UR. 	
Task 1: CH0, DU0, S1, RP1, PV0, A1, PL0, OO1 Task 2: T4 Task 3: N1a	Incorrec

Incorrect

Gemini without REK

Task 4: M0 Task 5: UR

Task 1: CH0, DU0, S1, RP1, PV0, A1, PL0, 000 Task 2: T4 Task 3: N1b Task 4: M0 Task 5: UR

Incorrect

Fig. 5. A representative result from the pancreatic cancer staging experiment (Case 98). In this case, both staging and retrieval by NotebookLM were correct, whereas staging by Gemini 2.0 Flash with REK and without REK was incorrect. A subset of the REK excerpts retrieved by NotebookLM is available in Supplementary file 5, while the full set (from ① to ⑨) can be found in Supplementary file 2. REK=reliable external knowledge

Case 48 CT findings:

An infiltrative pancreatic cancer measuring 48 mm is observed in the tail of the pancreas. Serosal invasion and retropancreatic tissue invasion are noted. The splenic vein is obstructed by the tumor, suggesting invasion. No other local invasion factors are identified. No lymph node metastases are present. No other metastases are observed.

Output by NotebookLM with REK:

Based on the image findings and the provided information from the sources, here's a breakdown of the tasks: Task 1: Diagnose the local invasion factors of pancreatic cancer • Based on the image findings, the local invasion factors are: Serosal invasion is present ①. Retropancreatic tissue invasion is present ①. Portal venous system (splenic vein) invasion is present ①②. • Therefore, the diagnosis is: CH0, DU0, S1, RP1, PV1, A0, PL0, OO0 ①. • Task 2: Determine the T classification of pancreatic cancer • The tumor is located in the tail of the pancreas and measures 48 mm, which is greater than 40 mm but not greater than 60 mm (3)(4). • Serosal and retropancreatic tissue invasion are present (1). • Portal venous system invasion is present (1)(2). • According to the JPS eighth edition, T3 is defined as a tumor that extends beyond the pancreas but does not involve the CA or SMA (1)(5). T4 is defined as a tumor that involves the CA or SMA (1)(5). • Given that the tumor extends beyond the pancreas, but does not involve the CA or SMA, the T classification is T3 (1). • Task 3: Determine the N classification of pancreatic cancer • The image findings state that no lymph node metastases are present. Incorrect $\circ\,$ Therefore, the N classification is N0, indicating no regional lymph node metastasis (6). (Task 5) • Task 4: Determine the M classification of pancreatic cancer The image findings indicate that no distant metastases are observed. • Therefore, the M classification is M0, indicating no distant metastasis (6). • Task 5: Determine the resectability classification of pancreatic cancer • The tumor is in the tail of the pancreas. • The tumor invades the splenic vein (a part of the portal venous system), obstructing it (1)(2). Based on the resectability classifications: • Resectable (R) indicates no tumor contact with the SMV or PV, or less than 180 degrees contact/invasion without occlusion \overline{O} . Borderline Resectable (BR-PV) indicates tumor contact/invasion of the SMV/PV of 180 degrees or more, or occlusion of the SMV/PV, not exceeding the inferior border of the duodenum (7). Unresectable (UR-LA) indicates tumor contact/invasion of the SMV/PV of 180 degrees or more, or occlusion of the SMV/PV extending beyond the inferior border of the duodenum (8). • Since the splenic vein is obstructed, the tumor is considered at least borderline resectable ⑦. However, since the image findings do not clarify whether the occlusion extends beyond the inferior border of the duodenum, it is difficult to distinguish between BR and UR. Therefore, the classification is BR.

Correct answer:

Task 2: T3

Task 3: N0

Task 4: M0

Task 5: R

Task 1: CH0, DU0, S1, RP1, PV1, A0, PL0, OO0

The LLM misinterpreted the splenic vein as the portal vein (PV).

Fig. 6. A representative result from the pancreatic cancer staging experiment (Case 48). In this case, although NotebookLM appropriately retrieved REK excerpts, the LLM misinterpreted the information, leading to an incorrect staging. A subset of the REK excerpts retrieved by NotebookLM is available in Supplementary file 5, while the full set (from ① to ⑧) can be found in Supplementary file 2. *REK*=reliable external knowledge, *LLM*=large language model

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that its performance did not meet clinical standards [9]. Similarly, in our experimental settings, pancreatic cancer staging by Gemini 2.0 Flash exhibited poor performance. In contrast, providing the pancreatic cancer staging guidelines in Japan as REK in the prompt field led to a slight improvement in accuracy. Moreover, a clear improvement was observed in NotebookLM, where Gemini 2.0 Flash was enhanced with RAG technology (Figs. 2 to 4). The superiority of NotebookLM in cancer staging was also demonstrated in our previous study on lung cancer [6]. Taken together, these findings suggest that RAG technology may enhance the accuracy of cancer staging by LLMs.

Although NotebookLM exhibited superior performance in cancer staging, classification errors persisted even when relevant excerpts from REK were appropriately retrieved, as the LLM misinterpreted the information (Fig. 6, Supplementary file 6^{\dagger}). Misinterpretations (or hallucinations) remain a serious concern in the field of LLM research, and no complete solution has been found [10]. Therefore, even a highly accurate LLM poses risks if used in medical practice without physician oversight, reinforcing the need to limit its role to a supplementary tool. For guideline-based tasks like cancer staging, LLM-generated classifications without reliable supporting evidence are unlikely to reduce physicians' workload, as they would still need to consult the guidelines just as they would without LLM assistance. However, this study demonstrated that the RAG-LLM, NotebookLM, can explicitly provide retrieved REK excerpts as evidence for staging (see Figs. 5 and 6, as well as Supplementary files 5 and 6^{\dagger} for examples) with relatively high accuracy (Fig. 2), potentially allowing physicians to verify facts more efficiently. Future studies should evaluate whether the partial provision of REK through RAG technology effectively alleviates physicians' burden.

As discussed above, RAG-LLMs have the potential to assist physicians with diagnosis and classification; however, data management issues remain a concern for practical medical applications. Submitting patient information, such as radiology reports, to internet-based LLMs like Gemini (Google) or GPT (OpenAI) is generally discouraged due to information security concerns. In light of this, open-source LLMs that can be downloaded and run locally are increasingly being recommended in the field of radiology [11, 12]. Therefore, in the future, it will be necessary to pursue the clinical application of offline or on-premises RAG-LLMs instead of NotebookLM.

The remaining limitations and future perspectives of this study are as follows. First, the extent to which RAG enhances LLM performance may depend on the LLM's capability as well as the length and complexity of the REK. If the LLM can fully comprehend and process the entire REK, directly inputting it into the prompt field may seem sufficient, potentially leading to the assumption that partial information extraction, as performed in RAG, is unnecessary. Nevertheless, if the REK is too extensive for physicians, extracting relevant information using RAG techniques may still be beneficial in assisting physicians with staging. Second, the retrieval accuracy we defined is affected by the length of the REK. In our experiment, the total word count of the retrieved excerpts for each case was roughly 20 % of the REK (see Supplementary file 2^{\dagger} for raw data). However, if the excerpts encompassed the entire REK, the retrieval accuracy would inevitably reach 100 %, making the result trivial (which did not occur in this experiment). Therefore, assessing retrieval accuracy based solely on its numerical value is not appropriate. Third, unlike in actual clinical settings, we evaluated the LLM's staging accuracy using fictional cancer CT findings and Japan's pancreatic cancer staging guidelines in English rather than Japanese. To rigorously assess its applicability in real clinical practice, validation with actual clinical data is necessary. Fourth, while our previous study [6] and this research have evaluated the utility of a RAG-LLM (NotebookLM) in cancer staging, future studies should also explore its applicability to other clinical tasks, such as identifying differential diagnoses based on imaging findings.

[†]Supplementary files 1 to 6 can be found in the ancillary files uploaded with this paper on arXiv.

5 CONCLUSION

NotebookLM, a RAG-LLM, demonstrated superior accuracy in a pancreatic cancer staging experiment compared to Gemini 2.0 Flash. Since Gemini 2.0 Flash is also the underlying LLM used in NotebookLM, this result suggests that RAG technology has the potential to enhance the staging accuracy of LLMs. Additionally, NotebookLM effectively retrieved relevant excerpts from the given REK, allowing physicians to assess the reliability of its responses and highlighting the potential of RAG-LLMs in supporting clinical diagnosis and classification. Due to information security concerns, the internet-based RAG-LLMs, including NotebookLM, are unlikely to be suitable for medical applications, underscoring the need for locally operating RAG-LLMs in the future.

6 DECLARATIONS

Author contributions

- Conceptualization: Hisashi Johno
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Competing interests

There are no competing interests with regard to this manuscript.

Ethics approval

Since the study used only fictional patient data, ethical approval was not required.

Informed consent

Not applicable.

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Data availability statement

Most of the data supporting the findings of this study are included in the article and its Supplementary files. Further details and additional data can be obtained from the corresponding author upon reasonable request.

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