Responses to the Reviewer's comments
Manuscript No: 89102
Title: Deep Learning-Based Magnetic Resonance Imaging Reconstruction for Improving the Image Quality of Reduced-Field-of-View Diffusion-Weighted Imaging of the Pancreas

Comment 1: How does reduced-field-of-view DWI address artifacts such as motion, ghosting, and distortion in abdominal imaging, particularly in the pancreas? What are the specific challenges associated with imaging of the pancreas using DWI?

Response 1: Thank you for the comment. Reduced-field-of-view DWI has been reported to reduce artifacts such as ghosting, susceptibility (distortion), and aliasing. Pancreatic MRI is occasionally disturbed by these artifacts because it is located near the GI tract and the center of the abdomen. Although the pancreas is occasionally affected by motion artifacts caused by respiration or peristalsis because it is located in the retroperitoneal space, reduced-field-of-view DWI is also effective in reducing motion artifacts. We have modified the 3rd sentence (underlined) in the 2nd paragraph of the **Introduction** as follows:

"In particular, imaging of the pancreas has been shown to improve image quality, such as visualization of anatomical structures, contrast-to-noise ratio (CNR), and lesion conspicuity, and reduce artifacts, such as ghosting, susceptibility, motion, and aliasing artifacts, compared to full-FOV DWI."

Comment 2: Can you elaborate on the potential benefits of combining reduced-FOV DWI with DLR to improve image quality in pancreatic imaging? What are the key advantages of the DLR in this context?

Response 2: Thank you for the comment. We have described our motivation for the introduction of DLR in our institute and applied it to reduced-FOV DWI in the 3rd sentence of the 2nd paragraph of ***MRI*** of the **Materials and Methods** section as follows:

"Our motivation for introducing DLR was to improve the image quality of FOCUS of the pancreas because it suffers from a low SNR and the limitation of not providing good results at higher b-value settings."

Based on our results, we have described the advantages of DLR in the **Conclusion** section as follows:

"The use of DLR improved the image noise and CRs on FOCUS without prolonging the scan time."

Therefore, we have not added any sentences to the main text; however, we appreciate this valuable comment.

Comment 3: In terms of image quality, what are the differences between FOCUS-DLR+ and FOCUS-DLR- compared to FOCUS-conv? How do these differences affect the visualization of anatomical structures and lesions in the pancreas?

Response 3: Thank you for the comment. The differences between FOCUS-DLR+ and FOCUS-DLR- compared to FOCUS-conv are described in the 2nd paragraph of ***Qualitative image assessment***s and the 2nd paragraph of ***Quantitative image assessments*** of the **Results** section.

Based on these results, we concluded that FOCUS-DLR+ is effective for visualizing anatomical structures and lesions in the pancreas. We have added a new 2nd sentence to the 3rd paragraph of the **Discussion** section as follows:

"We suggest that FOCUS-DLR+ may be effective in visualizing anatomical structures and lesions in the pancreas."

Comment 4: How does DLR affect the sharpness of the pancreatic contour in DWI images and what clinical implications does this have for diagnosing pancreatic conditions?

Response 4: Thank you for the comment. The clinical implications for the diagnosis of pancreatic conditions are speculated to be that DLR may improve the detectability of pancreatic lesions. It may also be effective in distinguishing pancreatic lesions from extrapancreatic lesions if the pancreatic lesions are present in the peripheral area of the pancreas.

We described our speculations in the 2nd paragraph of the **Discussion** as follows:

"Another benefit of DLR for denoising is that it can control the level of denoising of DWI to make the images appear more natural to the human eye. DLR can improve $CR_{pancreas\text{-}fat}$ on FOCUS using a b-value of 600 s/mm^2, and $CR_{pancreas\text{-}fat}$ and $CR_{lesion\text{-}pancreas}$ on FOCUS using a b-value of 0 s/mm^2. We speculated that a higher CR would clarify the pancreatic parenchyma and lesions. In fact, FOCUS-DLR− showed higher $CR_{lesion\text{-}pancreas}$ than FOCUS-DLR+ using a b-value of 600 s/mm^2. This result could be related to an increase in SIs of the pancreatic parenchyma on FOCUS-DLR+ compared to that on FOCUS-DLR−. However, the results of $CR_{lesion\text{-}pancreas}$ in FOCUS with a b-value of 600 s/mm^2 did not indicate that the detection of pancreatic cystic lesions would be affected by the use of DLR. Instead, DLR is helpful to determine whether there is a lesion inside or outside of the tissue."

Therefore, we have not added any sentences to the main text; however, we appreciate this valuable comment.

Comment 5: Can you explain the significance of CRs between the pancreatic parenchyma and adjacent fat tissue, and how does DLR influence these ratios at different b-values? What does this mean for lesion detection and characterization?

Response 5: Thank you for the comment. We speculate that the CRs between the pancreatic parenchyma and adjacent fat tissue may decrease with increasing b-value on DWI. This was because the SI of the pancreatic parenchyma decreased with the selection of a higher b-value. However, we believe that CRs between the pancreatic parenchyma and solid malignant tumors would improve because solid malignant tumors generally show hyperintensity on DWI with higher b-values. Therefore, we speculate that DLR improves lesion detection; however, we could not prove this speculation in this study. Furthermore, it is unknown how DLR influences the characterization of the lesion. This is a limitation of the present study. Therefore, we have modified the last sentence of the **Discussion** section as follows:

"In summary, we could not estimate how DLR affected the calculation results of ADCs and lesion characterization."

We also added the new 9th sentence in the limitations of the **Discussion** as follows:

"The mechanism by which DLR affects lesion detectability, especially in small pancreatic carcinomas, remains unknown."

This response is related to Comments 6, 8, 9, 10, 13, 14, 18, and 19.

Comment 6: What are the potential clinical applications of DLR-enhanced DWI to differentiate between benign and malignant pancreatic cystic lesions, and how do quantitative evaluations support these applications?

Response 6: Thank you for the comment. As we have responded to Comment 5, we speculated that DLR may improve lesion detection; however, we cannot prove our speculation from our study. Furthermore, it is unknown how DLR influences the characterization of the lesion. This is a limitation of the present study. Therefore, we have modified the last sentence of the **Discussion** section as follows:

"In summary, we could not estimate how DLR affected the calculation results of ADCs and lesion characterization."

We also added the new 9th sentence in the limitations of the **Discussion** as follows:

"The mechanism by which DLR affects lesion detectability, especially in small pancreatic carcinomas, remains unknown."

This response is related to Comments 5, 8, 9, 10, 13, 14, 18, and 19.

Comment 7: Given the variations in ADC measurements between FOCUS-DLR+, FOCUS-DLR-, and FOCUS-conv, how should radiologists interpret ADC values in the context of DLR-enhanced DWI for pancreatic imaging?

Response 7: Thank you for the comment. We believe that the most important finding was that the ADCs of the pancreatic parenchyma and the lesions varied depending on the field strength and MR parameter settings. Therefore, we believe that radiologists should avoid direct comparisons between FOCUS-DLR+, FOCUS-DLR-, and FOCUS-conv. However, we are not sure whether our speculation

is correct because we cannot prove our speculation from our study. We have described the limitations in the 6th paragraph of the **Discussion** as follows:

"One limitation of this study is that we were unable to evaluate $ADC_{pancreas}$ or ADC_{lesion} referring to standard references of pathological findings or larger patient populations. In summary, we could not estimate how DLR affected the calculation results of ADCs and lesion characterization."

Therefore, we have not added any sentences to the main text; however, we appreciate this valuable comment.

Comment 8: Are there limitations or challenges associated with the use of DLR for pancreatic imaging that are not addressed in this study? How do these limitations affect the broader clinical utility of DLR?

Response 8: Thank you for the comment. As described in the limitations of this study, no patients with solid pancreatic tumors, such as pancreatic carcinoma or neuroendocrine tumors, were enrolled. Therefore, we were unable to evaluate the effect of DLR on the detection and characterization of the lesion, particularly in small pancreatic carcinomas. We believe that this will have the most important impact on the clinical utility of DLR. We have modified the last sentence of the **Discussion** section as follows:

"In summary, we could not estimate how DLR affected the calculation results of ADCs and lesion characterization."

We also added the new 9th sentence in the limitations of the **Discussion** as follows:

> "The mechanism by which DLR affects lesion detectability, especially in small pancreatic carcinomas, remains unknown."

This response is related to Comments 5, 6, 9, 10, 13, 14, 18, and 19.

Comment 9: What further research is needed to validate the findings of this study and establish standardized guidelines for the use of DLR in pancreatic imaging? Are there plans to conduct larger-scale studies or investigate DLR in solid

pancreatic tumors?

Response 9: Thank you for the comment. In addition to the limitations of this study, as described in the main text, we recognize that a larger-scale multicenter study may be necessary to validate our results and establish standardized guidelines for the use of DLR in pancreatic imaging. However, we have not yet made such a plan. Therefore, we have added a new 4th sentence to the limitations section of the Discussion as follows:

"A large-scale, multicenter study would be necessary to validate our results."

Comment 10: In clinical practice, how can the combination of reduced-FOV DWI and DLR potentially improve early detection of pancreatic tumors, improve the prediction of tumor malignancy, or aid in the assessment of pancreatic cystic lesions? What are the implications of these findings for patient care and outcomes?

Response 10: Thank you for the comment. We speculated that DLR would improve lesion detection; however, we were unable to prove our speculation in our study. Moreover, we have no idea how DLR affects the characterization of the lesion. We could also not predict how the combination of reduced-FOV DWI and DLR would affect patient care and outcomes. Therefore, it may be necessary to conduct a large-scale multicenter study to evaluate these factors. Therefore, we have modified the last sentence of the **Discussion** section as follows:

"In summary, we could not estimate how DLR affected the calculation results of ADCs and lesion characterization."

We have also added the new 4th and 9th sentences to the limitations of the **Discussion** as follows:

"A large-scale, multicenter study would be necessary to validate our results."

> "The mechanism by which DLR affects lesion detectability, especially in small pancreatic carcinomas, remains unknown."

This response is related to Comments 5, 6, 8, 9, 13, 14, 18, and 19.

Comment 11: How does the introduction of DLR into the MRI reconstruction pipeline affect the SNR in pancreatic imaging with reduced-FOV DWI? Are there trade-offs between denoising and preserving image sharpness?

Response 11: Thank you for the comment. Based on our results, we concluded that the use of DLR improved the image noise and CRs on FOCUS without prolonging the scan time. However, we believe that there is a risk of excessive denoising if we select an inappropriate parameter setting for DLR. In such cases, DLR may decrease not only image noise, but also SIs of anatomical structures. Therefore, we believe that a preliminary scan of healthy volunteers would be helpful to find the appropriate parameter settings prior to examination of the patients.

We have not added any sentences to the main text; however, we appreciate this valuable comment.

Comment 12: Can you provide insight into the technical aspects of DLR, such as deep convolutional networks and training databases? How do these components contribute to their effectiveness in reducing image noise and artifacts?

Response 12: Thank you for the comment. We explain DLR on ***MRI*** in the **Materials and Methods** section**.** However, the details of the machine learning and training processes are unknown because they are patents from GE Healthcare (black box). Therefore, we have not added any sentences to the main text; however, we appreciate this valuable comment.

Comment 13: Are there specific patient populations or clinical scenarios in which the combination of reduced-FOV DWI and DLR is particularly advantageous for pancreatic imaging, and how does it compare to traditional imaging methods in these cases?

Response 13: Thank you for the comment. We assume that the combination of reduced-FOV DWI and DLR would be advantageous in patients with a medical history of pancreatic carcinoma, intraductal papillary mucinous neoplasm, and chronic pancreatitis. These patients must undergo regular follow-up MRI examinations due to the risk of developing pancreatic carcinoma. Furthermore, the combination of reduced-FOV DWI and DLR may be more useful than full-FOV DWI

for the detection of small pancreatic carcinomas. We have revised the 2nd and 5th sentences in the 3rd paragraph of the **Discussion** as follows:

"We suggest that FOCUS-DLR+ may be effective in visualizing anatomical structures and lesions in the pancreas."

"Reduced-FOV DWI can provide a higher spatial resolution than full-FOV DWI."

Therefore, we have not added any sentences to the main text; however, we appreciate this valuable comment.

This response is related to Comments 5, 6, 8, 9, 10, 14, 18, and 19.

Comment 14: Given that DLR was introduced to improve the image quality for FOCUS, are there implications for the detection of small pancreatic lesions or the ability to predict tumor aggressiveness? How does the DLR contribute to these aspects?

Response 14: Thank you for the comment. We assume that the combination of reduced-FOV DWI and DLR may be more useful than full-FOV DWI for the detection of small pancreatic carcinomas. We have revised the 2nd and 5th sentences in the 3rd paragraph of the **Discussion** as follows:

"We suggest that FOCUS-DLR+ may be effective in visualizing anatomical structures and lesions in the pancreas."

"Reduced-FOV DWI can provide a higher spatial resolution than full-FOV DWI."

Meanwhile, we speculate that DLR may improve the detection of lesion, but we were unable to prove this speculation in this study. Furthermore, it is not known how DLR affects lesion characterization. We believe that a large-scale multicenter study is necessary to evaluate these factors. Therefore, we have modified the last sentence of the **Discussion** section as follows:

"In summary, we could not estimate how DLR affected the calculation results of ADCs and lesion characterization."

We also added the new 9th sentence in the limitations of the **Discussion** as follows:

"The mechanism by which DLR affects lesion detectability, especially in small pancreatic carcinomas, remains unknown."

This response is related to Comments 5, 6, 8, 9, 10, 13, 18, and 19.

Comment 15: What are the practical considerations for implementing DLR in routine clinical practice, including the training and expertise required of radiologists and technologists? Are there any additional costs or resource implications?

Response 15: Thank you for the comment. For DLR, training and expertise are not necessary for radiologists or technologists. However, we do not have a clear answer to the additional costs or resources for the use of DLR because it depends on a maintenance contract between a hospital and a medical equipment manufacturer. We have explained DLR on ***MRI*** in the **Materials and Methods**. Therefore, we have not added any sentences to the main text; however, we appreciate this valuable comment.

Comment 16: Are there other organs or anatomical regions within the abdomen where reduced-FOV DWI and DLR can offer similar benefits in terms of image quality improvement and artifact reduction?

Response 16: Thank you for the comment. Except for the pancreas, we assume that the combination of reduced-FOV DWI and DLR would be advantageous to assess the gallbladder, pituitary gland, prostate, rectum, spine, uterine cervix, and vagina. We would not like to describe our presumption in the main text due to our planned future studies; however, we appreciate this valuable comment.

Comment 17: Can you discuss the possible impact of DLR on patient comfort and compliance during MRI, particularly for those with pancreatic conditions that may require frequent follow-up imaging?

Response 17: Thank you for the comment. We believe that there are no potential

impacts of DLR on patient comfort and compliance during MRI scans because DLR is applied in the post-processing pipeline after the scan. DLR can shorten the MR examination time, and the shortened examination time may influence patient comfort and compliance during MRI scans; however, we did not have any evidence to support this. Therefore, we would not like to describe our thoughts in the main text due to the lack of evidence, but we appreciate this valuable comment.

Comment 18: In the context of pancreatic cystic lesions, how might the improved image quality and denoising capabilities of DLR influence the ability to differentiate various cystic lesions, including IPMNs and other types?

Response 18: Thank you for the comment. We assume that the improved image quality and denoising capabilities of DLR would influence its ability to differentiate between various cystic lesions; however, a larger-scale, multicenter study is necessary to investigate this. We have modified the last sentence of the **Discussion** section as follows:

"In summary, we could not estimate how DLR affected the calculation results of ADCs and lesion characterization."

We also added the new 4th sentence in the limitations of the **Discussion** as follows:

"A large-scale and multicenter study would be necessary to validate our results."

This response is related to Comments 5, 6, 8, 9, 10, 14, and 19.

Comment 19: Are there ongoing developments or future directions in DLR technology that could further enhance its effectiveness in pancreatic imaging or address some of the limitations identified in this study?

Response 19: Thank you for the comment. As described in the **Conclusion**, we concluded that the use of DLR improved image noise and CRs on reduced-FOV DWI without prolonging scan times. However, DLR did not improve motion artifacts. We also describe the limitations of the **Discussion**. We recognize that we should investigate the detection of lesions in small pancreatic carcinomas, the characterization of lesions between malignant and non-malignant lesions, and

between pancreatic cystic lesions. Therefore, we have modified the last sentence of the **Discussion** section as follows:

"In summary, we could not estimate how DLR affected the calculation results of ADCs and lesion characterization."

We have also added the new 4th and 9th sentences to the limitations of the **Discussion** as follows:

"A large-scale and multicenter study would be necessary to validate our results."

"The mechanism by which DLR affects lesion detectability, especially in small pancreatic carcinomas, remains unknown."

This response is related to Comments 5, 6, 8, 9, 13, 14, 18, and 19.

Comment 20: Lastly, what are the implications of the significantly shorter scan time associated with FOCUS-DLR+/− compared to FOCUS-conv? How could this affect clinical workflow and patient performance in a clinical setting?

Response 20: Thank you for the comment. DLR can shorten scan time, but we believe that the bottleneck in examination time may be the patient's preparation for MRI examination. However, DLR cannot shorten the preparation time. We believe that this is a different discussion from our study on how DLR affects clinical workflow and patient throughput in a clinical setting. Therefore, we would not like to describe our thoughts in the main text due to the lack of evidence, but we appreciate this valuable comment.

Responses to Journal Editorial Board Comments

Manuscript No: 89102

Title: Deep Learning-Based Magnetic Resonance Imaging Reconstruction for Improving the Image Quality of Reduced-Field-of-View Diffusion-Weighted Imaging of the Pancreas

Comment: The aim of this article was good and the research was well conducted, but I am concerned that the generalization of the results of the study is problematic as no sample size measurements were taken at the beginning of the study, and I hope that a multi-center study will be conducted to confirm the reliability of the results. Deep learning itself has a black box effect, so further explanation of the DLR methodology used in this paper is needed, such as the key mathematical methods required for DLR.

Response: Thank you for the comment. Regarding the sample size of our study and the recommendation of a multi-center study, editor's concern is fully understandable for us. We already described them as the first limitation in the limitations of the **Discussion** as follows:

"First, we analyzed a small number of patients from a single center. It may be difficult to avoid bias in our results and speculations. A large-scale, multicenter study would be necessary to validate our results. The retrospective design of this study is also a potential source of bias."

Therefore, we have not added any sentences to the main text; however, we appreciate this valuable comment.

Regarding the black box effect and methodology of DLR, it is also fully understandable for us. We thought that we performed commonly used analysis methods in this study, but it was unclear whether or not our methods were appropriate for the assessment of the effectiveness of DLR. Therefore, we added a new limitation in as the third limitation in the limitations of the **Discussion** as follows:

"Third, we used the vendor-supplied DLR that was already trained before being installed on MRI machine. On the other hand, the machine learning model is widely regarded as a black box. It meant that we could not know detailed processes of DLR to improve the image quality of FOCUS-DLR+. Although we evaluated our data using

common analysis methods, it might be necessary to prove whether or not our methodology was appropriate to evaluate the effectiveness of DLR."

We appreciate valuable comments.