January 29, 2023

Dear Editorial Board,

World Journal of Clinical Cases

Thanks for accepting our paper " Manuscript NO: 83021, Minireviews) " to publish in the World Journal of Clinical Cases. Please see below for our response to the reviewer's question. We also applied this item in the attached manuscript. You can change the edited items with yellow highlights. Also, grammar edits have been done and can be seen by track changes. We hope these changes can satisfy the reviewer's point of view.

Thanks,

Farzan Vahedifard, Sharon Byrd

Department of Radiology, Rush University Medical Center, Chicago, IL

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This is a review of techniques for performing MRI imaging of the fetal brain. It covers a number of techniques, and I believe that there are virtually no problems in this regard. However, there are many editorial problems, such as indented paragraphs and inconsistent indentation.

1- The chapter "Limitation of Fetal brain MRI" on p. 3 and the chapter "Limitations of AI in Fetal" on p. 19 are parallel. and "Limitations of AI in Fetal" on p. 19, which is a source of confusion for readers. Since the contents are different, they could be in different chapters, but their positions need to be re-examined.

   Answer: Thanks for your comments. We solved the grammatical errors with the opinions of several native and academic professors in the current version, hoping to satisfy your concerns.

   The page 3 limitation is the Limitation of "Fetal brain MRI". These limitations are for just Brain MRIs in neonates. Regardless of AI. The page 19 limitation is: ""Limitations of "AI in Fetal MRI": These limitations are for "Artificial Intelligence in Brain MRI". For more specifications, we added the explanation.

2- In Page 3, In the last sentense of Chapter "Limitations of Fetal brain MRI", "." (period) is missing. It is unclear whether the sentence ends here or not. It is also unclear whether the preceding (?) is a bibliographic reference or not.

   Answer: Thanks.

   In the last sentence of page 3, we put a period now. The sentence is ended, and the last sentence was shortened to more clarification.

   We also removed the (?) from the paragraph.

3- In Page 13, "Expanding the Unet:" is the title of a chapter or section?

Answer: this is a subsection. So we added the bold title to this section "Example of segmentation: "Expanding the Unet model""

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The topic is useful, a good finding for the further investigstion

Answer: Thanks for your comment. Hoping the edits can improve the papers as well.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The study offers a review of the Roles of Artificial Intelligence and Deep Learning Models in Fetal Brain Magnetic Resonance Imaging.This paper is potentially interesting. But i would suggest the author could revise the draft deeply.

1. The major problem is that this draft is full text of description in words. I would suggest the author summary the main traits or findings of cited literature by using some tables. Then the readers could compare the cited studies and get the message and quickly.

Answer: Thanks for your valuable comments. As you asked, we summarized some parts of the paper (which you can see by track change). Also, in the revised version, we provided a summarized, narrative, and comprehensive table, for including the most important findings in just one table. Please see below what we updated as table 1:

Table 1- Different Applications for Artificial Intelligence for Fetal Brain MRI (The details are described in the manuscript)

A.	AI For Preprocessing of Fetal Images	✓ Automatic image quality assessment to detect artifacts on T2 HASTE sequences during fetal MRI (14, Gagoski et al.) ✓ Automatically detects fetal landmarks (using 15 key points – upper limb and lower limb joints, eyes, and bladder) (15, Xu et al.) ✓ Fetal motion correction (16, Hou et al.)

		✓ Predicting fetal motion directly from acquired images in real-time (17, Singh et al.)
B.	AI For Post-processing of Fetal Images	✓ U-net-based brain extraction algorithm to autonomously segment normal fetal brains (19, Li et al.) ✓ Localize, segment, and perform super-resolution reconstruction for the automated fetal brain (20, Ebner et al.)
C.	AI For Reconstruction of Fetal Imaging:	✓ Fully automatic framework for fetal brain reconstruction, consisting of four stages (22, Ebner et al.)
D.	AI For Gestational Age Prediction:	✓ Predicting GA from fetal brain MRI acquired after the first trimester, which was compared to a biparietal diameter (BPD) (26, Kojita et al.) ✓ An end-to-end, attention-guided deep learning model that predicts GA (28, Shen et al.)
E.	AI For Fetal Brain Extraction	✓ The automatic brain extraction method for fetal MRI employs a multi-stage 2D U-Net with deep supervision (DS U-net) (33, Lou et al.) ✓ A brain mask for an MRI stack using a two-phase random forest classifier and one estimated high-order Markov random field solution (32, Ison et al.)
F.	AI For Fetal Brain Segmentation:	✓ U-net-like convolutional neural network (Auto-net) (41, Salehi et al.) ✓ CNN using images with synthetically induced intensity inhomogeneity as data augmentation (42, Salehi et al.) ✓ Pipeline for performing ICV localization, ICV segmentation, and super-resolution reconstruction in fetal MR data in a sequential manner (43, Tourbier et al.) ✓ Automatic method for fetal brain segmentation from magnetic resonance imaging (MRI) data, and a normal volumetric growth chart based on a large cohort (44, Link) et al. ✓ Fetal Brain magnetic resonance Acquisition Numerical phantom, to simulate various realistic magnetic resonance images of the fetal brain a~~long with~~nd its class labels (45, Dumast et al.)

		✓ Single-Input Multi-Output U-Net (SIMOU-Net), a hybrid network for fetal brain segmentation. Was inspired by the original U-Net fused with the holistically nested edge detection (HED) network (46, Rampun et al.) ✓ Incorporating spatial and channel dimensions-based multi-scale feature information extractors into its encoding-decoding framework (47, Long et al.)
G.	AI For Fetal Brain Linear Measurement:	✓ AI for the anteroposterior (A/P) diameter of the pons and the A/P diameter and superior/inferior (S/I) height of the vermis (51, Deng et al.) ✓ A fully automatic method that computes three key fetal brain MRI parameters: 1- Cerebral Biparietal Diameter (CBD), 2- Bone Biparietal Diameter (BBD), 3-Trans Cerebellum Diameter (TCD) (52, Avisdris et al.)
H.	AI For Automatically Localizing Fetal Anatomy	✓ Automatically localizing fetal anatomy, notably the brain, using extracted superpixels (52, Alansary et al.)
I.	AI For Classification of Brain Pathology:	✓ Classification using several machine-learning classifiers, including diagonal quadratic discriminates analysis (DQDA), K-nearest neighbor (K-NN), random forest, naive Bayes, and radial basis function (RBF) neural network classifiers. (56, Attallah et al.)
J.	AI For Placenta Detection:	✓ U-net-based CNN to separate the uterus and placenta (62, Shehedi et al.) ✓ automatic placenta segmentation by deep learning on different MRI sequences (63, Farida et al.)
K.	AI for functional Fetal Brain MRI	✓ An auto-masking model with fMRI pre-processing stages from existing software (64, Rutherford)

2. Another problem is that the English writing level is not very good. such as"All three of these problems make it difficult to segment (?) ""Limitations of AI in Fetal :" and so on.

Answer: Thanks for your comments. We solved the grammatical errors with the opinions of several native and academic professors in the current version, hoping to satisfy your concerns.

- We removed the (?) mark from that sentence, and corrected the paragraph.

We clarify the limitations in this manner: The page 3 limitation is the Limitation of "Fetal brain MRI". These limitations are for just Brain MRIs in neonates. Regardless of AI. The page 19 limitation is: ""Limitations of "AI in Fetal MRI": These limitations are for "Artificial Intelligence in Brain MRI." For more specifications, we added the explanation in the manuscript.

-

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The manuscript falls within the scope of the journal. Description and discussion of the are well done and well-founded in this narrative review paper. However, the text needs improvement. The importance is justified. Questions are formulated. In the literature search, inclusion and exclusion criteria were not completely defined. Key statements are suported by the references. Study design and levels of evidence should be demonstrated. Validity, limitations, consistency and homogeneity are missing. Is there difference between 3 Tesla and 1.5 Tesla MRI? This question is relevant in fetal examination. See attached file with specific suggestions

- Answer: Thanks for your comments

1- We added this section for inclusion and exclusion:

- **Inclusion Criteria:** This narrative review paper investigated the role of AI and Machine Learning methods in fetal brain MRI. The databases for the search were MEDLINE using PubMed, SCOPUS, Web of Science, EMBASE, Cochrane Library, and Google Scholar, up to June 2022. First, we searched keywords including "artificial intelligence", "machine learning", "deep learning", "Fetal brain", "Fetal MRI", as well as "AI + Fetal", "AI + Brain MRI", and "AI or ML + neonates".

- **Exclusion Criteria**: After the second evaluation, only relevant models of AI and Machine Learning methods in fetal brain MRI were included. Animal and Basic science studies were also excluded.

2- For limitations, we specified two sections:

The page 3 limitation is the Limitation of "Fetal brain MRI". These limitations are for just Brain MRIs in neonates. Regardless of AI. The page 19 limitation is: ""Limitations of "AI in Fetal MRI": These limitations are for "Artificial Intelligence in Brain MRI." For more specifications, we added the explanation in the manuscript.

3- About 1.5 vs 3 T, we added this section to paper:

"MRI 3T vs 1.5 T in Fetal MRI: In fetal MRI, the use of 3-T magnets has improved access to advanced imaging sequences and improved anatomical evaluation. A 3.0-T MRI offers a greater signal-to-noise ratio and better spatial resolution than a 1.5-T MRI; however, when it comes to fetal MRI, there are concerns about the possibility of the fetus receiving greater radiofrequency energy. MRI examinations of fetal 1.5- and 3.0-T were found to have equivalent energy metrics in most cases. Three-dimensional steady-state free precession and two-dimensional T1-weighted spoiled gradient echo may require modifications to reduce the amount of energy delivered to the patient."

4- We solved the grammatical errors with the opinions of several native and academic professors in the current version, hoping to satisfy your concerns.

5- For validity and homogeneity, we tried to classify each application (such as segmentation and classification) in each section separately. Also, in the revised version, we provided a summarized, narrative, and comprehensive table, for including the most important findings in just one table. Please see below what we updated as table 1

Table 2- Different Applications for Artificial Intelligence for Fetal Brain MRI (The details are described in the manuscript)

A.	AI For Preprocessing of Fetal Images	✓ Automatic image quality assessment to detect artifacts on T2 HASTE sequences during fetal MRI (14, Gagoski et al.) ✓ Automatically detects fetal landmarks (using 15 key points – upper limb and lower limb joints, eyes, and bladder) (15, Xu et al.) ✓ Fetal motion correction (16, Hou et al.) ✓ Predicting fetal motion directly from acquired images in real-time (17, Singh et al.)
B.	AI For Post-processing of Fetal Images	✓ U-net-based brain extraction algorithm to autonomously segment normal fetal brains (19, Li et al.) ✓ Localize, segment, and perform super-resolution reconstruction for the automated fetal brain (20, Ebner et al.)
C.	AI For Reconstruction of Fetal Imaging:	✓ Fully automatic framework for fetal brain reconstruction, consisting of four stages (22, Ebner et al.)
D.	AI For Gestational Age Prediction:	✓ Predicting GA from fetal brain MRI acquired after the first trimester, which was compared to a biparietal diameter (BPD) (26, Kojita et al.) ✓ An end-to-end, attention-guided deep learning model that predicts GA (28, Shen et al.)
E.	AI For Fetal Brain Extraction	✓ The automatic brain extraction method for fetal MRI employs a multi-stage 2D U-Net with deep supervision (DS U-net) (33, Lou et al.) ✓ A brain mask for an MRI stack using a two-phase random forest classifier and one estimated high-order Markov random field solution (32, Ison et al.)

F.	AI For Fetal Brain Segmentation:	✓ U-net-like convolutional neural network (Auto-net) (41, Salehi et al.) ✓ CNN using images with synthetically induced intensity inhomogeneity as data augmentation (42, Salehi et al.) ✓ Pipeline for performing ICV localization, ICV segmentation, and super-resolution reconstruction in fetal MR data in a sequential manner (43, Tourbier et al.) ✓ Automatic method for fetal brain segmentation from magnetic resonance imaging (MRI) data, and a normal volumetric growth chart based on a large cohort (44, Link) et al. ✓ Fetal Brain magnetic resonance Acquisition Numerical phantom, to simulate various realistic magnetic resonance images of the fetal brain a~~long with~~nd its class labels (45, Dumast et al.) ✓ Single-Input Multi-Output U-Net (SIMOU-Net), a hybrid network for fetal brain segmentation. Was inspired by the original U-Net fused with the holistically nested edge detection (HED) network (46, Rampun et al.) ✓ Incorporating spatial and channel dimensions-based multi-scale feature information extractors into its encoding-decoding framework (47, Long et al.)
G.	AI For Fetal Brain Linear Measurement:	✓ AI for the anteroposterior (A/P) diameter of the pons and the A/P diameter and superior/inferior (S/I) height of the vermis (51, Deng et al.) ✓ A fully automatic method that computes three key fetal brain MRI parameters: 1- Cerebral Biparietal Diameter (CBD), 2- Bone Biparietal Diameter (BBD), 3-Trans Cerebellum Diameter (TCD) (52, Avisdris et al.)
H.	AI For Automatically Localizing Fetal Anatomy	✓ Automatically localizing fetal anatomy, notably the brain, using extracted superpixels (52, Alansary et al.)
I.	AI For Classification of Brain Pathology:	✓ Classification using several machine-learning classifiers, including diagonal quadratic discriminates analysis (DQDA), K-nearest neighbor (K-NN), random

		forest, naive Bayes, and radial basis function (RBF) neural network classifiers. (56, Attallah et al.)
J.	AI For Placenta Detection:	✓ U-net-based CNN to separate the uterus and placenta (62, Shehedi et al.) ✓ automatic placenta segmentation by deep learning on different MRI sequences (63, Farida et al.)
K.	AI for functional Fetal Brain MRI	✓ An auto-masking model with fMRI pre-processing stages from existing software (64, Rutherford)