Dear editors,

Thank you very much for your comments and suggestions.

We have revised the manuscript, according to the comments and suggestions of reviewers and editors, and responded, point by point to, the comments as listed below. Since the paper has been revised significantly throughout the text, we feel it is better to highlight the amendments in the revised manuscript.

I would like to re-submit this revised manuscript to World of journal Radiology, and hope it is acceptable for publication in the journal.

Looking forward to hearing from you soon.

With kindest regards,

Yours Sincerely

Xiao-Ming Zhang

Answers to Reviewers' questions were as follows:

1. This paper focused on technologies of DWI techniques, rather than biological or clinical aspects of pancreatic cancer. The most typical characteristic of pancreatic cancer is the dense fibrosis due to desmoplasia. In fact, many papers suggested relationship between DWI and pancreatic fibrosis of pancreatic cancer or pancreatitis. But authors didn't cite and review those papers. And they mainly focused on cellularity of pancereatic cancer, but, so far, no paper about cellularity and DWI of pancreatic cancer has been published.

Answer: Firstly, We agree with the referee that one of the characteristics of pancreatic cancer is the dense fibrosis. We are sorry for the misunderstanding due to unclear descriptions in our previous manuscript. We have mentioned relationship between the pancreatic cancer and the ADC value. The change of ADC value may due to tumor cell growth, tumor cell atypia and the richness of organelles and the decrease of extracellular space from dense cellularity and extracellular fibrosis. I have highlighted it in the paper, and I cite some paper and make complements. Wang Y,

Chen ZE, Yaghmai V,et al[59] showed that tumor cellularity and/or extracellular fibrosis may account for the change of ADC value in the pancreatic tumors. In 2015 ,**Barral M, et al [16]** ,the cited reference, also reported that pancreatic fibrosis due to cephalic tumor should be considered when using normalized ADC, and it clearly pointed out that pancreatic adenocarcinoma is usually associated with low ADCs in comparison to healthy pancreatic parenchyma because of the presence of fibrosis and increased cell density in these malignant lesions, which are associated with impeded free-water diffusion.

2. Authors wrote as following; "DWI can reflect biologic abnormalities at an early stage". What kind of abnormalities at early stage of cancer can be reflected? Is it really possible?

Answer: Diffusion MR imaging serves as one of the common functional MRI techniques and is the only technique that can be used to reflect the diffusion movement of water molecules in vivo. When the normal tissue underwent malignant transformation, tumor cell growth will change the cellularity. Tumor cell atypia , the richness of organelles, the decrease of extracellular space from dense cellularity and extracellular fibrosis also will change. Thus, to some extent, tumor cell growth may limit the diffusion of water molecules. So it is possible that biologic abnormalities at an early stage can be detected.

3. Authors wrote as following; "In this review, the various diffusion MR imaging techniques for pancreatic cancer will be discussed", but some of DWI techniques in this article have not been applied to pancreatic cancer. I am not sure whether such techniques should be written in the review article.

Answer: There is no research about the DKI for pancreatic cancer in pubmed. But in china, there is one research about the value of DKI in differentiating pancreatic cancer from chronic mass-forming type pancreatitis. Its results confirmed that the clinical application value of DKI model in diagnosis of pancreatic cancer. But what a pity it

didn't publish in pubmed, so I can't cite it in our paper. DKI is also one of the diffusion MR imaging techniques. It is a straightforward extension of DTI, which requires only minor changes in data acquisition and processing. The theory of DKI describes the non-Gaussian diffusion behavior in tissues. In theory, the pancreatic cancer occurs with tumor cell invasion and the proliferation of interstitial cells and connective tissue. The change in the tissue structure leads to the change of MK value. So I think this part can be reserved. Hope it can be acceptable. In the latest Pubmed SCI research, the DKI have been already used in pancreas (Noda Y, Kanematsu M, Goshima S, Horikawa Y, Takeda J, Kondo H, Watanabe H,Kawada H, Kawai N, Tanahashi Y, Bae KT. Diffusion kurtosis imaging of the pancreas for the assessment of HbA1c levels. J Magn Reson Imaging. 2015 Jun 12. doi: 10.1002/jmri.24982).So We speculate the research for DKI in pancreatic cancer has a great prospect.

4. Authors wrote as following; Ichikawa T et al.[59] reported that the ADC value of pancreatic cancer is higher than that of normal pancreas tissue." But [59] included only one pancreatic cancer patient, thus this paper is not proper in this context. If authors want to write review paper, they need to read cited papers carefully, and understand them precisely. Therefore, authors cannot say, "the variable values of the ADC of pancreatic cancer have led to reports of both lower and higher ADC values than those of normal pancreatic tissue or pancreatitis".

Answer: I am sorry that I have not read cited papers carefully. I agree with that one pancreatic cancer is not proper. I accept the comment. In the revised version of the manuscript, I have removed the reference. After that, most of the rest of cited references have shown that the ADC value of pancreatic cancer is lower than that of the normal pancreas.

5. Section 3.DKI for pancreatic cancer. No paper about DKI applied to pancreatic cancer was cited. If authors want to review DKI in pancreatic cancer, they need to cite study of DKI in pancreatic cancer. If they can't, this part should be deleted.
Answer: The question is similar to the question 3. In order to ensure the integrity of

the structure, so I think this part should retain. Hope it can be acceptable.

6. Figures in this paper have problems in aspect ratio. Please check.

Answer: I have checked all the pictures, and submitted the decomposable figures in another independent file, which can be edited by editors easily.

Replies to the Editors note and suggestions:

1. Add the running title

Answer: I have added the running title "DWI for PA".

2. Author contributions

Answer: I have revised the writing of all authors' name in abbreviation.

3. Supportive foundations

Answer: I have added the supportive foundations. "This work was supported by National Nature Science Foundation of China, No. 81271643."

4. Core tip

Answer: I have added the core tip.

5. "Please provide all authors abbreviation names and manuscript title here. World J ** 2015; In press"

Answer: I have added it.

6. "don't forget to submit some files [Conflict-of-Interest Statement (COI), Copyright (need **handwritten** signature of all authors in order) and language Certificate (.pdf)] and Audio core tip (.mp3)"

Answer: I have submitted the Conflict-of-Interest Statement, the Language Certificate and Audio core tip. But I have to explain for the Language Certificate. For manuscripts submitted by Non-Native Speakers of English, the authors are required to

provide a language editing certificate. In the Language Certificate, the paper named "Different diffusion MR imaging for pancreatic cancer", after the documents receiving the certification should be English-ready for publication, I have accepted their suggestions for the change of title. Hence, finally, I change our title as "Various diffusion MR imaging techniques for pancreatic cancer". We think this title is more suitable.

7. Search all abbreviations in your manuscript and do like this when they were used firstly.

Answer: I have checked the full text, and make sure that all abbreviations are acceptable.

8. Please distinguish the title level, level I used all capital letters and bold, level II used Italic effect and bold, level III was just bold.

Answer: I have revised the title level.

9. Please put data of Figures and tables behind references.

Answer: I put the Figures behind reference, and I revised them as the decomposable figures so that you can edit them easily.

10. Please add PubMed citation numbers and DOI citation to the reference list and **list all authors.** Please revise throughout. The author should provide the first page of the paper without PMID and DOI.PMID

Answer: I have revised all the references and list all authors. But some cited references didn't have the DOC number.For these reference, I only add the pubmed citation number.

I have to apologize for giving you so much trouble. Thank you very much!