PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	PEDAL Protocol: A prospective single arm paired comparison of multiparametric MRI and 18F-DCPFyl PSMA PET/CT to diagnose prostate cancer
AUTHORS	Tran, Vy; Hong, Anne; Sutherland, Tom; Taubman, Kim; Lee, Su-Faye; Lenaghan, Daniel; Sethi, Kapil; Corcoran, Niall; Lawrentschuk, Nathan; Woo, H; Tarlinton, Lisa; Bolton, Damien; Spelman, Tim; Thomas, Lauren; Booth, Russell; Hegarty, Justin; Perry, Elisa; Wong, Lih-Ming

VERSION 1 - REVIEW

REVIEWER	Ferro, Matteo European Institute of Oncology
REVIEW RETURNED	02-May-2022

GENERAL COMMENTS	The primary objective of this study is to compare the diagnostic accuracy of 18-fluorine PSMA (18F DCFPyL PSMA) PET scans to multiparametric magnetic resonance imaging (mpMRI) to detect primary prostate cancer at prostate biopsy I suggest to define these critical questions: - Evaluate costs with DCA and benefit on potential use of Prostate specific membrane antigen positron emission tomography (PSMA-PET) Discuss potential integration of Biomarkers in your study Protocol as : Cancers (Basel). 2021 Sep 21;13(18):4723. doi: 10.3390/cancers13184723 Minerva Urol Nephrol. 2021 Aug;73(4):442-451. doi: 10.23736/S2724-6051.21.04098-4. Epub 2021 Mar 26. Futurible application on reclassication biopsy during AS: Eur J Nucl Med Mol Imaging. 2021 Feb;48(2):477-482. doi: 10.1007/s00259-020-04944-2. Epub 2020 Jul 22

REVIEWER	Song, Bin Sichuan University West China Hospital Department of Radiology
REVIEW RETURNED	16-May-2022

GENERAL COMMENTS	The manuscript presented a detailed and well-designed study protocol for comparing the diagnostic accuracy of PSMA-PET/CT scans to mpMRI to detect primary prostate cancer in a multicenter prospective setting. The eligibility criteria, imaging procedures, outcome evaluation, and diagnostic accuracy assessment were

	clearly defined. In general, it is able to consider this paper for publication on BMJ open. Minor flaw: 1. Table 1: The author stated this is a non-randomised phase III trial. I'm confused about the term 'within 3 years of randomization' in exclusion criteria 2 and 3. Can the authors explain this to me? 2. page 12 line 4: A full stop between 'software' and 'Reporting' is missing. 3. page 14 line 7: There is an extra comma between 'cancer' and 'the'.

VERSION 1 – AUTHOR RESPONSE

1. emission tomography (PSMA-PET).
    - Thank you for this comment, and we agree that cost evaluation of some form is important in a study like ours. We have added a decision cost analysis component as a secondary outcome. Please see lines 275, 277 (table), 342-350.
2. Discuss potential integration of Biomarkers in your study Protocol as:
    A. Cancers (Basel). 2021 Sep 21;13(18):4723. doi: 10.3390/cancers13184723
    B. Minerva Urol Nephrol. 2021 Aug;73(4):442-451. doi: 10.23736/S2724-6051.21.04098-4. Epub 2021 Mar 26.
    - Biomarkers have been increasingly examined in recent times, with promising results. While our study focuses on the utility of PSMA PET/CT, we recognise the importance of considering biomarkers as an adjunct to diagnosis of clinically significant prostate cancer. Please see lines 87 and 383-394 for further discussion of biomarkers.
3. Futurible application on reclassication biopsy during AS: Eur J Nucl Med Mol Imaging. 2021 Feb;48(2):477-482. doi: 10.1007/s00259-020-04944-2. Epub 2020 Jul 22
    - This is an excellent point, and is included in our introduction and discussions. Please see lines 115-118, as well as lines 383-394

Reviewer #2 – Dr. Bin Song, Sichuan University, West China Hospital, Department of Radiology

Comments:

Comments to the Author:

4. Table 1: The author stated this is a non-randomised phase III trial. I'm confused about the term 'within 3 years of randomization' in exclusion criteria 2 and 3. Can the authors explain this to me?
    - Thank you for pointing this out. The table reflects an inaccuracy that is now rectified. Please see line 183 (table)
5. Page 12 line 4: A full stop between 'software' and 'Reporting' is missing.
    - These punctuation errors are now rectified. Please see line 239.
6. Page 14 line 7: There is an extra comma between 'cancer' and 'the'.
    - This is corrected. Please see line 286.