## PEER REVIEW HISTORY

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## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Comparison of the ultra-low-dose Veo algorithm with the gold standard filtered back projection for detecting pulmonary asbestos-related conditions: a clinical observational study |
| **AUTHORS** | Tekath, Marielle; Dutheil, Frederic; Bellini, Romain; Roche, Antoine; Pereira, Bruno; Naughton, Geraldine; Chamoux, Alain; Michel, Jean-Luc |

## VERSION 1 - REVIEW

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| **REVIEWER** | Giuseppe Mastrangelo<br>University of Padova, Padova (Italy) |
| **REVIEW RETURNED** | 31-Mar-2014 |

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| **GENERAL COMMENTS** | The paper is new and interesting. It presents, however, minor but essential concerns that are the following.<br><br>1. The paragraph “Interpretation of CT images” (page 6) is unclear. It seems that there were three radiologists: two viewed the images with a third “more experienced radiologist” acting as “gold standard”. I suggest adding more details to clarify the study design.<br><br>2. “Quality of FBP and Veo images” (page 7) is another unclear paragraph, particularly the statement on lines 36-37: “Objective image noise (Standard Deviation) and average CT numbers (in Hounsfield’s units) …”. It seems that authors have expressed the objective noise in Hounsfield’s units, then calculating the average and standard deviation of the values. Again, I suggest explaining things better.<br><br>3. The first paragraph on page 10 should to be rephrased in order to make clear the results shown in table 1.<br><br>4. In the paragraph “Pleural plaques” (page 10), pleural plaques were 297 in the first statement. In the second the numbers become 259 (Veo algorithm) and 287 (FBP algorithm). The reader does not understand the reason of these differences. It may be that the third radiologist found 297 plaques, but this is unsure. In the next statement of the same paragraph, it can be read: “the agreement for pleural plaques depiction was 84%, with a kappa of 0.05”. I fear that 0.05 could be a mistake.<br><br>5. In the paragraph “Pulmonay nodules” (page 11) the nodules were 167 in the first statement, but this number becomes 134 (for Veo method) and 133 (according to FBP method) in the following lines. The problem is: how were the 167 nodules diagnosed?<br><br>6. Furthermore, please notice that: (line 14, page 5) this study is not “prospective” because patients were examined at one point in time; |

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| | (line 12, page 6) a radiologist with two years of experience cannot be defined “experienced”; (line 41, page 8) “General estimated equation models” should be “generalized estimating equation models”; (Table 2) the title could probably be: “Mean and standard deviation of objective noise values (in Hounsfield’s units, HU) and signal to noise ratio measurements”, but it is not certain; (Table 3) in the title, “accurately” should probably be “accuracy”. |

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| **REVIEWER** | Lesage, François-Xavier<br>occupational diseases<br>university hospital of Reims<br>France |
| **REVIEW RETURNED** | 03-Apr-2014 |

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| **GENERAL COMMENTS** | This is a concordance study, between a ultra-low-dose algorithm known as Veo, and a gold standard method for detecting pulmonary asbestos-related conditions.<br>The reduction of radiation delivered is a major concern. Hence, this study is really relevant.<br><br>First at all, I found that this article was written professionally.<br><br>This study is correctly conducted. The protocol is suitable in my opinion, and the statistical analysis are relevant.<br><br>However, I have to main comments:<br><br>-The authors concluded to a best used for follow-up of patient. In my opinion, such a recommendation is premature. Only two radiologists participated to this study (with a low interobservers agreement for pleural plaque detection !). Their findings argue for this conclusion, but the level of proof is too weak in my opinion.<br><br>-Authors compared Veo and the gold standard. But it’s important to discuss the other reconstruction algorithms, such as iDose, ASIR, … There is no data concerning these algorithm. Is the Veo more relevant that the other algorithm for follow-up these patients? It’s really important to discuss this point.<br><br>Overall, this is a really interesting study, concerning a relevant topic. The manuscript is well written. |

## VERSION 1 – AUTHOR RESPONSE

Reviewer 1
Reviewer Name: Giuseppe Mastrangelo
Institution and Country University of Padova, Padova (Italy)

The paper is new and interesting. It presents, however, minor but essential concerns that are the following.

1. The paragraph “Interpretation of CT images” (page 6) is unclear. It seems that there were three radiologists: two viewed the images with a third “more experienced radiologist” acting as “gold standard”. I suggest adding more details to clarify the study design.
In order to clarify the study design, we added the initials of the two radiologists in brackets and we

rephrased the sentences as follow: « Each CT acquisition was viewed independently by two radiologists (2 to 7 years of experience, Drs RB and AR). The low-dose images with Veo reconstruction were interpreted before the standard CT and on separate weeks to minimize recall bias. A third simultaneous reading of the Veo and FBP acquisitions by the more experienced radiologist (AR) evaluated the concordance of pleuroparenchymal abnormalities."

2. "Quality of FBP and Veo images" (page 7) is another unclear paragraph, particularly the statement on lines 36-37: "Objective image noise (Standard Deviation) and average CT numbers (in Hounsfield's units) …". It seems that authors have expressed the objective noise in Hounsfield's units, then calculating the average and standard deviation of the values. Again, I suggest explaining things better.
Objective image noise is information accessed from CT scan software. We rephrased the sentences as follow: "Objective image noise is the mean of the Standard Deviation of the signal intensity (in Hounsfield's units) measured with circular regions of interest (ROI) on different anatomical levels, 10 mm in diameter.19 ROIs were drawn within the descending thoracic aorta at the level of the left main bronchus, within the tracheal lumen up to the tracheal bifurcation, and on the lung. The signal to noise ratio (SNR) was also calculated using the equation SNR = signal intensity / objective noise". Thus, we did not express the objective image noise in HU and subsequently calculate the average and SD of the values, we simply reported the objective image noise given by the software.

3. The first paragraph on page 10 should to be rephrased in order to make clear the results shown in table 1.
The first paragraph now reads: "Tables 1 and 2 provide results from subjective image noise assessed by the two radiologists using, average of objective noise data and SNR available in the manufacturer's software. The two protocols differed significantly in objective image noise. The ultra-low-dose Veo acquisition reduced objective image noise from 13 to 23% and increased SNR from 5 to 33% compared with the standard FBP acquisition. However, the two readers rated higher subjective image noise in axial and coronal planes with Veo than FBP, with the exception of parenchymal analysis in the coronal plane for the reader 1."

4. In the paragraph "Pleural plaques" (page 10), pleural plaques were 297 in the first statement. In the second the numbers become 259 (Veo algorithm) and 287 (FBP algorithm). The reader does not understand the reason of these differences. It may be that the third radiologist found 297 plaques, but this is unsure. In the next statement of the same paragraph, it can be read: "the agreement for pleural plaques depiction was 84%, with a kappa of 0.05". I fear that 0.05 could be a mistake.
We hope the response to the comment 1 is sufficiently clear. 287 nodules were depicted the first time using FBP algorithm. However, the third simultaneous reading of Veo and FBP resulted in the detection of 10 more plaques. In order to clarify the understanding of the manuscript, we added the following sentence highlighted in yellow: "A total of 297 pleural plaques (Figure 2) were observed in 20 participants (74%). Detection of plaques did not differ between Veo (259; 87%) and FBP (287; 97%) (p=0.10). Thus, the third simultaneous reading of Veo and FBP resulted in the detection of 10 plaques that were not detected during the first reading of FBP images."

5. In the paragraph "Pulmonay nodules" (page 11) the nodules were 167 in the first statement, but this number becomes 134 (for Veo method) and 133 (according to FBP method) in the following lines. The problem is: how were the 167 nodules diagnosed?
The response is similar to the one provided in the previous comment: 133 nodules were depicted the first time using FBP algorithm. However, the third simultaneous reading of Veo and FBP resulted in the detection of 34 more nodules. In order to clarify the understanding of the manuscript, we added the following sentence highlighted in yellow: "Among the 167 recorded nodules, the detection rate did not differ (p = 0.98) between Veo (134/167) and standard FBP (133/167), with the same 80%

detection rate. Thus, the third simultaneous reading of Veo and FBP resulted in the detection of 34 nodules that were not detected during the first reading of FBP images."

6. Furthermore, please notice that: (line 14, page 5) this study is not "prospective" because patients were examined at one point in time;
We replaced "prospective" with "observational".

(line 12, page 6) a radiologist with two years of experience cannot be defined "experienced";
We removed "experienced" from the sentence.

(line 41, page 8) "General estimated equation models" should be "generalized estimating equation models";
We made this change.

(Table 2) the title could probably be: "Mean and standard deviation of objective noise values (in Hounsfield's units, HU) and signal to noise ratio measurements", but it is not certain;
The title of the table 2 "Objective noise, mean of the SD values and SNR measurements" has been rephrased "Objective noise and Signal to Noise Ratio measurements" in order to avoid confusing the reader.
However, we confirmed that the objective image noise is the mean of the Standard Deviation of the signal intensity for one participant (and thus, in the table, we reported mean+/-SD of the objective noise of all participants, i.e. mean+/-SD of the mean of the SD of signal intensity).

(Table 3) in the title, "accurately" should probably be "accuracy".
Apologies, "accurately" has been replaced with "accuracy", thanks.

Reviewer 2
Reviewer Name: FX Lesage
Institution and Country: occupational diseases, university hospital of Reims, France

This is a concordance study, between a ultra-low-dose algorithm known as Veo, and a gold standard method for detecting pulmonary asbestos-related conditions. The reduction of radiation delivered is a major concern. Hence, this study is really relevant.

First at all, I found that this article was written professionally.

This study is correctly conducted. The protocol is suitable in my opinion, and the statistical analysis are relevant.

However, I have to main comments:
-The authors concluded to a best used for follow-up of patient. In my opinion, such a recommendation is premature. Only two radiologists participated to this study (with a low interobservers agreement for pleural plaque detection !). Their findings argue for this conclusion, but the level of proof is too weak in my opinion.
We have reworded the recommendations to include: "these results should be confirmed on a larger sample size before the use of Veo in clinical routine practice in asbestos-related conditions, especially regarding the low prevalence of interstitial abnormalities in this study."

-Authors compared Veo and the gold standard. But it's important to discuss the other reconstruction algorithms, such as iDose, ASIR, … There is no data concerning these algorithm. Is the Veo more

relevant that the other algorithm for follow-up these patients? It's really important to discuss this point. We added this section in the discussion: "Comparison of Veo with other low-dose algorithms
To date, no studies using other algorithms to reduce radiation exposure have investigated asbestos-related conditions. Thus, because the Veo algorithm appears to reduce the more radiation delivered than other low-dose algorithm such as "iDose", "100% ASIR" or "IRIS"15-20, we chose only to compare Veo with the gold standard FBP."

Overall, this is a really interesting study, concerning a relevant topic. The manuscript is well written.