

July 22, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (ESPS Manuscript NO: 10665).

Title: entitled " Quantifying Synovial Inflammation: Emerging Imaging Techniques

Author: Deepak Tripathi, Vikas Agarwal

Name of Journal: *World Journal of Rheumatology*

ESPS Manuscript NO: 10665

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1.

- (1) **Comment 1.** Page 6, paragraph title: Please define "Ultrasonography" as US and use the abbreviation US instead of ultrasonograph (lines 1, 4, 10 of page 6 and line 8 of page 7).

Answer: Corrected (yellow highlight)

- (2) **Comment 2.** Page 6: "Synovitis at the knee in RA patients was first evaluated using GSUS at 5.0 MHz in a study evaluating Yttrium-90 synovectomy (17)

- (3) ." This sentence should be moved from its current location to the end of the first paragraph.

Answer: Corrected. Sentences change and shifted to mentioned paragraph.

- (4) **Comment 3.** Page 6: The power Doppler ultrasound is introduced in the first paragraph but the advantages of this technique are explained in the second paragraph. Substantial reorganization of this section is required.

Answer: Reorganized.

- (5) **Comment 4.** Page 7, line 11: It would be better to state, ... confirm that changes in power Doppler signals correlate quite well...".

Answer: Corrected. (Yellow highlight)

- (6) **Comment 5.** Page 7: "It is sensitive to intravenously administered contrast agents which can be used to augment very slow rates of flow". The end of the sentence is not clear.

Answer: Corrected. Sentence has been removed.

- (7) **Comment 6.** Page 9: Three of these developed joint involvement outside the PET field of

view used in the study. What do the authors meant by joint involvement? It is arthritis in joints?

Answer: Corrected. A sentence has been modified. (Yellow highlight)

- (8) **Comment 7.** Page 10, line 3: Anti-tumour necrosis factor could be deleted from the sentence. The abbreviation anti-TNF therapy is currently used in the field.

Answer: Corrected.

- (9) **Comment 8.** Page 12, line 1 and page 14, line 6: parameters

Answer: Corrected.

- (10) **Comment 9.** Page 12, line 13: This study provided proved that...

Answer: Corrected

Reviewer 2

- (1) **Comment 1:** In assessing synovial inflammation, plain radiography and CT scan have no place as they detect only bony changes.

Answer: We agree with the reviewer that these two techniques do not detect synovial inflammation but they do provide information regarding bony changes caused by synovial inflammation and cartilage destruction. In this review we exploring about the non-invasive imaging techniques for the assessment of synovial inflammation. Plain radiography (Modified Sharp score) even today is the gold standard for evaluating response to disease modifying drugs or biologicals in the clinical trials of rheumatoid arthritis. CT scan also provides information regarding bone erosions and cartilage loss. Since these techniques have been evaluated for assessing joint inflammation, hence we have discussed these two techniques in our review. Moreover, comparative information across various techniques will give readers a precise idea about the significance of modern imaging techniques.

- (2) **Comment 2:** The authors need to outline advantages and disadvantages for each imaging modality.

Answer: We added table-1 for the comparison of each imaging modality.

- (3) **Comment 3:** For instance, for the ultrasound they do not mention examiner's experience, for the PET-CT the authors do not mention the cost.

Answer: We mention the cost of the PET-CT in the table-1.

- (4) **Comment 4:** Minor points: Page 4, line 13: remove:proteoglycans, MMP blockers, CD22
Page 4, line 16: delete: the primary cause.

Answer: Corrected

Reviewer 3:

Major

- (1) **Comment1:** Ref 12 is written in French on “Transrectal ultrasonography of the prostate” Chapelon JY, Fourcade C, Cathignol D, Devonec M, Dubernard JM, Sarkissian J, Kamel G. La Nouvelle Presse Medicale [1981, 10(42):3491-3492]. This reference was quoted in page 6 as “B-mode grey-scale US (GSUS) allows synovial thickening to be detected in regions of synovium and tenosynovium”. Please clarify.

Answer: Corrected. We thank the reviewer for pointing out the typographical error. Ref 12 has been replaced with reference “Maria Alcalde, Maria Antonietta, D’Agostino, George A. W. Bruyn, Ingrid Moller, Annamaria Iagnocco, Richard J. Wakefield, Esperanza Naredo. A systematic literature review of US definitions, scoring systems and validity according to the OMERACT filter for tendon lesion in RA and other inflammatory joint diseases. Rheumatology. 2012; 51; 1246-1260.”

- (2) **Comment 2:** should include table/s that will compare the advantage or disadvantage among different imaging techniques, it will help the reader to easily understand author’s preposition.

Answer: We added table-1 for the comparison of each imaging modality.

- (3) **Comment 3:** Page 14, discussion was made with reference 61. But I could not find figure 1 in reference 61. Where does figure 1 come from? State permission on reproduction of published figure OR describe how this figure is derived.

Answer: Figure 1 refers to the figure in the present paper not from reference 61.

Minor

- (4) **Comment 4:** References: many has different format e.g reference nos (a) 1, 2, 4 in different format of author names (b) 4, 9, 20 in different format using et al (3) 21 has no pages etc. Amend the references according to journal format as instructed.

Answer: Corrected

References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Rheumatology*.

Sincerely yours,



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