Author’s response to reviews

Title: Dual energy CT findings in gout with rapid kilovoltage-switching source with gemstone scintillator detector

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Author’s response to reviews:

Janitzia Vazquez-Mellado, MD PhD (Reviewer 1):

1.1*The authors consider that DECT is an alternative method to synovial fluid microscopy. In my opinion, is just a complementary method. DECT is not available in many institutions from undeveloped countries.

Author reply: This is true, DECT is not easily available in large parts of the world.

Action taken: None.

1.2*The authors report that there are at least 5 types of DECT scanners available, maybe the studies that consider the evaluation with different DECT types and moreover comparison with ultrasonography in the same patients, could be more useful.

*The data of different DECT types and ultrasonography including all the scope of gout (early onset, long duration, severe) feasibility, costs, required time and quality of the images, related clinical data and limitations are desirable.

Author reply: We completely agree, comparative studies between different DECT techniques and maybe also involving ultrasound is needed.

Action taken: None.
Methods.

1.3*The data acquisition was retrospective, including only 55 patients attended between 2015 and 2018. Did them were all the available patients in whom DECT GSI was realized or were selected for any reason? Consecutive? how many gout patients were attended on that period?

Author reply: Thank you for this important remark. We identified all individuals who had performed DECT of the feet between 2015 and 2018 and if they had or received a diagnosis of gout in their medical records, prior or after DECT examination, they were included in the study. Furthermore, all patients fulfilled the ACR/EULAR classification criteria for gout. See answer to Reviewer 2: 2.10.

Action taken: We have added the following to the beginning of the the Methods section of the Abstract (page 1, line 19) and the Methods section of the article (page 3, line 102) and it now reads: “Patients with new or established gout who all fulfilled the ACR/EULAR classification criteria for gout [12] and had been examined with DECT GSI scanning of the feet at Sahlgrenska University Hospital, Mölndal between 2015 and 2018 as part of clinical diagnostics or disease monitoring of gout were identified. They all had at least one ICD-10 diagnosis of gout (M10) in their medical records.”

1.4*DECT images evaluation and scoring were done by an experienced radiologist and a junior radiologist, them read the images together twice. We have no data about inter-observer (maybe not possible in this case) and intra-observer evaluations?

Author reply: All images were examined by one experienced radiologist and one junior radiologist who read and scored all images together. If disagreement, images were read together until consensus was reached. This procedure was performed twice. Intraobserver agreement between the two readings was calculated and found satisfactory, $K=0.66$, 95% CI=0.61–0.71.

Action taken: None

1.5 We have not data about DECT GSI in other diseases or control patients. Artifact are the unique concern?.

Author reply: Thank you for this remark. The vast majority of studies on the DECT technique has been performed with CT scanners with two X-ray tubes (dual source) and published data in DECT GSI is really scarce. Artifacts are most certain not the only concern but the design of our study does not allow us to compare with other techniques.

Action taken: None.
1.6 The limitations of the study should be considered.

Author reply: Thank you for this remark. We have added two limitations regarding lack of control group without gout and the inability to compare results with other DECT techniques.

Action taken: We have added the following sentences to Discussion (page 8, line 235): “Fourth, the lack of a control group without gout limited the estimation of artifacts. Fifth, examination of the study subjects with other DECT techniques would have rendered important information but was not possible due to the retrospective design of the study. We are however planning a prospective study with this design.”

1.7 Minor points.

*Reference 3: authors are missing

Author reply: Thank you for this remark. We have inserted the full reference.


1.8 * Maybe is better to use gender instead of "sex"

Author reply: Thank you for this remark.

Action taken: We have replaced sex with gender throughout the manuscript.

1.9 * Table 1, include first all the clinical or biochemical data and artifacts in the last lines of the table.

Author reply: Thank you for this remark. However, we would prefer to display the tables as they are since we don’t want to mix the study population characteristics with the results from the readings (artifacts).

Action taken: None
1.10 *Figure 1 is repetitive.

Author reply: Thank you for this remark. We agree upon Figure 1 being partly repetitive but think it is good to also display the data in a figurative way.

Action taken: None

Angelo Gaffo (Reviewer 2): This is an informative study. I cannot identify a good pre-specified research hypothesis outside of just reporting on the performance of this novel DECT technology. The authors try to correlate their findings about burden of urate deposition to some clinical features collected but this - again - does not appear hypothesis driven and is quite disorganized.

2.1 Page 1, line 12: best term is "monosodium urate crystals in tissues"

Author reply: Thank you for this remark. We have inserted monosodium.

Action taken: After inserting monosodium the sentence now reads (page 1, line 11): “Dual energy CT (DECT) has repeatedly been shown to be able to detect monosodium urate crystals in tissues, hence being an alternative method to synovial fluid microscopy.”

2.2 Page 1, line 19: "incident and prevalent gout" are confusing terms in this context - these are epidemiological term, not clinical. Do the authors mean new and established cases of gout? Probably that would be a better term - more clear for the reader

Author reply: Thank you for this remark. We have changed incident and prevalent to new and established cases of gout.

Action taken: We have changed incident and prevalent to new and established cases of gout throughout the manuscript.
2.3 Page 2, line 29: is not clear what statistic is quoted here (is that a beta coefficient 0.64?)

Author reply: Thank you for this remark. The “ρ” stands for Spearman’s Rho.

Action taken: We have changed ρ to “Spearman’s Rho” at page 2 line 35 and page 6 line 183.

2.4 Page 2, line 30: "artefacts". Here and throughout the manuscript what is called "artefacts" should be "artifacts"

Author reply: Thank you for this remark.

Action taken: We have replaced artefacts with artifacts throughout the manuscript.

2.5 Page 2, line 32: "readings" should be "readers"

Author reply: Scoring of the images were done by an experienced radiologist and a junior radiologist, they read the images together twice, thus two readings.

Action taken: None

2.6 Page 3, line 59: “two technical DECT solution”, but earlier in the introduction is described as 5 types of DECT technology. This is confusing.

Author reply: Thank you for this remark. We have changed the sentence: “There are great differences between the two technical DECT solutions.”

Action taken: The new sentence reads (page 3, line 75): “There are great differences between the different technical DECT solutions.”

2.7 Page 3, line 74: "incident and prevalent" as before

Author reply: See 2.2

Action taken: See 2.2

2.8 Page 4, line 91: can the authors explain more about "beam hardening" and "noise". These terms are unfamiliar to the rheumatologist
“Furthermore, noise with single pixels or areas smaller than 1 mm are seen as well as coloring associated with beam-hardening artifacts, in particular in relation to metallic implants and in relation to bone cortex, or motion artifacts[8].”

with the following sentences to make it more understandable (page 3, line 66):

“Other recorded artifacts that might result in false coloring at the DECT image are motion artifacts, noise, and beam hardening artifacts [8]. Noise is a randomly unwanted change in pixel values which in the DECT context means that a single pixel being colored might be considered false. The signal to noise ratio (S/N) varies significantly between different technical solutions throughout the imaging process and is always of concern while assessing radiological image quality. Beam hardening is an artifact due to the phenomenon that low energy x-ray photons do not always pass the whole way through the patient and thus the x-ray beam becomes “hardened” i.e. more energetic during its passage, which in particular is seen in relation to metallic implants and sometimes in relation to bone cortex.”

2.9 Page 4, line 117: "all patients fulfilled…..classification for gout". This probably should go in the methods - that all patients enrolled had to fulfill classification criteria

Author reply: Thank you for this remark. We have moved this sentence to the Methods section.

Action taken: The first sentence of the Methods section now reads (page 4, line 102): “Patients with new or established gout who all fulfilled the ACR/EULAR classification criteria for gout [12] and had been examined with DECT GSI scanning of the feet at Sahlgrenska University Hospital, Mölndal between 2015 and 2018 as part of clinical diagnostics or disease monitoring of gout were identified.”

2.10 Page 6, lines 131-134: the statistics in the last paragraph in the results are incompletely explained (e.g; what is 0.64?)

Author reply: Thank you for this remark. We have added information on the different statistics.
Action taken: The new sentences now read (page 6, line 181): “Agreement between the two combined readings of DECT images were good (Kappa =0.66, 95% CI=0.61–0.71). The total urate deposit score was significantly higher in the presence of tophus (p=0.0005) and correlated strongly to disease duration (Spearman Rho 0.64, p &lt;0.0001) while no association or correlation was seen to age, sex, erosive disease, urate levels, BMI, diuretic use, ULT use or renal function (table 3).”

2.11 Discussion: is there any reason to believe that DECT GSI would perform better than conventional DECT technology currently available?

Author reply: Thank you for this very important question. In the current study we are not able to answer this question but the very low frequency of artefacts in DECT GIS is very promising although this may not have a crucial impact. We are however planning a prospective study comparing performance of different DECT techniques on patients with gout.

Action taken: None.

2.12 I cannot find any reference in the body of the text to the figures presented.

Author reply: Thank you for this remark.

Action taken: We have added references to figures in the following places: page 6, line 175, 179, 180