Author’s response to reviews

Title: Image quality and pathology assessment in CT Urography: When is the low-dose series sufficient?

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Author’s response to reviews:

Editor in Chief,

BMC Medical Imaging,

15th June, 2019

RE: Major revision of submission BMIM-D-19-00110

Dear Editor,

Thank you for giving us this opportunity to revise our recently submitted manuscript in BMC Medical Imaging. We would like to thank the reviewers for the constructive feedback we have received. We have implemented corrections in the manuscript including the reference list. All changes that we have made to the manuscript are documented by using “track changes” option in Microsoft Word.

When amending the manuscript, we have considered the reviewers comments and suggestions carefully and a point by point response to the reviewer after each reviewer comment is provided below. We have made efforts to reduce both the introduction and discussion sections but to comply with the reviewer comments and suggestions for improvement, new text has been added where appropriate.
Best Regards,

Bharti Kataria (on behalf of all the authors)

Reviewer reports and responses:

Ahmed Abdel Khalek Abdel Razek (Reviewer 1): -Add the unique of this study compared to other studies discuss the same issue.

Reply: We have performed a simple study to compare image quality between the three phases of the CTU protocol and pathology assessment. Although we failed to separate the individual effects of dose and contrast enhancement on image quality, the study showed that differentiation between normal and pathological examination was possible with many high to medium categorical certainty scores. The literature search found a few studies that have compared a non-enhanced abdominal CT to intravenous urography or plain abdominal radiography, but to our best knowledge, there are no studies that have compared image quality between the three phases as our study. With the amendments we have made in the manuscript we believe we have discussed this issue.

We have added the following text to introduction section:

A number of studies on diagnostic performance of non-enhanced CT compared to intravenous urography (IVU) (26) and plain abdominal radiography (27) have been performed but there are, to our knowledge, no studies that have compared the image quality and pathology assessment between phases as the present study.

And the discussion section:

As the implementation of the LDCT has been very slow, this study provides an insight into the possible applicability of this protocol in clinical practice to reduce radiation dose for certain groups of patients.

-English language correction through the manuscript

Reply: Language corrections in the whole manuscript have been made after review by a native English speaker.

-Update of references as most of references are old
Reply: The oldest references are from 2008 (Safety and efficacy of computed tomography (SECT): A broad perspective (CT Safety and Efficacy) Euratom call 2003) which recommends various methods of reducing radiation dose in younger patients with symptoms of haematuria which are still relevant today. And (CT urography: definition, indications and techniques. A guideline for clinical practice) presenting guidelines for CT Urography imaging which are also followed today. Most of the other references are from 2014 to 2019 and up to date.

Ankur Goyal (Reviewer 2): * The results don't seem to correspond to the query raised in the title

Reply: It is true that there is no unequivocal answer to the question in the title. And we have now amended the conclusion accordingly.

Amended text reads:

Visualisation of renal anatomy in the three phases were as expected with each post-contrast phase showing favourable scores compared to the native phase. However, no statistically significant differences in the assessment of pathology were found between the three phases.

Since many certainty scores were in the high and medium categories, the LDCT seems to be sufficient to differentiate between normal and pathological examinations. In order to reduce the radiation burden in adolescents and children, as well as patients with negative outcomes and those that require repetitive imaging, the LDCT could be considered a suitable alternative as a first line imaging method. However, radiologists should be aware of its limitations.

* Abstract fine

* Introduction is very long. Please reduce

Reply: We have made efforts to shorten this section. However to comply with the reviewer comments and suggestions for improvement, new text has been added where appropriate.

* There are few interspersed English language corrections which need to be done

Reply: Language corrections in the whole manuscript have been made after review by a native English speaker.

* Methodology :

  o Please write details of CT equipment (dual energy dual source 2x128 slice etc)
This is a retrospective study approved by the regional ethical board. Of the 50 patients who were referred for a clinical CTU between 2016-03-14 and 2016-11-22 and examined on a 192-slice dual source scanner in single source mode (Siemens Healthineers, Erlangen, Germany), forty patients were included in the study. The acquisition data are presented in Table 1.

Were any of the phases acquired on dual energy mode?

Reply: No.

Why not? NCCT on DE could help in characterization of stone while nephrographic phase on DE could have obviated the need of NCCT.

Reply: Thank you, this is a valuable point and this option is available on the DE scanner. However, unfortunately it was not available in this retrospective material. We have corrected the table 1 legend to read as below in order to clarify that the scans were performed in single source mode. Although the scans are performed on a dual energy scanner, our clinical CT Urography protocol is based on single source scan mode.

Amended table legend: Acquisition parameters for CT Urography for a 192-slice dual source scanner in single source mode……..

* The results are those what are anticipated and there is nothing new. Just detection of lesion is not sufficient. Its staging is also important. Thus, even though a lesion projecting into PCS may be well-seen on delayed phase as well, even then nephrographic phase is necessary for staging and assessment of local resectability.

Reply: This is absolutely true but our intention was to compare image quality in the three phases and to verify if the NCCT provided sufficient image quality when assessing anatomical image criteria and to differentiate between a normal and pathological examination. If the NCCT is found to be sufficient to rule out pathology, then avoidance of further irradiation of the patient is achieved. Whereas, if pathology is detected, then the obvious choice is to continue with a number of contrast enhanced phases depending on the indication as per protocol.

* Discussion is too long and one seems to loose track of the research question

Reply: Thank you for pointing this out – we have made efforts to shorten this section. However to comply with the reviewer comments and suggestions for improvement, new text has been added where appropriate.
Dominik Spinczyk (Reviewer 3): The article presented for review is a valuable work in the scope of a compromise in the quality of imaging pathological changes and the dose of X-ray radiation absorbed by the patient.

Reply: Thank you for the positive feedback, your summary above highlights our intentions with this study to reduce radiation dose in certain patient groups such as younger patients or patients undergoing repetitive imaging.

Because this is a retrospective study, the limitations of such a method have been described.

Ernest Ekpo, Ph.D (Reviewer 4): This study examined various dose protocols and phases on CT urography optimisation. This is an interesting piece of work and is relevant to imaging personnel.

Reply: Thank you very much for the positive feedback.

However, the paper will benefit from a revision as detailed below:

Abstract: Good, however, the conclusion will benefit from a statement highlighting When the low-dose series is sufficient"

Reply: The conclusion has been amended to highlight a possible answer to our question in the title.

Amended text now reads:

Visualisation of renal anatomy in the three phases were as expected with each post-contrast phase showing favourable scores compared to the native phase. However, no statistically significant differences in the assessment of pathology were found between the three phases.

Since many certainty scores were in the high and medium categories, the LDCT seems to be sufficient to differentiate between normal and pathological examinations. In order to reduce the radiation burden in adolescents and children, as well as patients with negative outcomes and those that require repetitive imaging, the LDCT could be considered a suitable alternative as a first line imaging method. However, radiologists should be aware of its limitations.

Keywords: fine

Introduction

There are quite a number of factual statements that are not supported by references or poorly refereed. E.g "the benefits of CT imaging outweigh the risk for many of these patients";
"Optimisation is not only about..."; "Urolithiasis is a common health..."; "The standardized care pathway (SCP) was introduced in Sweden in 2015..."

Reply: We have updated the referencing and new references have been added.

Amended text reads:

1. Optimisation is not only about patient dose and image quality but also about the diagnostic task at hand, i.e. the correct examination technique for a specific diagnostic enquiry in accordance to the ALARA (radiation dose as low as reasonably achievable) and AHARA (image quality as high as reasonably achievable) principles (2, 3).

2. Urolithiasis is a common health problem with a high recurrent rate requiring considerable radiological imaging resources for this population, many of which are younger than 50 years of age (5).

3. The standardized care pathway (SCP) led to general recommendations of the use of medical imaging in patients with macroscopic hematuria ≥ 40 years (revised to ≥ 50 years in 2018), but even younger patients with risk factors are investigated (6).

P6 line 18: "Presented" Grammatical error, please use the correct tense.

Reply: Language corrections in the whole manuscript have been made after review by a native English speaker.

Methods of dose optimisation have been introduced but there is no clear rationale for this work. Please add a statement highlighting the rationale.

Reply: The first discussion paragraph has been moved to the introduction section to highlight the rationale for this work.

Amended text:

Both the Bonn call for action and the triple AAA campaign were introduced to strengthen the need for stringent measures in radiation protection for safe and appropriate use of ionizing radiation in medical imaging (17-19). Published literature on renal stone evaluation have validated the trend towards use of low-dose CT (LDCT) due to the high contrast between urinary stones and the surrounding soft tissue (15, 20) as well as in investigation of acute abdomen (16). However, implementation of the LDCT protocol in the clinical setting has been very slow partly due to the low quality of the images and lack of confidence in interpreting reduced-dose images (21). But with practice and growing experience it is possible to increase diagnostic confidence and acceptance of lower quality images (22). The diagnostic performance of non-enhanced CT compared to intravenous urography (IVU) (23) and plain film radiography (24) has been
evaluated but there are, to our knowledge, no studies that have compared the image quality and pathology assessment between phases as the present study.

Methods: The methods are appropriate but need to be better described

- Provide detailed explanation of how SSDE was calculated is needed to allow for reproducibility of the study

Reply: This information is now provided in the material & methods section. And to clarify how we calculated the SSDE we have added a reference and revised the sentence to read:

…… Size Specific Dose Estimate (SSDE) was calculated based on the AP and LAT dimensions of each patient at the level of the kidneys using the center slice approach as described in Boos at al. (25, 26).

The European guideline details the criteria to be used for image quality assessment, and methods such as the ICS, VGA, VGCA etc were developed based on these guidelines. The authors state that they used VGR, which I guess is the VGCA as shown in Table 2B.

Reply: We have used VGR and not VGCA and we apologize for not clearly stating this in the methods section, but this has now been amended.

Amended text: Statistical analysis within the Visual Grading Regression (VGR) (27) framework was performed with the software Stata 13.1 (Stata Corporation LP, College Station, TX, USA) using the multi-level mixed-effects ordered logistic regression (meologit) command for image quality scores (28).

It would be good to state exactly which four anatomical structures were used for the grading and the number of grading criteria used. I see that this is included in Table 2a, but it would be good to list the structures within the text to enhance understanding.

Reply: As requested the text has been amended to include the description of criteria as well as scoring options:

During the reading sessions the readers were asked to grade four anatomical structures (renal parenchyma, renal pelvis and calyces, proximal ureters and renal arteries), obtained from European guidelines for quality criteria on a five-point Likert scale with numerical scores from one to five allocated to response alternatives: criterion was fulfilled, criterion was probably fulfilled, indecisive, criterion was probably not fulfilled and criterion was not fulfilled (Table 2a). The readers were also asked to assess the presence of pathology in three categories; renal, abdominal and incidental findings. These were also graded on a five-point Likert scale based on
scores 1 to 5 with response alternatives: examination was considered to be normal, probably normal, indecisive, probably pathological and pathological (Table 2b).

The authors also need to describe how the calculation was performed to determine the VGCA score. Perhaps provide the formula and describe whether or not VGCA points were generated, if so how they were used to generate a VGCA curve.

Reply: As explained above VGCA was not performed. VGR is described in references (27) and (28).

Results

Assessment of pathology: "For all three pathology categories, the number of inconclusive scores were very low suggesting that normality and pathology could be assessed in all three phases with marginal differences in scores", where are the results to show this?

Reply: The number of scores are shown as annotations in the histograms above each bar/phase (Figure 3) for all criteria assessed as well as in tables 5 and 6 (additional files 1 & 2) at the after the references showing the scores in table form.

Amended text in figure legend to clarify this:

Figure 2 Distribution of number of scores (annotation above each bar) allocated to each criterion assessed by readers in a Computed Tomography Urography (CTU) protocol. All differences between phases are significant for Criterion 1 to 4. All differences between phases were non-significant for Criterion C5 to C7 (Additional file 1: Table 5)

Figure 3 Distribution of number of certainty scores (annotation above each bar) allocated to each criterion assessed by readers in a Computed Tomography Urography (CTU) protocol. The scores 1 and 5 were grouped for high certainty, scores 2 and 4 for medium certainty and a score of 3 for low certainty. Significance values are presented in supplementary data (Additional file 2: Table 6).

Figures 1-3 are fine, but these are too many and make understanding difficult. I would suggest generating a VGCA curve for each phase/dose level. This will provide a simple and easy to understand interpretation of the results

Reply: Our reason for choosing VGR as the statistical method has been added to the discussion section. The histograms are self-explanatory but to clarify further we have amended the figure legend to include description of the number of scores as annotation above each bar as well as tables 5 & 6 as additional files 1 & 2.
Amended text:

Discussion section: The statistical method we have used, VGR, allowed us to analyze the three phases in the same analysis, with subsequent pair-wise comparisons. VGR also has the ability to let the researcher estimate the potential dose reduction resulting from changes in the imaging protocol. However, the design of this retrospective study does not permit such an analysis.

Changes in Figure Legend for clarification: Please see response to previous question.

Discussion: The first paragraph would fit into the introductory section as a rationale for this work rather than where it currently is.

Reply: Thank you for this constructive feedback, we have revised the introductory section accordingly.

The findings of the study are summarised and compared to the literature, however there is no clear discussion regarding the implications of these findings and their relevance to policy and practice. There is also a need to discuss about "When the low-dose series is sufficient" and providing a justification for this.

Reply: We discuss the relevance in practice where one of our sites has adopted the LDCT protocol in imaging av acute abdominal patients and with practice widened the panorama of diagnoses that can be answered.

We discuss how the LDCT is useful in differential diagnoses and a valuable tool that can be used to decrease the radiation burden in adolescents and children as well patients exposed to repetitive imaging.

Some additional text and changes made provide some justification for this.

The conclusion reads like a repetition of the summary of results. I would like to see a concise conclusion focusing on the meaning of these findings and contribution to knowledge rather than restating the results.

Reply: We have revised the conclusion to read as follows:

Amended text now reads:

Conclusion:
Visualisation of renal anatomy in the three phases was as expected with each post-contrast phase showing favourable scores compared to the native phase. However, no statistically significant differences in the assessment of pathology were found between the three phases.

Since many certainty scores were in the high and medium categories, the LDCT seems to be sufficient to differentiate between normal and pathological examinations. In order to reduce the radiation burden in adolescents and children, as well as patients with negative outcomes and those that require repetitive imaging, the LDCT could be considered a suitable alternative as a first line imaging method. However, radiologists should be aware of its limitations.

References: See comment in the introduction. There are many factual statements that either have no references or poorly refereed.

Reply: Amended as suggested. See the comment above in the introduction

Tables: Fine

Reply: Thank you

Figures: They are too many. Use VCGA curves instead.

Reply: As explained above VGCA was not performed.

References in the response to reviewers:


25. Size specific dose estimates (SSDE) in paediatric and adult body CT examinations. In: The report of the AAPM task group no 204. AAPM; 2011.

