

Peer Review File

Article information: <http://dx.doi.org/10.21037/shc-21-5>.

**Review A:**

The work “Diameter versus volumetry: a narrative review on current recommendations to measure and monitor screening detected lung nodules” is a well-written, useful review on currently ‘hot’ and important topic with the aim “to report strengths and weaknesses of the two PN sizing approaches in LCS, and to discuss possible implications of PN size over- and underestimation”. In my consideration, it has been achieved.

I recommend this article for publication.

Comment 1: I would appreciate a little bit more information about non-solid nodules. Currently, nodule size assessment (diameter) is mainly used in the US, and Europe tends to use volumetry. Volumetry and currently used software are fairly well suited to measuring solid nodules but are less accurate in assessing non-solid nodules. LungRads criteria were updated in 2019 and the BTS on which European screening is based was not updated. The results of the latest research (NELSON) indicate the high efficiency of LCS based on volumetry.

Reply 1: Thank you for your comment. We provided further information on non-solid nodules. Please see paragraph “Focus on non-solid nodules”.

Comment 2: Add the dots: et al.

Reply 2: We added the dots as requested.

Comment 3: Specify/correct the data in the tables.

Reply 3: We specified the information reported within the tables.

Comment 4: Make minor corrections in the text as depicted in the table below.

Reply 4: We edited the text according to the suggestions.

Comment 5: Table 1 is clear, except few informations concerning the screening method where for LUSI, ITALUNG and Depiscan – ‘Annual screen’ is not specific (for how many years? – as for DLCST or single screen – as for UKLS); Smoking history for the randomization column: the number of pack years is not clear for NELSON, DLCST, MILD, LUSI, ITALUNG, DANTE, Depiscan.

Reply 5: Thank you for your comment. We edited Table 1 providing detailed information on both screening intervals and eligibility criteria.

Comment 6: Please see the attachment for the Narrative Review checklist.

Reply 6: We provided an updated version of the narrative review checklist.

### **Review B:**

Re: Diameter v volumetry. The authors attempt review current recommendations to measure monitor screening studies. The following points are noted:

Comment 7: Incidentally, the term “narrative” applied to review is idiosyncratic pertaining to no know standard description or methodology and should be deleted.

The term “Brief” applied to sections should also be deleted.

Reply 7: Thank you for your comment. The term “narrative” was added as per request by the Editorial Office. We removed the term “Brief” as suggested.

Comment 8: Abstract/Introduction: The stated purpose of this report is ostensibly in an unbiased assessment of the “strengths and weaknesses” of two approaches to measuring nodules by performing a review of established databases – in fact from the start - even before objectively reviewing the available literature - conclude that volumetrics is clearly superior. As stated in the Abstract – “Although either method shows individual strengths... nodule volumetry is currently deemed more accurate and reproducible.” Unfortunately, the case for this is hardly documented by this review. What is missing is a systematic assessment of the advantages and disadvantages of each method separately and then concluding with a final discussion emphasizing the applicability of each approach when applied given practices - for ex. to large university settings v small community practices.

Reply 8: Thank you for your comment. We modified the abstract removing the sentence “Although either method shows individual strengths and weaknesses, nodule volumetry is currently deemed more accurate and reproducible. Several LCS trials demonstrated that such approach is indeed associated with lower inter- and intra-observer variability as compared with manual bidimensional measurement.”

Comment 9: Material and Methods: In support of the above assessment the authors really only cite a small number of references truly applicable to a comparison of the two methods (see for good ex. Han et al #'s 19 and 43). While a number of references directly apply to one or the other approaches alone, a clear majority of these are solely concerned with volumetric assessment – and these still only measure less than 15 references total.

The remainder of the author’s references fall into several categories – only tangentially concerned with direct comparisons of the two methods. These include:

references to a number of completed imaging trials from various countries (few if any with direct methodologic comparisons); discussion of current guidelines for assessing nodules – including references to non-screening guidelines (see Fleischner guidelines # 46); and an entire discussion on overdiagnosis and use of advanced computer methods for identifying and measuring nodules including deep learning techniques – the latter several in particular not germane to the stated intent of this review.

Especially surprising is the authors inclusion of an entire section devoted to the positive results of screening (Brief focus on LCS trials) – this is entirely unnecessary! In this regard, the authors failure to extensively reference the LungRADS guidelines is especially difficult to understand when discussing current guidelines– referenced only once in this paper – given the near universal use of this in the US.

Reply 9: Thank you for your comment. We added few more references specifically referred to the comparison of the two approaches (e.g., #31, #34, #41) and removed inappropriate citations. We also removed the paragraph on LCS trials and extensively referred to the LungRADS guidelines throughout the manuscript.

Comment 10: Several statements by the authors are actually misstatements: for example – in the Introduction they state that “PN management mostly relies on size” when in fact nodule density is every bit as important in reference to current guidelines in particular. In fact, the author’s treatment of major differences in nodule measurements as effected by type of nodule is only inconsistently mentioned throughout most of this report. It would be greatly advantageous if this aspect of their topic was directly addressed from the start best in separate sections. For example – it is only late in the author’s presentation that the problems associated with measuring the solid components of part solid nodules is broached – and then leading to a discussion of advanced AI techniques without extensively discussing this in the context of routine volumetric assessment.

For example, the authors similar authors assertion that “...inter an intra-observer variability is expected to range between 1.5 and 2 mm ... it increases to almost 3 mm by using a single diameter” uses as a citation Silva #14 an article primarily concerned with structured reporting – hardly adequate validation.

The authors also play down the problems associated with differences in manufacturer’s differences in semi-automated volumetrics – only towards the end of this report acknowledging the problems associated with differences in reproducible results especially between different volumetric measurements made using different volumetric programs.

Reply 10: Thank you for your comment. We replaced the sentence “PN management mostly relies on size” with “PN management mostly relies on density and size” in both the Abstract and Introduction sections. We also moved up the paragraph entitled

“Focus on subsolid nodules” and expanded on issues related to subsolid nodules measurement. Moreover, we replaced the citation #14 with references #39 and #40.

Comment 11: Inappropriate citations: Another major problem with this review is that the authors disconcertingly often cite literature inappropriate to the context. There are too many instances to cite all of these. See for example:

A. Introduction: “In the last two decades PNs being detected in up to 66% - with one citation primarily concerned with structured reported (#14 Silva)

B. In the same paragraphs as above – citing the Fleischner guidelines as evidence of PN management mostly relying on size when these same guidelines recommend either size or volume.

C. In Diameter v Vol in LCS trials – the authors cite Oudkerk #40 a European position paper in support of the assertion that volumetrics offer better precision and reproducibility compared to manual measurements.

Similar concerns are noted throughout the manuscript. The authors are request to reassess their specific citations to insure that they truly support the author’s assertions

Reply 11: Thank you for your comment. As per previous replies (9 and 10), we removed the inappropriate citations.