Editorial

2D or 3D measurements of pulmonary nodules: preliminary answers and more open questions

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Accurate size measurements of pulmonary nodules on CT are a prerequisite for accurate nodule management, given that all current management guidelines are based on nodule size (1-4). Nodule size is most commonly measured manually using electronical calipers, with the long- and perpendicular short-axis being measured on two-dimensional images (5). As a management criterion alternative to size, three-dimensional nodule volume has been discussed in the literature (6) and has also received mention in recent management guidelines for incidental nodules (1,3).

In this evolving context, we read with interest the recent research letter of Heuvelmans *et al*. (7). In this letter, the authors describe discrepancies between two-dimensional size- and three-dimensional volume measurements of pulmonary nodules. The pulmonary nodules in this study were all selected from the Dutch-Belgian Randomised Lung Cancer Screening Trial (Dutch acronym: NELSON). First, the authors determined three-dimensional nodule volume using a computer-based approach. Second, based on the computer measurements, the authors determined the maximum size of long- and short-axes and re-calculated nodule volume based on those two-dimensional axes, assuming a spherical nodule shape. Third, the two sets of volume measurements were compared. The authors found that volume measurements based on two-dimensional axes overestimated nodule volume by 47% to 85%, as referenced to the three-dimensional computer-based approach. The authors conclude that three-dimensional methods should be given preference over the traditional two-dimensional approach for lung nodule dimension assessment. Although we generally agree that three-dimensional volumetry will likely become the standard method for assessing pulmonary nodules in the future, we would like to add some cautious comments to the findings reported in the current letter, and on its subsequent conclusions.

In the current study, the authors define "intranodular diameter variation" as the difference between the maximal and the minimal diameter of a given nodule. These maximal and minimal diameters were not manually measured but automatically calculated by the software platform. The authors assume that intranodular diameter variation likely represents maximal variation of independent manual measurements. They found a 2.8 mm median intranodular diameter variation, which exceeds the commonly accepted threshold for interobserver variability when nodules are measured manually (8). The authors conclude that diameter-based measurements may result in inaccurate nodule classification. However, the assumption on which this conclusion is based, namely the equalization of intranodular diameter variation and interobserver variability of manual measurements, is equivocal and relies on several discussable points. First, it would require that automated measurements correctly reflect manual measurements. However, the authors provide no data to support this. Second, the assumption implies a comparison between non-independent measurements. Yet, in this study, maximal and minimal diameters were calculated at the same time

by the same volumetry software. Third, the authors conclude that manual measurements are likely causing an inaccurate nodule classification because of their inherent interobserver variability. This statement would require that we can equalize the difference between maximal and minimal diameter ("intranodular diameter variation", as defined by the authors) to the difference between several average diameters (which would reflect real interobserver variability). Indeed, as recently determined, the average diameter is the only required parameter when assessing a nodule smaller or equal to 10 mm (5).

The authors report that nodule volumes calculated from two-dimensional measurements lead to a significant overestimation, as compared to three-dimensional measurements. From a statistical perspective, these two approaches are not independent, as they are based on the same segmentation process. This might decrease inherent measurement variability, but does not exclude systematic measurement errors. This point is not addressed because no reference standard is provided and we, therefore, do not know how accurate the three-dimensional measurements truly are. Interestingly, in a phantom study with small nodules using the same software platform than the one used in the current paper, Xie *et al*. (9) showed that automated three-dimensional measurements underestimate actual nodule size. Overall, the current findings might simply reflect the fact that pulmonary nodules are not perfectly spherical, and that the assumption of perfect sphericity of pulmonary nodules should be generally questioned, as acknowledged by the authors. However, the findings also show that calculating nodule volume with long- and short-axis diameters and based on the assumption of perfect sphericity has the potential to artificially augment nodule volume and, therefore, reflects a "worst case scenario" that will, as a consequence, result in the most cautious possible management approach. This most cautious possible management approach might be of clinical value in patients at a particularly high risk for lung cancer.

The authors appropriately emphasize the well-published issue of intra- and inter-reader variability between radiologists when manually measuring lung nodules (8,10-12). However, the authors do not equally emphasize the variability issues of computer-based lung nodule measurements. Variability can indeed arise from the radiologists' interaction with a given nodule, as some nodule boundaries need to be manually re-drawn. This can be the case if the nodule is adjacent to a vascular or bronchial structure, or adjacent to parenchymal abnormalities (6). In the current study, the authors do not report in how many nodules manual re-drawing was required. Furthermore, it is known that technical CT scanner parameter parameters during acquisition and reconstruction of images can artificially cause substantial volume differences, beyond expected interscan variability (13,14). This is a relevant limitation to the generalizability of volume-computing software. Then, there is variability caused by the volumetry software platforms themselves. Several studies have shown that different software platforms and even different segmentation algorithms within the same software platform cannot be used interchangeably (15,16). This causes another relevant problem, as many patients to undergo consecutive examinations on different CT scanner models operating with constantly upgraded software packages, and, potentially, in different geographical locations. Finally, one should keep in mind that automatic or semi-automatic volume measurements perform poorly in subpleural and subsolid nodules, which currently excludes a substantial number of nodules from the assessment with this technology (6).

Although the authors meticulously document variability between a two- and a three-dimensional measurement approach, the impact of this variability on clinical management and patient outcome is not investigated. Numerous studies have previously documented variability between measurement approaches and modalities for pulmonary nodules and a certain degree of variability inherent to these approaches, both manual and automated, is well known (5). It would have been interesting if the authors had simulated "management scenarios" based on the two measurement approaches and compared the respective results. Indeed, the important question might not so much be whether one measurement method is more "accurate" than another, but rather whether one measurement method can better predict prognosis and outcome than another. Of note, this method might not necessarily be the most "accurate" one in terms of size or volume measurements. The time for such management- and outcome-centered studies will have come once the final data of the NELSON trial are published and can be compared to the data of previous large screening trials such as the National Lung Screening Trial. This might then tell us which nodule size or volume parameters are the most clinically relevant, rather than the most diagnostically accurate and, thereby, emphasize the general paradigm shift towards outcome-centered imaging research.

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Footnote

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References

1. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for management of incidental pulmonary nodules detected on CT images: From the Fleischner Society 2017. Radiology 2017;284:228-43.
2. Gould MK, Donington J, Lynch WR, et al. Evaluation of individuals with pulmonary nodules: When is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. Chest 2013;143:e93S-120S.
3. Callister ME, Baldwin DR, Akram AR, et al. British thoracic society guidelines for the investigation and management of pulmonary nodules. Thorax 2015;70 Suppl 2:ii1-54.
4. American College of Radiology [Internet]. Lung CT Screening Reporting & Data System (Lung-RADS) [cited 2017 Dec 20]. Available online: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads
5. Bankier AA, MacMahon H, Goo JM, et al. Recommendations for measuring pulmonary nodules at CT: A statement from the Fleischner Society. Radiology 2017;285:584-600.
6. Devaraj A, van Ginneken B, Nair A, et al. Use of volumetry for lung nodule management: Theory and practice. Radiology 2017;284:630-44.
7. Heuvelmans MA, Walter JE, Vliegenthart R, et al. Disagreement of diameter and volume measurements for pulmonary nodule size estimation in CT lung cancer screening. Thorax 2017. [Epub ahead of print].
8. Revel MP, Bissery A, Bienvenu M, et al. Are two-dimensional CT measurements of small noncalcified pulmonary nodules reliable? Radiology 2004;231:453-8.
9. Xie X, Willemink MJ, de Jong PA, et al. Small irregular pulmonary nodules in low-dose CT: Observer detection sensitivity and volumetry accuracy. AJR Am J Roentgenol 2014;202:W202-9.
10. Heidinger BH, Anderson KR, Nemec U, et al. Lung adenocarcinoma manifesting as pure ground-glass nodules: Correlating CT size, volume, density, and roundness with histopathologic invasion and size. J Thorac Oncol 2017;12:1288-98.
11. Heidinger BH, Anderson KR, Moriarty EM, et al. Size measurement and T-staging of lung adenocarcinomas manifesting as solid nodules </=30 mm on CT: Radiology-pathology correlation. Acad Radiol 2017;24:851-9.
12. Ridge CA, Huang J, Cardoza S, et al. Comparison of multiplanar reformatted CT lung tumor measurements to axial tumor measurement alone: Impact on maximal tumor dimension and T stage. AJR Am J Roentgenol 2013;201:959-63.
13. Ravenel JG, Leue WM, Nietert PJ, et al. Pulmonary nodule volume: Effects of reconstruction parameters on automated measurements--a phantom study. Radiology 2008;247:400-8.
14. Honda O, Sumikawa H, Johkoh T, et al. Computer-assisted lung nodule volumetry from multi-detector row CT: Influence of image reconstruction parameters. Eur J Radiol 2007;62:106-13.
15. Zhao YR, van Ooijen PM, Dorrius MD, et al. Comparison of three software systems for semi-automatic volumetry of pulmonary nodules on baseline and follow-up CT examinations. Acta Radiol 2014;55:691-8.
16. Ashraf H, de Hoop B, Shaker SB, et al. Lung nodule volumetry: Segmentation algorithms within the same software package cannot be used interchangeably. Eur Radiol 2010;20:1878-85.

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