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Consistency evaluation of lung nodules measurements among different automated measurement systems in the field of computed tomography

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Оценка согласованности различных систем автоматического измерения патологических образований солидного типа в легочной ткани при компьютерной томографии

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Резюме

Introduction: The size of nodules in the lungs is an important criterion in deciding what further tactics to use. There are several measurement approaches: determination of maximum size, average size, nodule volume and volume doubling time (VDT). Each of these requires validity, reproducibility and accuracy, which are not always achieved in routine practice. **Aim:** To evaluate the performance of different programs in the automated measurement of nodules and solid masses in lung tissue and the reproducibility of the results. **Materials and methods.** To conduct a comparative evaluation of automated nodule size estimation, we used four software products: Program A — Vitrea (manufactured by Canon, version 6.3.2047.65), Program B — Vitrea (manufactured by Canon, version 7.14.2.227), Program C — AW Server (manufactured by GE, version 3.2 Ext.4.0), and Program D — Hiveomics Platform (Hiveomics Ltd., version 1.2). We selected 62 nodules and solid masses for statistical processing. **Results.** During the study, all software products had technological defects (unable to process the study technical/other reasons) that prevented the measurement of all nodules and masses accepted for participation. Statistically significant differences were found when comparing the mean effective diameters obtained from the measurements. These differences were observed between automatic nodule measurement systems from different manufacturers and between older generation software products and the AI algorithm. There were no statistically significant differences observed in the measurements of mean effective diameters between the AI-based automatic nodules analysis system and the results obtained after physician delineation correction on earlier versions of automatic volumetry systems. **Conclusion.** The study of average volume values in all groups showed no statistically significant differences, confirming the universality of the use of this parameter in clinical practice.

Keywords: pulmonary nodules; volume; effective diameter; reproducibility of measurements, computed tomography

Резюме

Обоснование. Размер очагов в легких — важный критерий, учитывая который планируется дальнейшая тактика. Существуют разные подходы к измерению: определение наибольшего размера, среднего размера, объема очага, а также времени удвоения объема (VDT). Для каждого из них необходимы достоверность, воспроизводимость и точность, что далеко не всегда реализуется в рутинной практике. **Цель исследования:** оценить возможности различных программ при автоматическом измерении образований солидного типа в легочной ткани и воспроизводимость результатов. **Материалы и методы.** Для сравнительной оценки автоматической оценки размеров очага нами использовались 4 программных продукта: Vitrea (производства Canon, версия 6.3.2047.65) — программа A, Vitrea (производства Canon, версия 7.14.2.227) — программа B, AW Server (производство GE, версия 3.2 Ext.4.0) — программа C, Hiveomics Platform (Hiveomics Ltd., version 1.2) — программа D. Для статистической обработки было отобрано 62 очага и образования солидного типа. **Результаты.** В ходе исследования у всех программных продуктов отмечался тот или иной технологический брак (невозможность обработать по тем или иным причинам исследования), не позволивший измерить все очаги и образования, принятые к участию в исследовании. Были получены статистически значимые различия при сравнении средних эффективных диаметров, полученных в результате измерения: между системами автоматического измерения очагов от разных производителей; между программными продуктами более старого поколения и алгоритмом ИИ. Не отмечено статистически значимых различий между измерениями средних эффективных диаметров системой автоматического анализа очагов на основе ИИ в сравнении с результатами, полученными после коррекции оконтуривания врачом на более ранних версиях автоматических систем волюметрии. **Заключение.** В результате исследования средних значений объемов во всех группах не было выявлено статистически значимых различий, что подтверждает универсальность использования этого параметра в клинической практике.

Ключевые слова: очаг в легком, объем, эффективный диаметр, воспроизводимость измерений; компьютерная томография

Introduction

Lung cancer ranks among the leading causes of cancer-related mortality worldwide [1]. This pathology can also serve as the substrate for pulmonary nodules visualized on computed tomography (CT). Therefore, key questions arise regarding the management of such patients and the necessity of follow-up imaging, which are determined by evaluating various parameters and characteristics of pulmonary nodules [2]. The size of the nodules is an important criterion used to plan further management strategies. Different approaches to measurement exist, including determination of the maximum diameter, mean diameter, lesion volume, and volume doubling time (VDT) [3]. Each of these requires reliability, reproducibility, and accuracy, which are not always achievable in routine practice, since measurements are often performed manually. Such an assessment is rather subjective, as the obtained result depends on numerous factors (the selected CT slice and series, viewing mode, contrast phase, measurement plane etc.). As a result, the described measurements are characterized by high variability and low interobserver agreement, which has been demonstrated in several studies [4, 5].

In a study conducted by M.M. Suchilova et al., the results of measuring 293 pulmonary nodules by three independent observers were analyzed. When using linear measurements, Fleiss' kappa was only 0.027 (indicating slight agreement), which is extremely poor. The result was substantially better when measuring volume, where Fleiss' kappa reached 0.672 (substantial agreement) [4].

Thus, one of the potential solutions to this problem may be the implementation of automatic measurement systems for pulmonary nodules, which can improve the accuracy of determining one of the most important parameters described in current international guidelines. Their use is particularly relevant for the accurate determination of the T criterion in tumor staging according to the TNM classification [6]. For the management of patients with incidentally detected nodules, according to the recommendations of the Fleischner Society (updated in 2017), the Lung-RADS system for low-dose chest CT screening, as well as the British Thoracic Society (BTS) guidelines covering both patient categories, one of the key criteria is the nodule size, which must be determined as precisely as possible. Accurate measurement enables correct assessment of malignancy risk, appropriate follow-up intervals, and the need for additional diagnostic procedures [7–9].

The BTS guidelines also consider nodule volume and VDT, for which automated assessment is equally relevant [9]. Moreover, when evaluating tumor response to therapy according to RECIST 1.1 criteria, precise measurement of target lesion diameters is critical, as their sum serves as the baseline for subsequent changes and for determining treatment response dynamics — classifying the disease course as improving, stable, or progressive [10].

Objective of the study: to evaluate the capabilities of various software tools for automatic measurement of solid-type pulmonary nodules and lesions, and to assess the reproducibility of the results.

Materials and Methods

This study utilized a radiological image database developed at the Saint Petersburg Research Institute of Phthisiopulmonology, Ministry of Health of the Russian Federation. The database comprises 150 radiological studies of patients with various histologically verified peripheral pulmonary nodules (Database registration certificate: RU-2019621712).

For the current analysis, solid-type nodules (N=81) were selected. Only chest CT scans with solid pulmonary nodules without CT signs of cavitation were included. The term cavitation was defined as the presence of any air-containing inclusions (air density) within the structure of a nodule. Such cases were excluded because there are no universally accepted criteria in the literature distinguishing between a mass and a cavity based on the volume of gas-containing inclusions.

All CT studies were performed with a slice thickness of 1–1.25 mm and reconstructed using a standard algorithm. Only non-contrast-enhanced CT series were included in the analysis. All examinations were anonymized prior to inclusion in the database. The studies were performed on CT scanners from various manufacturers.

The distribution of pulmonary nodules is presented in Table 1.

The initial assessment of nodules size was performed by a radiologist specializing in thoracic imaging with over 10 years of professional experience. Measurements were conducted using an electronic caliper on a Vitrea workstation. Only the maximum axial diameter was used for evaluation. These measurements were carried out solely for the preliminary assessment of the testing database and were not used for direct comparison with measurements obtained from automated software tools.

According to the maximum axial dimension, the nodules were evenly distributed between those measuring ≤2.0 cm and >2.0 cm. Only 4% nodules included in the study were smaller than 1.0 cm in axial diameter. This distribution is explained by the inclusion of only verified lesions in the study, as most lesions smaller than 1.0 cm are typically managed by follow-up rather than surgery.

Table 1

Characteristics of nodules included in the study according to the maximum axial dimension measured by a radiologist

Size of nodules	Number of nodules	%
Less than 1 cm	3	4
1–2 cm	38	46
More than 2 cm	40	50

All pathological findings included in the study were verified (according to the database description) in accordance with established diagnostic standards for each nosological category. The verification criteria were as follows:

- For malignant and benign tumors — histopathological examination of surgically resected specimens;
- For tuberculosis — a combination of histological evidence consistent with tuberculosis and confirmation of Mycobacterium tuberculosis by culture or PCR-based DNA detection;
- For non-specific inflammatory processes manifesting as round lesions — confirmation by complete radiological resolution following therapy;
- For arteriovenous malformations — confirmation by angiographic studies.

By nosological category, the composition of the test database was as follows:

- 49% (n=40) — malignant neoplasms;
- 24% (n=19) — localized forms of tuberculosis;
- 27% (n=22) — benign lesions (localized non-specific inflammatory processes, hamartomas, and arteriovenous malformations).

Four software products were used for comparative analysis of automated lesion measurements:

- Program A: *Vitrea* (Canon, version 6.3.2047.65);
- Program B: *Vitrea* (Canon, version 7.14.2.227);
- Program C: *AW Server* (GE, version 3.2 Ext.4.0);
- Program D: Hiveomics Platform (Hiveomics Ltd., version 1.2).

Inclusion criteria for software selection:

1. Availability of a registration certificate as a medical device.

2. Accessibility of the software product for testing.

3. The presence of functionality for detection and analysis of round pulmonary nodules described in the product documentation.

All automated measurement results were independently reviewed by two radiologists specializing in thoracic imaging to verify the accuracy of lesion contouring. In cases of disagreement, the final decision was made by an expert with over 20 years of thoracic radiology experience.

Program A (Vitrea, Canon, version 6.3.2047.65) allows for automatic determination of nodules volume in the lungs. In addition to volume, it provides the effective diameter, as well as maximum, minimum, and mean lesion density values. Measurement is performed semi-automatically: after the radiologist selects the nodule, the software automatically delineates the boundaries for volumetric analysis. However, this delineation is not always accurate. For example, when the nodule is subpleural or in close

contact with a vessel, the software may fail to distinguish between them and include adjacent structures in the calculated volume.

A manual correction tool allows the user to adjust the nodule boundaries, ensuring more accurate measurements — a notable advantage of this software.

As part of this study, we performed an additional comparison of the diameter and volume measurements obtained before and after manual correction by the radiologist, referring to these two stages as A1 and A2, respectively.

Additionally, we conducted an analysis of nodules using another version of the Vitrea workstation (version 7.14.2.227), featuring a similar but more recent software package for pulmonary nodules analysis (Program B). For this version, only the results of the automatic analysis were included in the evaluation, without subsequent manual correction.

Program C (AW Server, manufactured by GE, version 3.2 Ext.4.0) provides three maximum diameters measured in the axial, sagittal, and coronal planes, as well as the nodule volume in cubic millimeters. For this program, we also included in the analysis only the automatic measurements, without performing any manual adjustments.

Program D — the Hiveomics Platform — is a web-based application for the automatic measurement and assessment of findings on chest computed tomography using computer vision technology. In this study, version 1.2 was used, which includes tools for automatic detection, segmentation, and evaluation of identified pulmonary nodules. The processed results are visualized as additional DICOM series generated by the Hiveomics algorithm.

The additional DICOM series enables verification of the accuracy of detection and segmentation of nodules identified by the algorithm, by displaying both the processed axial CT images in the lung window and the algorithm's visual output, which consists of several components:

- The upper section of the series contains several general quantitative parameters for the entire study;
- The central section displays the DICOM series processed by the algorithm;
- The lower section includes a scroll bar showing the current slice position, with red-colored markers indicating the detected nodules and lesions.

An additional pop-up window provides detailed information for each nodule identified by the algorithm, including: the nodule ID number, the nodule dimensions, the nodule volume.

Results

Only solid lesions that were successfully processed by all programs were included in the statistical analyses (N = 62). Pairwise comparisons of diameters and volumes were conducted across Program A (A1 and A2), Program B, Program C, and Program D.

Comparison of mean nodules sizes across the groups was performed using the effective diameter as the primary metric. In Program A, the effective diameter is calculated automatically, in Programs B and D, the software automatically measures the maximum axial diameter, the maximum perpendicular diameter (short-axis diameter), and the mean diameter, in Program C, the software calculates the maximum axial, maximum perpendicular, and maximum vertical diameters.

The effective diameter was calculated using the formula proposed by C. Anam et al. [11].

$$Deff = \sqrt{D_{max}} \qquad axial \times Dshort\ axis$$

This formula represents one of several possible methods for determining the effective diameter. Since the technical documentation for Program A specifies the use of this particular formula, we applied it to Programs B and D as well, in order to improve the comparability of results across software platforms.

The comparison of nodules volumes was performed based on the mean volume value (in mm^3). Each software program employs its own segmentation algorithm, characterized by individual threshold settings, smoothing methods, and small-object filtering. Therefore, even when axial diameters are similar, the resulting calculated volume of the nodules may differ.

All computations were performed using the Python programming language, with statistical analyses carried out using the SciPy v1.11.4 and Pingouin v0.5.3 libraries.

The main characteristics of the nodules are presented in Table 3. The standard deviation and confidence intervals of the variables were determined using the bootstrap method.

The bootstrap is a statistical technique in which multiple resampled subsets are drawn from the available dataset, and statistical calculations are repeated on each subset to estimate variability and confidence intervals.

Table 2

Results of automatic analysis of studies with pulmonary nodules performed using different software products

Nodules	Program A	Program B	Program C	Program D
Number of nodules taken for study	81			
Number of processed nodules	80 (98%)	81 (100%)	70 (86%)	74 (91%)
Incorrectly contoured nodules from among those processed	13 (16%)	13 (16%)	5 (7%)	11(14%)

Table 3

Comparison of the results of measurements of effective diameters and volumes when measured by different programs

Variable	Program A1	Program A2	Program B	Program C	Program D
Effective diameter, mm, average [std; 95% CI]	17.0 [0.2; 16.7 : 17.4]	17.54 [0.25; 17 : 18]	18.3 [0.23; 17.8 : 18.7]	23.3 [0.32; 22.6 : 23.9]	20.6 [0.3; 20 : 21.2]
Effective diameter, mm, median [std; 95% CI]	15.9 [0.34; 15.6 : 16.4]	16 [0.28; 15.6 : 16.4]	17.4 [0.36; 16.9 : 18]	22.8 [0.43; 22.4 : 23.3]	19.1 [0.58; 17.9 : 19.7]
Volume, mm 3, average [std; 95% CI]	5643 [284; 5088 : 6208]	5055 [377; 4371 : 5804]	3839.7 [155; 3538 : 4151]	4371.92 [180; 4015 : 4729]	5024.1 [246; 4556 : 5517]
Volume, mm 3, median [std; 95% CI]	2099.2 [136; 1978 : 2308]	2137.6 [114; 1986 : 2308]	2097 [137; 1979 : 2309]	2533.5 [264; 1975: 2695]	2309.5 [239; 2251: 2952]

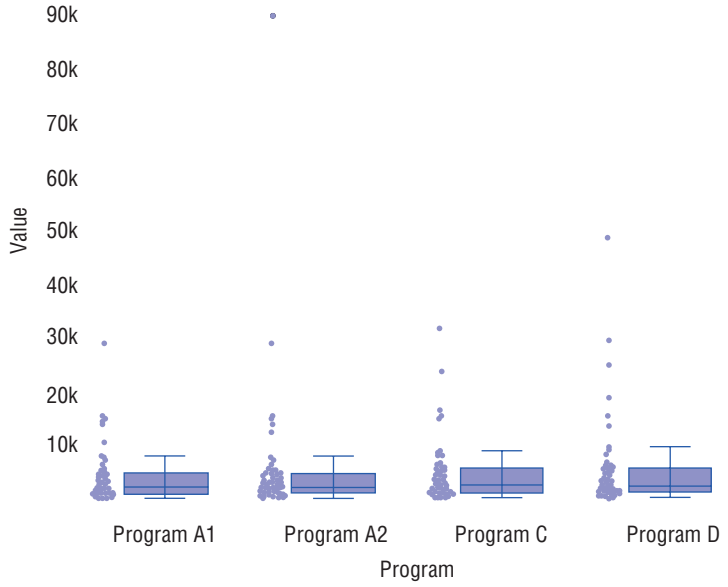

Fig. 1. Distribution of nodule diameter values measured by different software programs

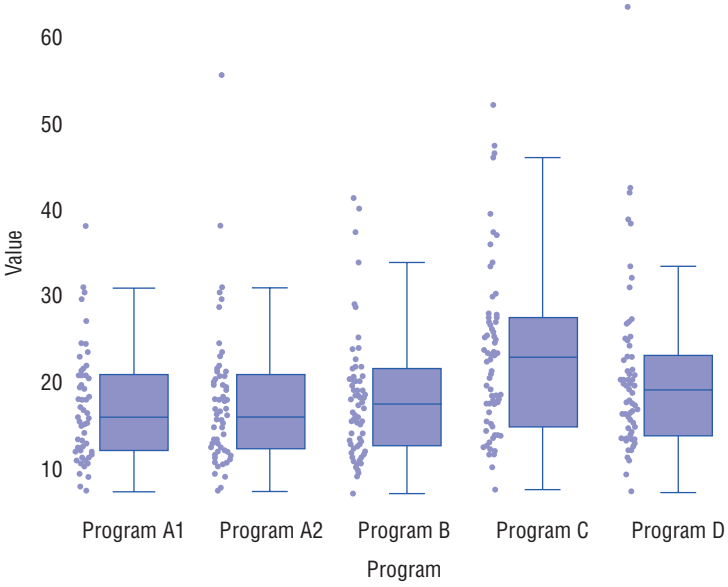

Fig. 2. Scatter of nodule volume measurements obtained by different software programs

The data distribution was visualized using a Box and Whisker Plot. The structure of this plot consists of the following components: the box represents the interquartile range (IQR), which contains 50% of the data. The lower and upper boundaries of the box correspond to the first (25%) and third (75%) quartiles, respectively. The line inside the box indicates the median of the dataset. The whiskers extend from the edges of the box to the most distant data points that lie within 1.5 × IQR from the first and third quartiles. They may also represent the minimum and maximum values that do not exceed this range. Points located beyond the whiskers are considered outliers (Figure 1, 2).

To assess the normality of the distribution, a normality test was applied, specifically the Shapiro–Wilk test, which is most effective for small sample sizes. This test evaluates the hypothesis that the data are drawn from a normally distributed population. The hypothesis is rejected when the p-value is less than 0.05, indicating a non-normal distribution. In the present study, all variables demonstrated deviation from normality.

Comparison of variance equality was performed using pairwise comparisons of subsamples. Unequal variances were observed in the following subsamples: Program C vs. Programs A1, A2, and B. In all other subsamples, variances were equal.

Comparison of diameters and volumes between the results of Programs A, B, and C and those of Program D was performed using a two-tailed Student's t-test for subsamples with equal variances, and the Mann–Whitney U test — a nonparametric test that does not assume normality or equality of variances — in cases where variances differed.

All statistical parameters were computed based on 1,000 bootstrap resamples. The results of the comparisons are presented in Tables 4 and 5.

Statistically significant differences ($p<0.05$) were observed when comparing the mean diameters between Program C and Programs A and B, as well as between the subsamples of Program A1 and Program D. No statistically significant differences were found between the other groups.

No statistically significant differences in mean volumes were found among the groups.

Table 4

Pairwise comparison of diameter measurements by program

Group 1	Group 2	p-value	Result
Program A1	Program A2	0.7	No statistically significant differences were observed
Program A1	Program B	0.32	No statistically significant differences were observed
Program A1	Program D	0.02	There are statistically significant differences
Program A2	Program B	0.59	No statistically significant differences were observed
Program A2	Program D	0.051	No statistically significant differences were observed
Program B	Program D	0.12	No statistically significant differences were observed
Program C	Program A1	0.0002	There are statistically significant differences
Program C	Program A2	0.0003	There are statistically significant differences
Program C	Program B	0.003	There are statistically significant differences
Program C	Program D	0.14	No statistically significant differences were observed

Table 5

Pairwise comparison of volume measurements by program

Group 1	Group 2	p-value	Result
Program A1	Program A2	0.44	No statistically significant differences were observed
Program A1	Program B	0.96	No statistically significant differences were observed
Program A1	Program D	0.3	No statistically significant differences were observed
Program A2	Program B	0.46	No statistically significant differences were observed
Program A2	Program D	0.98	No statistically significant differences were observed
Program B	Program D	0.32	No statistically significant differences were observed
Program C	Program A1	0.55	No statistically significant differences were observed
Program C	Program A2	0.66	No statistically significant differences were observed
Program C	Program B	0.59	No statistically significant differences were observed
Program C	Program D	0.59	No statistically significant differences were observed

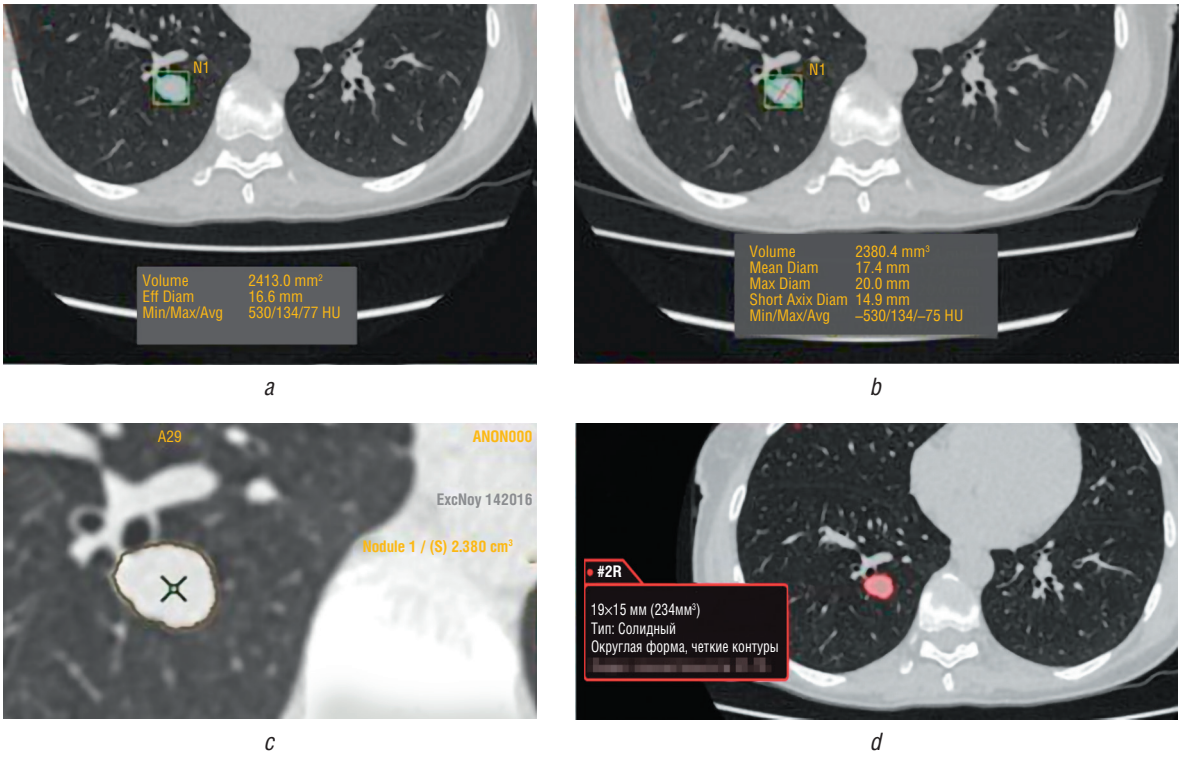

Fig. 3. Volumetric measurements of the same nodule performed using four different software products. All four programs demonstrate accurate segmentation and minimal variation in the measured nodule volumes

Discussion

The study revealed that statistically significant differences ($p<0.05$) were observed when comparing the mean effective diameters between Program C and Programs A and B. This indicates the presence of substantial discrepancies in diameter measurements between workstations from different manufacturers, regardless of software version or whether radiologists performed manual adjustment of the final result in one of the programs.

At the same time, no statistically significant differences were found between Program C and Program D — i.e., between a workstation using a semi-automatic algorithm and a fully automatic analysis system. However, the p-value itself provides additional insight: the lowest p-value for Program C was obtained when compared with Program A, which represents an older-generation workstation.

A similar trend was seen for the p-value between Program D and Program A1, where statistically significant differences were observed, suggesting notable discrepancies in diameter measurements between the older-generation workstation without manual correction and the deep learning–based algorithm.

Statistical analysis of the mean effective diameters across the five groups demonstrated that both modern platforms (Program C and Program D) differed significantly from the older-generation software (Program A). At the same time, the fully automatic analysis system (Program D) showed no significant differences from either the newer workstation (Program B) or the semi-automatic measurements obtained after manual contour correction (Program A2). This indicates comparable results between semi-automatic diameter measurement performed on a workstation and fully automatic diameter measurement obtained by an AI algorithm, which requires no additional user intervention or time investment by the radiologist.

The second most comparable result was found between Program A1 and Program A2, indicating that manual correction of semi-automatic diameter measurements did not result in a statistically significant difference within this sample.

Comparison of volumetric measurements across software products did not reveal statistically significant differences. An important factor explaining the lack of significant differences is the high variability of data within the sample, leading to broader 95% confidence intervals. When confidence intervals for two groups overlap, statistical testing fails to detect significant differences ($p>0.05$), as overlap suggests no substantial shift in the underlying distributions. Combined with heterogeneity in lesion size, this broad variability mitigates even visible differences in mean volume values, preventing achievement of statistical significance.

Nevertheless, some results deserve attention: the highest p-value was obtained when comparing Program A2 and Program D, meaning that volumes obtained af-

ter manual correction by a radiologist were most similar to those automatically calculated by the AI algorithm. In contrast to diameter comparisons, the volume comparison between Program A1 and Program A2 yielded a lower p-value, indicating more noticeable changes in volume after manual adjustment of the semi-automatically derived values. This observation is further supported by the relatively low p-value found when comparing Program A1 and Program D.

When comparing our results with previous studies, it should be noted that numerous investigations have demonstrated high variability due to human factors in the measurement of pulmonary nodules, underscoring the need for automated quantitative assessment of lesion size [4, 5, 12].

A number of studies have focused on volumetry, assessing the influence of factors such as slice thickness, radiation dose, and respiratory motion artifacts on volumetric accuracy.

The most critical factor highlighted in the literature is the accuracy of nodule segmentation performed by automatic and semi-automatic systems.

Another key issue addressed in prior research is the reproducibility of measurements performed by different software products.

One of the largest studies in this area was conducted in 2008 by Bartjan de Hoop et al. The aim of that study was to assess the variability of volumetric measurements of the same nodule across six different software platforms in 20 patients with pulmonary metastases. The following segmentation algorithms were evaluated: Advantage ALA (GE, v7.4.63), Extended Brilliance Workspace (Philips, EBW v3.0), Lungcare I (Siemens, Somaris 5 VB 10A-W), Lungcare II (Siemens, Somaris 5 VE31H), OncoTreat (MEVIS, v1.6), and Vitrea (Vital Images, v3.8.1). The authors assessed both the accuracy of segmentation and the interchangeability of measurement results across these platforms. Their findings demonstrated considerable differences between segmentation and volumetric measurements obtained using different software packages [13].

In a more recent study by Penha D et al. (2022), two measurement tools were evaluated: VuePACS ver. 11.4.01.1011 (Carestream; Tool 1) and Syngo via VB20 (Siemens; Tool 2). These systems showed high inter-software reproducibility, though both radiologists reported that Tool 2 provided more accurate segmentation and measurement results [14].

These findings collectively suggest that with continued development, automatic analysis systems are becoming increasingly precise and reproducible measurement tools.

In our study, statistically significant differences were observed between older-generation software and the modern AI-based algorithm, as well as between two different versions of the same manufacturer's product. Our findings further confirm the critical importance of accurate lesion segmentation for volumetric assessment, emphasizing that the implementation of machine learning is a promising direction for improving this process.

This study has several limitations. We analyzed only solid pulmonary nodules, with the majority of cases exceeding 1.0 cm in maximum axial dimension. Therefore, the conclusions should not be extrapolated to all available automatic nodule measurement systems. We did not evaluate reproducibility across different reconstruction algorithms (only standard reconstruction protocols were included) or compare measurements obtained without intravenous contrast or across different contrast-enhancement phases. These aspects warrant further investigation in future studies addressing the important issue of reproducibility in automated pulmonary nodule measurement.

Conclusion

Statistically significant differences in mean effective diameters were identified when comparing measurements:

- between automatic nodule measurement systems from different manufacturers;
- between earlier versions of semi-automatic volumetric analysis software and more advanced systems.

No statistically significant differences were observed between the mean effective diameters obtained by the automatic analysis system and those obtained after manual contour correction by a radiologist using earlier semi-automatic volumetric tools.

Analysis of mean nodule volumes across all groups revealed no statistically significant differences, confirming the robustness and potential universality of this parameter for use in clinical practice.

The implementation of such systems may potentially reduce radiologists' workload by eliminating the need for manual measurement of quantitative parameters, thereby saving time and improving workflow efficiency.

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