Improved precision of repeat image change measurement of pulmonary nodules using moment-based z-compensation on a zero-change dataset

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ABSTRACT

CT scanners often have higher in-plane resolution than axial resolution. As a result, measurements in the axial direction are less reliable than measurements in-plane, and this should be considered when performing nodule growth measurements. We propose a method to measure nodule growth rates by a moment-based algorithm using the central second order moments for the in-plane directions. The interscan repeatability of the new method was compared to a volumetric measurement method on a database of 22 nodules with multiple scans taken in the same session. The interscan variability was defined as the 95% confidence interval of the relative volume change.

For the entire database of nodules, the interscan variability of the volumetric growth method was (-52.1%, 30.1%); the moment-based method improved the variability to (-34.2%, 23.3%). For the 11 nodules with scans of the same slice thickness between scans, the variability of the volumetric growth method was (24.0%, 30.1%), compared to (-12.4%, 12.7%) for the moment-based method. The 11 nodules with scans of different slice thickness had a variability for the volumetric method of (-68.4%, 30.2%) and for the moment-based method, (-46.5%, 24.4%). The moment-based method showed improvement in interscan variability for all cases.

This study shows promising preliminary results of improved repeatability of the new moment-based method over a volumetric method and suggests that measurements on scans of the same slice thickness are more repeatable than on scans of different slice thickness. The 11 nodules with the same slice thickness are publicly available.

Keywords: pulmonary nodule, moment analysis, growth rate

1. INTRODUCTION

The growth rate of a pulmonary lesion has been shown to be an important indicator of malignancy.[1,2] As CT scanner technology improves, particularly in the area of resolution, ever smaller nodules can be detected and measured. There has been much research into methods for accurately measuring pulmonary nodules, but it is often difficult to assess the performance of such algorithms without ground truth – studies have shown that variation exists between different measuring methods[3,4] and observers.[5] These variations are due to factors such as type of scanner and scanner parameters,[6,7] the presence of attached structures such as blood vessels,[8] and nodule morphology.[9]

To assess the performance of automated methods without a ground truth measurement, studies may use phantoms or nodules where no change in size occurs. The use of phantoms is problematic because they often are not able to accurately represent all the complexities of actual nodules. Thus, many studies attempt to measure using nodules which do not change in size. These studies can be divided into two groups – those that use "coffee break" scans, where several scans are taken within minutes of each other, and thus should exhibit no change,[10] and those using stable nodules where scans are obtained using normal protocols. Coffee break scans are ideal for quantifying the error in measurement, since the nodules would not have changed in size between the scans. Stable nodules are assumed to have no significant growth, but this is often difficult to verify.

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Among the studies using coffee break scans, Gietema et al showed a 95% confidence interval for the difference in measured volumes of (-21.2%, 23.8%).[11] In their study, two low-dose CT scans at 0.75 mm collimation were obtained for each patient. Volumes were measured using Siemens LungCare and only nodules that had no contact with the pleura or vessels were included, which resulted in a dataset of 218 nodules. Wormanns et al assessed the precision of a prelease version of Siemens LungCare on 151 nodules from ten subjects.[12] Patients were scanned twice and asked to leave the table between scans. Scans were acquired with 1.25 mm slice thickness. The range of nodule diameters was 2.2 to 20.5 mm. The limits of agreement for repeatability was -20.4% to 21.9%. Goodman et al studied the interobserver and interscan variability of pulmonary nodule volume measurements made using GE Advanced Lung Analysis. The interobserver variability was (-3.3%, 7.6%) while the interscan variability was 13.1%±25.6%. The interscan variability is computed over several observers, so it may not be directly comparable to the previous two studies.

Studies using stable nodules have the advantage of not exposing patients to additional radiation, as required by "coffee break" studies, but even in short time intervals, stable nodules may have changed in size. In a study by Reeves et al on fifty stable nodules, a percent volume change standard deviation of 11.54 was found using their standard method; using a rule-based adjustment reduced the standard deviation to 9.68.[13] An adaptive threshold improved the results only slightly. Kostis et al assessed the reproducibility of volume measurements on 94 pulmonary nodules.[14] Nodules were on 1.0 or 1.25 mm scans and ranged in size from 2 – 10 mm. For all nodules with any interval between scans, the mean percent volume change (PVC) was 1.79 with an SD of 16.1 for a confidence interval of -29.8 – 33.4%. For nodules 2-5 mm in diameter, the confidence interval was -34.3 – 38.3%; for nodules 5-8 mm, -18.6 – 22.9%; and for nodules 8-10 mm, -16.2 – 13.1%, suggesting that the confidence interval is smaller for larger nodules.

Most current automated nodule measurement methods simply segment the nodule and sum up the number of voxels included in the segmentation and multiply by the voxel size to obtain a volume measurement. However, most CT scanners acquire anisotropic images, where the resolution in-plane is higher than the axial resolution. Making use of this fact may improve the reliability of nodule volume measurements. We propose a method that accounts for the anisotropic nature of CT scans using a moment-based method compare the repeatability of this new method to a previously published volumetric method.

2. METHODS

The moment-based z-compensation method first requires segmentation of the nodule followed by moment analysis. Segmentation of the nodule is performed using a semi-automated algorithm described by Reeves et al[13] that requires the manual specification of a seed point within the nodule. The algorithm determined the center and approximate size of the nodule, resampled the nodule into isotropic space, and performed vessel and pleural wall removal if necessary. The result of the algorithm is a binary image indicating which voxels belong to the nodule. The standard volumetric method simply sums up the number of voxels included in the segmentation and multiplies by the voxel size to obtain the volume of the nodule. The moment-based method takes the result of the nodule segmentation and applies further processing to account for the lower axial resolution, as compared to the in-plane resolution, of most CT scanners. Before describing the moment-based method, a brief overview of moments is presented.

2.1 Moments

Moment analysis of images has been used for various tasks including such diverse applications as shape characterization for the identification of airplanes,[15] nodule characterization algorithms,[16,17] and morphological characterization of intracranial aneurysms.[18] The general equation for a moment of order $p+q+r$ for a 3D image is:

$$m_{pqr} = \sum_x \sum_y \sum_z x^p y^q z^r f(x,y,z)$$

where x, y, and z are the voxel coordinates and $f(x,y,z)$ is the intensity of the voxel. For a binary image, $f(x,y,z)$ is either 0 or 1. Note that this function is sensitive to the location of the region under consideration. This is undesirable since the same nodule in different locations should, for the purpose of growth analysis, result

in the same value, assuming no change in size. This is addressed by using central moments, which have the following form:

$$\mu_{pqr} = \sum_x \sum_y \sum_z (x - \bar{x})^p (y - \bar{y})^q (z - \bar{z})^r f(x, y, z)$$

where $\bar{x} = \frac{m_{100}}{m_{000}}$, $\bar{y} = \frac{m_{010}}{m_{000}}$, and $\bar{z} = \frac{m_{001}}{m_{000}}$.

2.2 Moments for growth analysis

In our moment-based method, the second-order central moments are computed on the segmented nodule image. These second-order moments represent the axes of the ellipsoid of inertia of the nodule. The in-plane moments μ_{200} and μ_{020} were used to estimate the volume of the nodule using the following equation:

$$V \approx k \left(\sqrt{\frac{\mu_{200}}{\mu_{000}}} * \sqrt{\frac{\mu_{020}}{\mu_{000}}} \right)^{3/2}$$

The second-order moments are normalized by the zero-order moment (volume) to account for increases in nodule volume orthogonal to the direction under consideration. This results in the following expanded equation:

$$\frac{\mu_{200}}{\mu_{000}} = \frac{\sum_x \sum_y \sum_z (x - \bar{x})^2 f(x, y, z)}{\sum_x \sum_y \sum_z f(x, y, z)}$$

which for the case of a binary image, is similar to the expression for sample variance. To convert to meaningful units, the square root of the expression is taken, and this is used as an analogue of the diameter of the nodule in one dimension. These diameters are then used to compute an estimate of the volume of the nodule. Although μ_{002}, the second-order moment corresponding to the z-direction, is not used in the expression above, both μ_{200} and μ_{020} are computed over all the voxels in the segmented nodule image, so all the image data are still being used.

To compute the actual volume of the nodule, the expression needs to be scaled by a constant k, but since we are concerned about relative volume change, k drops out of the expression and we need not be concerned with its value. A relative volume difference is then computed. For the nodules used in this study, the ideal case of perfect measurement would result in a relative volume difference of 0%. The relative volume difference (RVD) was computed according to the following equation:

$$RVD = \frac{V_2}{V_1} - 1$$

The computed RVD were used to compute the interscan variability, which is defined as the 95% confidence interval of the RVD as suggested by Gietema et al.[11] The standard volumetric method and the new moment-based method were then compared on the basis of interscan variability.

2.3 Data

The dataset for this study consisted of twenty-two cases with multiple scans taken a few minutes apart in the initial stages of a lung biopsy so that there was no change in the nodule volume between the scans. All cases had a nodule of solid consistency, as determined by a radiologist, with at least two scans that included the entire nodule. In eleven cases, the scans were taken using the same slice thickness, with ten of the eleven cases at 1.25 mm slice thickness and one at a slice thickness of 2.5 mm. In the remaining eleven cases, scans were taken at different resolutions, with at least one scan at a slice thickness of 1.25 mm. In three cases, the second scan had a 5.0 mm slice thickness while eight had 2.5 mm. The mean size of the nodules in the dataset was 14.1 mm with a standard deviation (SD) of 5.6 mm. For the eleven cases with scans of the same slice thickness, the mean size was 14.8 mm with a SD of 4.6 mm while the eleven cases with scans of different slice thickness had a mean size of 13.4 mm with a SD of 6.5 mm. A plot of the size distribution of the nodules in the dataset is shown in Figure 1. Scans were obtained using either a GE LightSpeed QX/i or LightSpeed Ultra scanner, using 120 kVp and a current in the range of 40-250 mAs.

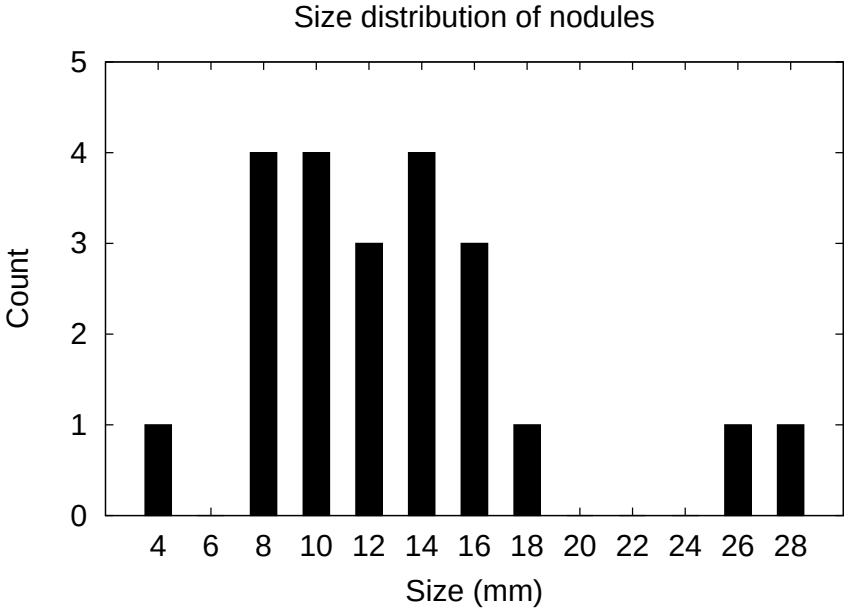


Figure 1. Size distribution of nodules in the dataset. The value along the x-axis indicates the minimum size of nodules in the bin.

Table 1. Interscan variability of volumetric and moment-based methods

Dataset	Interscan variability (%)	
	Volumetric method	Moment-based method
Full (22 nodules)	(-52.1, 30.1)	(-34.2, 23.3)
Same slice thickness (11)	(-24.0, 18.2)	(-12.4, 12.7)
Mixed slice thickness (11)	(-68.4, 30.2)	(-46.5, 24.4)

3. RESULTS

The new moment-based method was compared to a previously published volumetric method on the basis of interscan variability. Interscan variability is presented as the upper and lower bounds of the 95% confidence interval of the relative volume difference of the cases in the study. On cases with scans of the same slice thickness, which is comparable to cases used in previously published studies, the volumetric method had an interscan variability of -24.0% to 18.2%. The moment-based method had a lower interscan variability of -12.4% to 12.7%. The full results are presented in Table 1.

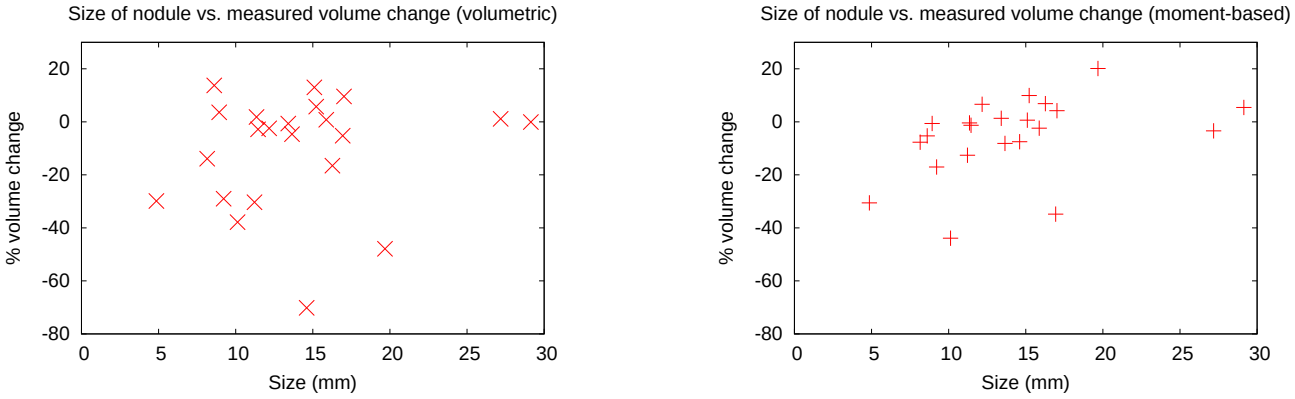
As the conventional method of expressing pulmonary nodule size is in diameter, the interscan variability can be converted to a relative size difference; these values are included in Table 2. As an example of the actual impact on size measurement the interscan variability may have, the size difference corresponding to the confidence intervals of the interscan variability in Table 1 are shown in Table 3 for a 10 mm nodule. Note that despite a large interscan variability in relative volume difference, the difference in size on a 10 mm lesion is less than 1 mm for cases of the same slice thickness.

Table 2. Interscan variability presented as relative size difference

Dataset	Interscan variability (size) (%)	
	Volumetric method	Moment-based method
Full (22 nodules)	(-21.8, 9.2)	(-13.0, 7.2)
Same slice thickness (11)	(-5.7, 8.7)	(-4.1, 4.3)
Mixed slice thickness (11)	(-31.9, 9.2)	(-18.8, 7.5)

Table 3. Interscan variability presented as size range for a 10 mm nodule

Dataset	Interscan size variability (mm)	
	Volumetric method	Moment-based method
Full (22 nodules)	(7.8, 10.9)	(8.7, 10.7)
Same slice thickness (11)	(9.1, 10.6)	(9.6, 10.4)
Mixed slice thickness (11)	(6.8, 10.9)	(8.1, 10.8)



(a) (b)

Figure 2. Scatter plot of measured volume change versus the initial size of the nodule for a) volumetric measurement method and b) moment-based method

4. DISCUSSION

A low interscan variability validates that a nodule growth measurement method is able to consistently measure the same nodule. This variability can then be used to establish error bounds on the measurement precision of the method. Previous studies of other methods have found interscan variability of approximately (-20%, 20%) using scans of the same slice thickness; our standard volumetric method, on the eleven nodules with scans of the same slice thickness, performed similarly with a variability of (-24.0%, 18.2%). The new moment-based method improved the variability to (-12.4%, 12.7%). Both methods performed worse on the eleven nodules with scans of different slice thicknesses, with the volumetric method interscan variability increasing to (-68.4%, 30.2%) and the moment-based method interscan variability increasing to (-46.5%, 24.4%), with the moment-based method still performing better than the volumetric method. This result suggests that pulmonary nodule growth assessment requires scans with the same slice thickness for the most accurate measurement.

The measurement precision of a volume measurement method has implications for the the accuracy of growth rate measurements. For a nodule with a 400 day doubling time on scans 1 year apart, a confidence interval of (-20%, 20%) on the volume measurement of the nodule on one scan would result in a doubling time ranging from 551 days to 327 days. If the confidence interval is reduced to (-13%, 13%), as with the new moment-based algorithm, the doubling time range is reduced to 485 days to 349 days. This range of doubling time values increases for a shorter time interval between scans and decreases for a longer time interval.

There was no clear relationship between the initial size of the nodule and the volume change measured by either the volumetric method or the moment-based method. Linear regression was performed to determine if there was any correlation between the size and measured volume change; neither method showed a significant relationship, with the volumetric method having an correlation coefficient $r^2 = 0.16$ and the moment-based method having an $r^2 = 0.01$. This can be seen in a scatter plot of the data in Figure 2.

Although the moment-based method had a lower interscan variability, it did not measure smaller volume change on every case. On ten cases, the moment-based method measured a higher relative volume difference than the volumetric method, but on these cases, the difference between the two methods was small, with an average difference between the two methods of 5.8%. On the other twelve cases where the moment-based method

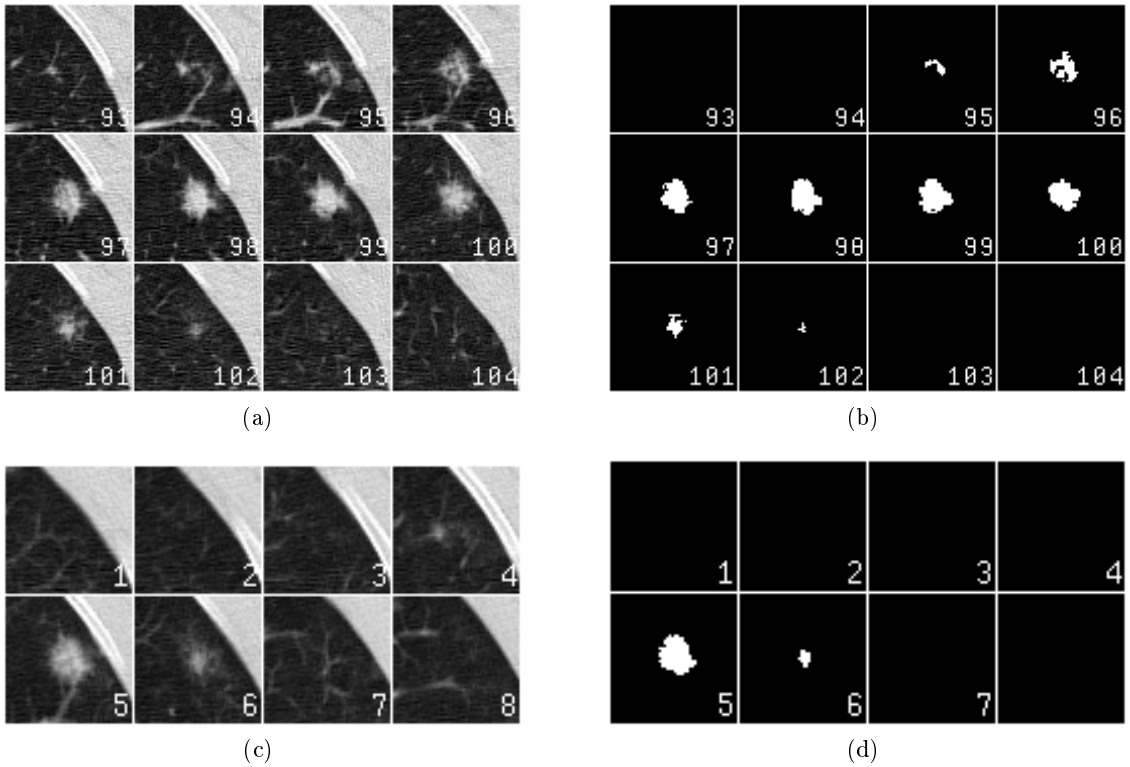


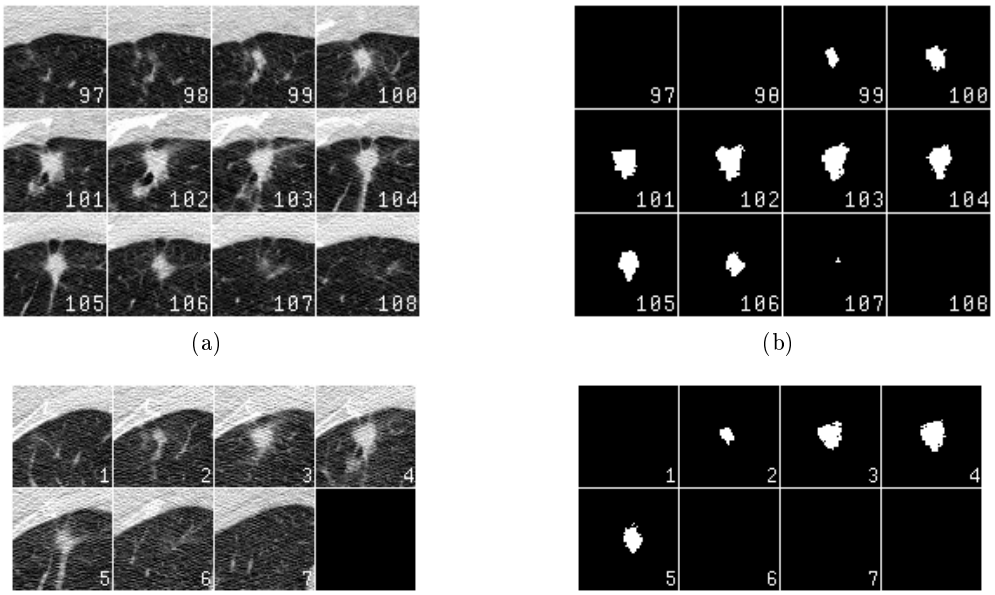
Figure 3. Example of a case with scans of the different slice thickness (1.25 mm top, 5.0 mm bottom) and high interscan variability. a) Montage of several slices through the nodule on the first scan, b) segmentation of the nodule on the first scan where white voxels are those belonging to the nodule, c) several slices on the second scan, and d) segmentation on the second scan. Scans are not to the same scale.

measured a lower relative volume difference than the volumetric method, the moment-based method had much lower values; on average, the moment-based method had measurements that were 14.0% lower.

In cases with different slice thicknesses between the two scans, the appearance of the nodule was different between the two scans. In some cases, the difference was great enough to cause a large difference in volume between the two scans, while in others the volume difference was minimal. One case with a large difference in volume is shown in Figure 3. In this case, one scan was acquired with a slice thickness of 1.25 mm while the other scan was acquired with 5.0 mm; the relative volume difference computed by the volumetric method was 37.8% while the relative volume difference computed by the moment-based method was 43.8%, with the larger volume measured on the first scan. In another case, even though the scans were obtained at different slice thicknesses, the volume change was small, as in Figure 4. For this case, the volumetric method had a volume difference of 2.8% while the moment-based method had a volume difference of 1.3%. Even in cases with scans of the same slice thickness, there was sometimes a marked difference in the appearance of the nodule between the two scans, as illustrated by the case in Figure 5, the nodule appears on an additional slice in the second CT scan; this is reflected in the segmentation shown on the right side of the figure. This case had a relative volume difference of 30.3% for the volumetric method and 12.6% for the moment-based method, with the larger volume on the first scan.

5. CONCLUSION

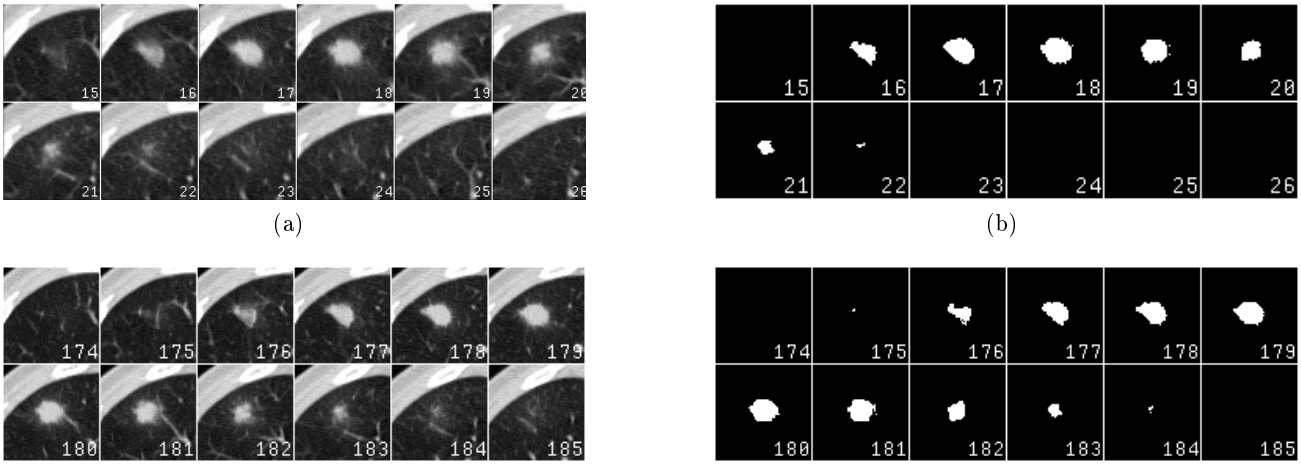
A new method for nodule growth measurement taking into account the anisotropy of CT scanners based on moment-analysis was developed. The interscan variability of the method was assessed on a zero-change dataset and was found to be lower than a volumetric method. Both methods had a larger variability when scans of mixed slice thickness were used, compared to when scans of the same slice thickness were used, suggesting that for the



(a) (b)

(c) (d)

Figure 4. Example of a case with scans of the different slice thickness (1.25 mm top, 2.5 mm bottom) and low interscan variability. a) Montage of several slices through the nodule on the first scan, b) segmentation on the first scan with voxels part of the nodule indicated in white, c) several slices on the second scan, and d) segmentation on the second scan. Scans are not to the same scale.



(a) (b)

(c) (d)

Figure 5. Example of a case with scans of the same slice thickness and high inter-scan variability. a) Montage of several slices through the nodule on the first scan, b) segmentation on the first scan, c) several slices on the second scan, and d) segmentation on the second scan. Note that there appears to be an extra slice between the two scans.

best accuracy, pulmonary nodule growth rate measurements should be performed on scans of the same slice thickness. To aid the community in the development and validation of nodule growth measurement algorithms, we have made the set of eleven nodules with scans of the same slice thickness publicly available on our website, `http://www.via.cornell.edu/crpf.html`.

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