Letters to the Editor

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Can the Extent of Low-Attenuation Areas on CT Scans Really Demonstrate Changes in the Severity of Emphysema?

From
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Editor:

In the September 2007 issue of *Radiology*, H. A. Gietema and colleagues (1) studied the reproducibility of computed tomographic (CT) lung densitometry in monitoring emphysema. They used Bland-Altman analysis to determine the limits of agreement from repeated CT scans and reported that the relative area (RA) of low attenuation varies the least at a threshold of −950 HU, concluding that this method and threshold should be used.

However, Bland-Altman analysis can be used only if the differences follow a normal distribution and if the variation in the differences is unassociated with the size of the measurement. Unfortunately, neither of these requirements was met in this study, which resulted in wrong conclusions. Figure 3 of the article shows that most differences in RA are close to zero, which results in a non-normal, peaked distribution. At −950 HU, the majority of the 157 samples have been projected to the origin. Furthermore, repeatability was dependent on the mean value, since smaller variations were found at lower RA values.

This should have triggered the authors to have a closer look at their data.

A known drawback of RA is the cutoff effect at 0%, as a patient simply cannot have a CT scan with an RA of less than 0%. Hence, this cutoff effect is dependent on the threshold used and on the severity of emphysema in the patient group. Dr Gietema and colleagues conclude that with a threshold of −950 HU, the smallest real increase (1.1%) is all that is needed. However, the use of the lowest threshold of −950 HU produces many data truncated at 0%. And because the same value of 0% is reliably reproduced at follow-up, the sensitivity to changes in emphysema is diminished to zero. This is unlikely to represent a true reflection of the increase in the extent of emphysema.

In conclusion, the data presented by Dr Gietema and colleagues actually show that RA is not a suitable outcome parameter for monitoring the progression of emphysema. The alternative method (the percentile point) does not have this profound cutoff problem and is therefore already recommended in an international workshop on lung densitometry (2).

References

1. Gietema HA, Schilham AM, van Ginneken B, van Klaveren RJ, Lammers JW, Prokop M. Monitoring of smoking-induced emphysema with CT in a lung cancer screening setting: detection of real increase in extent of emphysema. Radiology 2007;244(3):890–897.
2. Newell JD Jr, Hogg JC, Snider GL. Report of a workshop: quantitative computed tomography scanning in longitudinal studies of emphysema. Eur Respir J 2004;23(5):769–775.

Response

From
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We thank Dr Stoel and colleagues for their comments because they highlight an ongoing discussion about how to best detect and quantify emphysema progression.

The Bland-Altman method is a frequently used technique for analyzing the dependence of measurement variability on the size of measured values. In itself the Bland-Altman method is independent of the distribution of differences (1). Because the differences need to be normally distributed in order to be able to calculate 95% confidence intervals using the linear approach we chose, we had checked our data and found that the distribution of differences did not deviate significantly from a normal distribution. We are grateful that Dr Stoel and colleagues pointed out that we did not fully account for the truncation effect at 0% in our calculations. To minimize this truncation effect we should have excluded low scores (at least smaller than the upper limit of agreement) to obtain sufficiently precise estimates of the 95% confidence intervals. When we exclude such low emphysema scores, the upper limits of agreement change from 13% to 16.6% for −910 HU, from 4.5% to 6.0% for −930 HU, and from 1.2% to 1.9% for −950 HU. The suggested closer look at the data therefore did result in just a moderately higher change in the emphysema score (ES) before emphysema progression can be stated with 95% probability.

We do not agree with the other arguments of Dr Stoel and colleagues: As figure 3c in our study shows (2), an ES of 0% is usually not exactly reproduced at repeat CT (the x-axis represents the mean of the two measurements). In fact, an ES of 0% was found on both CT scans in only five (3%) of 157 cases for the −950 HU threshold, but there were 24 subjects with an ES of 0% in only one measurement. Consequently, the statement that "the sensitivity to changes in emphysema is diminished to zero" is incorrect, as is the conclusion that the ES (called the "RA" by Dr Stoel and colleagues) "is not a suitable outcome parameter for monitoring the progression of emphysema." Moreover, Madani et al (3) recently showed that the first percentile correlated best with histologic findings when using the percentile technique. One can speculate that such a low percentile might even be less sensitive to detect small changes in emphysema. The data are not yet out to decide which technique is best suited to detect an early increase in emphysema on a per-patient basis.

References

1. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1(8476):307–310.

2. Gietema HA, Schilham AM, van Ginneken B, van Klaveren RJ, Lammers JW, Prokop M. Monitoring of smoking-induced emphysema with CT in a lung cancer screening setting: detection of real increase in extent of emphysema. Radiology 2007;244(3):890–897.

3. Madani A, de Maertelaer V, Zanen J, Gevenois PA. Pulmonary emphysema: radiation dose and section thickness at multidetector CT quantification—comparison with macroscopic and microscopic morphometry. Radiology 2007;243(1):250–257.

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