Lung Cancer Growth Curves Based on CT Imaging

To the Editor:

We read with interest the recent article in CHEST (December 2009) by Lindell et al1 in which the authors state that this “study is the only one to have evaluated growth curves of lung cancers using multiple CT scans.” We would like to point out our previously published article that examined growth rates in 54 lung lesions, including 33 primary non-small cell lung cancers, based on volumetric measurements from thin-section CT imaging.2 Individual growth curves were plotted for the 20 lesions with ≥3 CT scans, including 13 non-small cell lung cancers. As in the study by Lindell et al, we found considerable variability in growth rates among the individual cancers that were analyzed. On the other hand, however, most of our lesions showed exponential growth, differing somewhat from the results of Lindell et al.

Lindell et al noted that their study was limited by the accuracy of two-dimensional measurements for volume calculation. Indeed, in our study, we found that calculated growth rates differed substantially, depending on the volume measurement technique used (ie, based on lesion diameter, lesion area, or direct volume measurement using automatic segmentation and direct volume measurement); presumably, direct volume measurements are superior to the other methods because primary lung cancers are not spherical and often grow asymmetrically. Despite the potential limitations of our studies, CT imaging-based growth rates are undoubtedly more accurate than the oft-quoted rates based on data derived from older chest radiography studies.3–5

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Response

To the Editor:

I would like to thank Quint et al and Kakinuma et al for their letters and making us aware of the article by Quint et al titled “Lung Lesion Doubling Times: Values and Variability Based on Method of Volume Determination.”4 Their article’s focus was on volume determination methods, whereas our article in a recent issue of CHEST (December 2009)5 was on the lack of exponential growth of a subset of lung cancers as shown by growth curves and the implications that this could have on prior studies that advocated using two volume measurements to determine volume doubling time. While their study did include growth curves for 20 lesions, only 13 of those were lung cancers, and although it is difficult to be sure from their growth curves, it appears that most, if not all, of their lung cancers were followed with only three CT scan exams. An early criticism of our manuscript during peer review was that it would be difficult to prove or exclude exponential growth based on only three data points, and it was recommended that we include only cases with at least four CT scan exams. Therefore, although Quint and colleagues did generate growth curves, it is our position that based on peer review feedback they did not plot growth curves that were analogous to the curves we plotted. We did perhaps err in not referencing the paper and explaining our reasoning. We do agree with their conclusion that “given the very slow growth of some lung cancers, short term follow-up CT may not always be capable of detecting volume changes indicative of malignancy. Therefore, stability on short term follow-up exams should be interpreted with caution.” However, based on our study we would expand on that to caution that even using a volume doubling equation based on two exams could potentially be misleading since the assumption of exponential growth has been called into question.

The differing results regarding exponential growth are interesting but perhaps somewhat explainable by our prospective screening method and different inclusion criteria. Compared with their study, our study’s criteria resulted in a population of lung cancers with a smaller initial size (none >8 mm vs a mean of 11–17 mm) and slower growth (volume doubling time mean of 771 days vs a mean range of 58–128 days) that were followed on more CT scan exams for a longer period of time (mean 1,025 days, median 1,051 days, range 404–1,666 days, or 55.5 months if assuming 30 days, vs a mean of 227 days, median 154 days, range 6 days–34.5 months). Since their study was retrospective and only included lesions with a histologic diagnosis, they selected for a different set of cancers. Cancers with a slower growth rate may not have changed sufficiently during the course of their study to have undergone resection and were therefore not included.