I believe there may be an error in Figure 11 of a recent article published by the International Early Lung Cancer Action Project (I-ELCAP) group in The Oncologist (reproduced here as Fig. 1) [1]. The figure displays the comparative survival of subjects with clinical stage I computed tomography–detected lung cancer who are treated promptly (i.e., treated subjects) compared with similarly diagnosed subjects who received no treatment (i.e., untreated subjects). Thus, the figure is intended to provide insights into whether or not early treatment of patients with screen-detected early-stage lung cancer alters outcomes, and if it does, screening for early cancer may be beneficial.

Two aspects of this figure have me puzzled. First, I cannot determine how the I-ELCAP study accrued five additional “untreated subjects” and also observed their outcomes during the small amount of time that passed between their October 2006 paper [2] (when they reported on eight “untreated subjects”) and their January 2008 paper [1] (when they reported on “13 untreated subjects”). In both papers, and in editorials and letters that refer to the papers, the I-ELCAP investigators stated that all of the untreated subjects (eight in the former study, 13 in the latter) had been followed to the outcome of death from lung cancer by the time the respective papers were published [1–6]. Thus, the additional five untreated subjects that appear in the paper in The Oncologist could not have been in active follow-up at the time of the earlier publication.

This means that all five of the additional subjects had to both enter the study and die from lung cancer during the time that passed between the papers. For this to occur, the time interval between the two publications had to be as long as the minimum follow-up time needed for all five subjects to both enter the study and die. But not that much time actually passed.

Table 1 shows the survival times for the 13 untreated subjects as shown in the authors’ figure. The survival time for the fifth subject is 20 months, which exceeds the time that passed between the two publications. Comparing publication dates, 15 months passed between October 26, 2006 and January 31, 2008. Using the most generous possible interval, 18 months passed between the last follow-up date of the first publication (May 30, 2006) and the date of manuscript acceptance for the second publication (November 14, 2007).

I recently wrote to The Oncologist about the other puzzling feature of Figure 11, which is somewhat related [7]. There does not appear to be any censoring among the untreated subjects. Yet, in any ongoing study of survival with rolling entry, there is inevitably censoring. Recent entrants to the study are particularly likely to be censored, as they will only have a brief follow-up. In the authors’ figure, the impact of the rolling entry on early censoring is clear in the
survival curve for treated subjects—there are numerous vertical tick marks.

It is therefore a little mystifying why there is no censoring in the untreated group. One would anticipate that some subjects who received no treatment would still be in follow-up (and thus censored) purely because their diagnosis occurred very recently relative to the end date of follow-up. Given the ambient rate of censoring in I-ELCAP that can be gleaned from their 2006 publication (and shown here in Fig. 2 along with the follow-up time for the 13 untreated subjects), the probability that none of these subjects were censored is also numerically quite low. It is 1.6% (the product of the individual 13 probabilities of not being censored). Not impossible, but highly improbable.

Put together, I worry that the data incorporated into the figure may be biased in a manner that reduces the survival estimate for untreated subjects. If, for example, the I-ELCAP investigators were only capturing information on untreated subjects after they died, this would explain why all subjects in the graph died, and none were censored. But the problem with this approach is that study inclusion is associated with study outcome, and in this case the bias would ensure that the death rate is always 100% (because no new subjects are added until they die). If such a bias is not present in the treated subjects graph, then the difference in survival of the two groups will appear larger than it actually is.

Author’s Note (August 5, 2008): After the above letter was submitted and accepted by The Oncologist, Dr. Henschke reported, on July 30, 2008, that most of the original eight “untreated” subjects described in the 2006 paper had been misclassified—there were only three actual patients with clinical stage I lung cancer at diagnosis in that study.
The other five had advanced cancer at the time of diagnosis, not stage I cancer as the original report stated. This misclassification would not explain the absence of censoring in Figure 11.

Figure 2. Probability of not being censored (curve) based on follow-up time along with the follow-up for each of the 13 “untreated subjects” in the International Early Lung Cancer Action Project (arrows).

REFERENCES


