Fixation Time Does Not Affect the Expression of Estrogen Receptor

To the Editor

We read with high interest the article by Ibarra et al\(^1\) in the Journal. The authors are to be congratulated for taking the initiative to add to the literature of fixation time for hormone receptors. However, the article that is published in the Journal is essentially a data point and not a valid scientific study.

The authors used breast cancers from 10 patients, all of whom are high expressers of estrogen receptor (ER). The authors processed these specimens on an accelerated tissue processor program that uses heat enhancement. For this article to be scientifically and clinically useful and not misleading, the authors need to include patients who have intermediate to low expression of ER, which comprises about one third of all patients with breast cancer. In addition, results from the processor used in the study must be compared with those from a conventional tissue processor (nonaccelerated, without heat enhancement).

The specimens used in this study were hand-carved to simulate breast core biopsy specimens, but we submit that they are not truly representative of breast core biopsy specimens that are procured by radiology. Radiology-procured breast biopsy specimens are typically fatty, 11-gauge, vacuum-assisted biopsy specimens that provide obstacles to fixation. They are not simple bare fragments of tumor tissue. They vary from 1.0 to 2 cm in length and vary in width, so to assume that the fabricated tissue in this study mirrors the real world is simply erroneous. In addition, most predictive/prognostic markers in the United States are performed on breast core biopsy specimens. Finally, progesterone receptor and HER-2/neu studies also need to be performed on the very same tissues. The authors make no attempt to mention this specific, critical need, a very serious and misleading flaw in this article.

To summarize, the paper by Ibarra et al\(^1\) is a data point, not a scientific, clinically useful study. We are hoping that a busy pathologist will not rely on the abstract content without reading the entire article. The abstract content alone is very misleading. It implies that a 1-hour fixation is adequate for hormone receptor studies.
Finally, in their discussion, Ibarra et al.\textsuperscript{1} attack the recommendations of the ad hoc group that formulated the recommendations for hormone receptor testing. Those recommendations were based on a combination of the evidence that existed at the time and the lack of evidence at the time. The cautionary signals that arose from the recommendations were a part of the real-world experience of hormone receptor testing, given the recent debacle in Newfoundland, Canada, and data from clinical trials that showed discrepancy of ER with central testing.

Hormone receptor testing and other predictive prognostic markers in breast cancer are highly complex

Reference

The Authors' Reply
We appreciate the interest of Drs. Dabbs and Bhargava in our article.\textsuperscript{1} However, it should be noted that this article was submitted as a pilot study, as indicated in the first line of the abstract, and addressed 1 preanalytic variable in ER immunohistochemical testing. Of course, further validation is warranted, including examination of cases with intermediate and low expression of ER.

The criticism of our selection of tissue processing was not well founded. The heated formalin stage of processing was bypassed and the only “heat enhancement” was in the paraffin station and is the same as we use for our standard longer process.

It may be true that the samples in this study were not totally equivalent to core biopsy fragments. However, the point of the exercise was to test tumor tissues sufficiently thin to simulate the penetration of the formalin in core biopsy specimens. Most image-directed core biopsy specimens from solid tumors at our institutions are essentially devoid of fat, quite similar to the tumor tissues processed in our study. By using geometrical considerations alone, our square “hand-carved” samples would seem to pose no more or less of a barrier to formalin penetration than cylindrical samples of equal thickness (up to 10 gauge). The choice of needle size for image-directed biopsies is quite variable, and frequently cores smaller than 11 gauge are obtained for solid tumor masses. The length of the core biopsy is irrelevant in affecting adequacy of fixation and processing.

Core biopsies performed for microcalcifications can be a different story; those, we agree, tend to be fatty fragments up to 8 gauge in diameter for which fixation and processing times may need to be lengthened.

References