Supplementary Online Content


**eAppendix.** Details of Statistical Analysis

This supplementary material has been provided by the authors to give readers additional information about their work.
eAppendix

Details of Statistical Analysis

We performed single predictor modeling to assess the association between specific ultrasound characteristics and cancer status using generalized estimating equations, with a compound symmetry (exchangeable) correlation structure to account for the correlated outcomes between multiple nodules within a patient. For variables that were statistically significant in single predictor model based on a 2-sided nominal significance level of $\alpha = .05$, we calculated diagnostic accuracy statistics. The estimates and confidence intervals for the accuracy statistics were generated directly from the data on the individual nodules without consideration that there may have been multiple nodules within a subject and each nodule was assumed to be independent of all other nodules. Consequently, the confidence intervals for nodule level accuracy estimates will be narrower than if within-subject correlation had been explicitly accounted for.

Alternative Analyses

We performed several sensitivity analyses to determine whether implicit assumptions in the primary analysis were reasonable. The primary analysis included all benign nodules as a single group; included all patients followed for a minimum of 2 years during which a cancer could be diagnosed; defined the sensitivity at two years; and included all cancers diagnosed up to 6 years following ultrasound. For our secondary analyses, we restricted benign nodules to those that occurred in the control group; lengthened the minimum follow up to 3 years; assessed the impact of defining the sensitivity at 12 and 36 months; and limited our inclusion of cancers to those diagnosed within 2 years of the ultrasound.