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Reduced Surgery Through Afirma GEC: Impact to Date and Potential for the Future

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OBJECTIVES

Afirma GEC benign results indicate a low risk of malignancy and offer the opportunity of clinical observation in lieu of diagnostic surgery for cytologically indeterminate thyroid nodules. Here we estimate the global impact of Afirma since its commercial launch, and speculate on the impact of raising its specificity while maintaining its high sensitivity.

METHODS

Veracyte quantified all Afirma GEC test results from January 1, 2011 through September 30, 2016. MTC and Parathyroid Classifier positive results were counted. PubMed was reviewed through November 21, 2016 for publications reporting surgical rates among Afirma GEC benign patients. The impact of improving the GEC specificity on further ruling-out patients from surgery was modeled.

RESULTS

The Afirma GEC has been performed on samples from 66,325 thyroid nodules. Considering adequate samples, Afirma GEC was benign in 27,154 (44.5%). Among 18 published studies evaluating 1554 patients tested with the GEC, 9.9% of GEC benign patients underwent surgery.[1-18] Extrapolation of this rate to all GEC benign results suggests that approximately 24,466 patients may have been spared surgery as a result of the GEC and more than $255M in surgical costs may have been averted (Figure 1). The MTC and Parathyroid Classifiers are included with each GEC test, and are also available for patients with SFM and M cytology. Positive results have occurred for the MTC classifier and the Parathyroid classifier in 246 and 375 nodules, respectively (Figure 2).

DISCUSSION

More than 27,000 Bethesda III/IV thyroid nodules have been reclassified as molecularly benign since the introduction of Afirma, facilitating consideration of clinical observation instead of diagnostic surgery in the great majority. Additionally, 621 nodules were identified as likely harboring MTC or parathyroid tissue in the biopsied nodule, a result likely to significantly improve patient care. Efforts are underway to improve the GEC specificity. Assuming a 24% prevalence of malignancy and maintaining the same test sensitivity (90.2%), improving test specificity from its current 51.6% to 65% or 75% would result in a rise in the rate of GEC benign results to 52% and 59%, respectively (Table 1). For each 1% rise in specificity there is an absolute gain in benign test results of 1 minus the prevalence of malignancy (e.g. 0.76%, if prevalence of malignancy is 24%).

CONCLUSION

Maintaining high test sensitivity while improving test specificity is expected to identify even more patients unlikely to benefit from surgical resection, and raise the test's positive predictive value. An enhanced version of the Afirma GEC is predicted to benefit a higher percentage of patients and increase its cost-effectiveness.

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FIGURE 1.

Estimated Unnecessary Surgeries Avoided

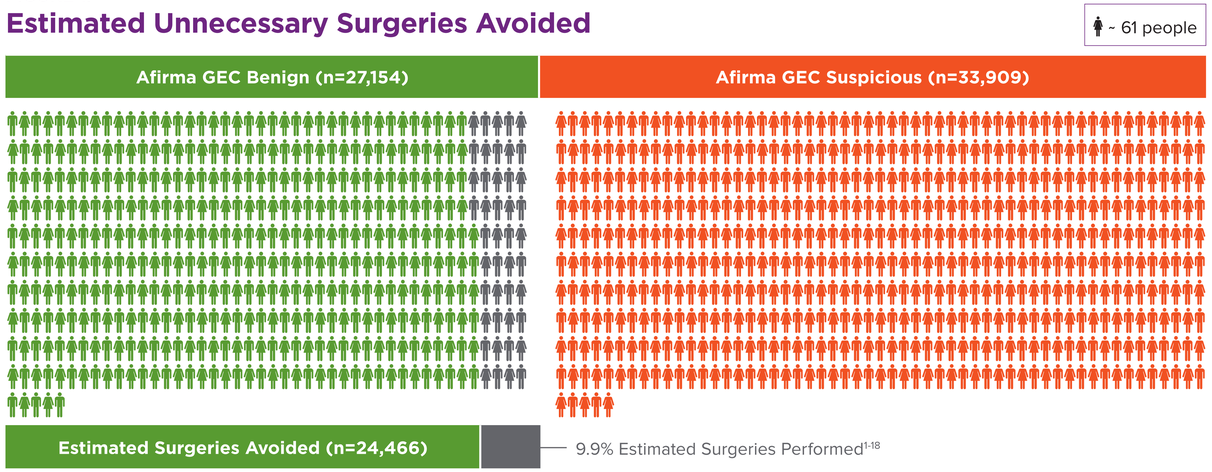

FIGURE 2.

Rare Neoplasm Identification with Afirma GEC

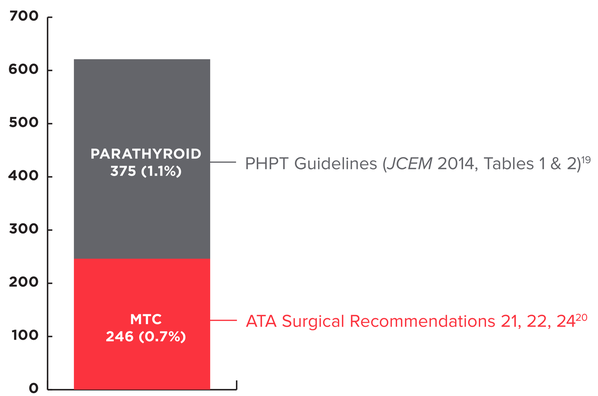

TABLE 1.

Effect of Increasing Specificity

Specificity	Benign Call Rate
52%	42%
65%	52%
75%	59%

Disclosure: Dr. Patel: Received Speaker's Honoraria from Veracyte; Dr. Kloos: Veracyte employee and equity owner