

## The 21-gene breast cancer assay in small (<1cm) tumors

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**Background:** Tumor size is a clinicopathologic factor often used in early stage breast cancer (EBC) management to estimate prognosis and make decisions about therapy. While in general, small tumors have a lower chance of recurring than large tumors, some patients with small tumors have poor outcomes. The 21-gene breast cancer assay (OncotypeDX) yields a Recurrence Score result that predicts the 10-yr risk of distant recurrence (DR) and the likelihood of chemotherapy (CT) benefit in patients (pts) with ER+ EBC. This study reviews the clinical evidence and experience of the 21-gene assay in subcentimeter (subCM) tumors and shows that the Recurrence Score is more reflective of the underlying tumor biology. **Methods:** A meta- analysis of Genomic Health validation and supportive studies reporting Recurrence Score result and tumor size was conducted in order to describe the distribution of Recurrence Score results. **Results:** There were 10 GHI-sponsored studies (7,094 pts) that presented Recurrence Score results as a function of tumor size. The studies varied in the recorded tumor sizes, ranging from  $\leq 0.5$  cm to  $> 5$  cm. Four studies specifically examined the distribution of Recurrence Score results in subCM tumors and identified a total of 629 pts out of 2,912 pts (21.6%) that fit the size criteria of  $< 1$ cm. A broad distribution of score results was observed in subCM tumors in the four studies combined: 61% low, 25% int, 15% high. **Conclusions:** These results demonstrate that not all pts with subCM tumors have low risk disease, and that the 21- gene assay can help inform the risk of DR more precisely as well as predict the likelihood of CT benefit. Approximately 40% of pts had intermediate or high score results, suggesting an increased potential for DR and CT benefit. The clinical implications of this meta-analysis are that size doesn't tell the whole story. There is underlying biology reflected in the Recurrence Score that can better inform the treatment decision for pts with ER+ EBC.

Study (N pts with tumor <1cm)	Low-risk RS (%)	Intermediate-risk RS (%)
GHI Kaiser (242)	61	21
NSABP-B20 (110)	64	20
NSABP-B14 (109)	60	25
GHI Breast Registry (168)	60	32