

2007 ASCO Breast Cancer Symposium – Abstract #88

A Kaiser-Permanente population-based study of ER and PR expression by the standard method, immunohistochemistry (IHC), compared to a new method, quantitative reverse transcription polymerase chain reaction (RT-PCR)

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Introduction: Accurate and precise measurement of ER and PR is of significant therapeutic importance in breast cancer. To evaluate quantitative RT-PCR assessment of ER and PR by *Oncotype DX*[™] as an alternative to IHC we compared central lab IHC to central lab RT-PCR

Methods: Breast cancer specimens from the Kaiser *Oncotype DX* study (Habel et al, Breast Can Res 2006) were evaluated by IHC for ER (SP1) (Cheung et al, JCO 2006) and PR (636) using 1% staining for positivity. Standardized quantitative RT-PCR analysis for ER and PR was performed using pre-defined cutoffs of 6.5 and 5.5 units, respectively, for positivity. Hormone receptor (HR) positivity was defined as ER and/or PR positive.

Results: Evaluable data was obtained in 607 pts (94% of the published cohort). A two-by-two table (below) compares IHC versus RT-PCR. The overall concordance (95% CI) between IHC and RT-PCR was 96% (94%-97%) for ER, 90% (87%-92%) for PR, and 95% (93%-97%) for HR (all p<0.0001). The kappa (95% CI) between IHC and RT-PCR was 83% (77%-89%) for ER, 76% (70%-82%) for PR, and 81% (75%-88%) for HR (all p<0.0001). Of the 20 discordant pairs that are ER negative by IHC but ER positive by RT-PCR, 17 (85%) are within 1 unit of the 6.5 cutoff. Of the 38 discordant pairs that are PR negative by IHC but PR positive by RT-PCR, 23 (61%) are within 1 unit of the 5.5 cutoff. Of the 7 discordant pairs that are ER positive by IHC but ER negative by RTPCR, 6 (86%) are within 1 unit of the 6.5 cutoff. Of the 22 discordant pairs that are PR positive by IHC but PR negative by RT-PCR, 19 (86%) are within 1 unit of the 5.5 cutoff.

Conclusions: There is a high degree of overall concordance between central IHC and central RT-PCR for ER, PR and HR status. RT-PCR by *Oncotype DX* for ER, PR and HR status is an alternative to IHC.

	<u>ER+</u> <u>IHC</u>	<u>ER-</u> <u>IHC</u>	<u>Total</u> <u>RT-PCR</u>	<u>PR+</u> <u>IHC</u>	<u>PR-</u> <u>IHC</u>	<u>Total</u> <u>RT-PCR</u>	<u>HR+</u> <u>IHC</u>	<u>HR-</u> <u>IHC</u>	<u>Total</u> <u>RT-PCR</u>
<u>RT-PCR+</u>	501	20	521	403	38	441	502	22	524
<u>RT-PCR-</u>	7	79	86	22	144	166	7	76	83
<u>Total IHC</u>	508	99	607	425	182	607	509	98	607