

30th Annual San Antonio Breast Cancer Symposium -- Abstract #3028

**Gene expression by standardized quantitative RT-PCR in the special histologic subtypes of estrogen receptor positive invasive breast cancer.**

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**Background:** Most invasive breast cancers are characterized histologically as ductal, lobular, or mixed. We report here the gene expression profiles obtained by the 21 gene *Oncotype DX*<sup>TM</sup> assay in these cancers and in the special histologic subtypes.

**Material and Methods:** 25,475 tumors tested in the Genomic Health laboratory from July 2005 through April 2007 were ER positive by RT-PCR (ER  $\geq 6.5$  units). Academic surgical pathologists reviewed specimens for invasive carcinoma and histologic subtyping using World Health Organization criteria (IARC 2003). Quantitative expression of 16 cancer-related genes was measured using RT-PCR by *Oncotype DX* on a scale from 0 to 15 (relative to 5 reference genes), where a one unit increment is associated with a 2-fold change in expression. Recurrence Score (RS) was calculated using the published equation. The proliferation index (PI), a component of the RS, was calculated as the average of the expression of the five proliferation genes (CCNB1, Ki-67, MYBL2, STK15, and Survivin). Descriptive statistics for the RS, gene groups, the individual genes among the different subtypes were obtained.

**Results:** The vast majority of the cancers (94.5%) were ductal, lobular, or mixed. RS's, quantitative ER, and quantitative proliferation for each subtype are shown in the table below. For all subtypes including the rarer ones, a wide range of RS's was observed, and included all three RS risk categories. The RS, on average, was lower for the classic lobular, solid/alveolar lobular, mixed ductal/lobular, tubular, cribriform, mucinous, and papillary subtypes and was higher for the and medullary-like subtype. Medullary-like tumors (4 of 1000 cases) generally had lower ER and higher proliferation gene expression, which may make them more responsive to chemotherapy. Tubular cancers (9 of 1000 cases) rarely had high RS's, related in part to lower proliferation gene expression. The lower average ER expression for tubular cancers in this cohort may reflect submission of selected cases and not typical high ER cases for RS testing. The proportion of cases with RS < 18, RS 18 – 30, and RS  $\geq 31$  and group gene expression values will also be presented.

**Discussion:** There is considerable variation in gene expression, as quantified by the *Oncotype DX* assay, both within and between the special subtypes of invasive breast cancer in this large observational cohort of estrogen receptor positive tumors.

Subtype	% of	RS	RS	RS	Quantitative ER	Proliferation
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	cases	(median)	(min)	(max)	(median)	Index (median)
Ductal	79.9	18.2	0	91	9.7	5.3
Lobular, classic	9.3	17.5*	0	65	9.5*	5.0*
Lobular, solid/alveolar	1.4	16.1*	0	62	10.5*	5.7*
Lobular, pleomorphic	0.7	18.9	1	71	9.6	5.3
Mixed	3.3	17.4*	0	80	9.7	5.2*
Tubular	0.9	15.2*	3	32	9.2*	4.3*
Cribriform	0.4	13.7*	0	54	10.1*	5.1*
Mucinous	3.2	16.6*	0	73	10.1*	5.2*
Micropapillary	0.4	20.0	0	74	10.1	5.8*
Medullary-like	0.4	33.1*	9	85	9.1*	6.5*
Papillary	0.2	7.8*	0	58	11.4*	5.7*

\*Significantly different compared to ductal (p<0.05)