Multigene Signature Methods and Results (SSF22 and 23) in Breast Cancer

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Background and Methods

Multigene signature methods (SSF22) and results (SSF23) for breast cancer (BCa) have been required for collection by SEER since 2010. Oncotype DX is the most widely used multigene signature assay in the United States and is included in oncology clinical practice guidelines for identifying women with early stage (node negative, hormone receptor positive, HER2 negative, tumor size > 0.5cm) BCa since 2008. Oncotype DX has been validated for risk stratification of distant recurrence and to predict the benefit of chemotherapy for node negative (LN-), hormone receptor positive (HR+) disease in 2004; for node positive disease (LN+) in 2008, and for ductal carcinoma in situ (DCIS) in 2011.
The objective of this study is to assess availability of SSF 22 and SSF 23, quality of manual data collection and testing according to guidelines among BCa patients.

We analyzed cases diagnosed with female BCa in 2010-2012 from SEER 18, for the November 2014 submission. Since the oncology practice guidelines recommended only Oncotype Dx at the time the cases were diagnosed we focused majority of the analysis in this report on the latter test. Cases were categorized whether or not they met the NCCN or ASCO guideline criteria for testing. The Oncotype Dx Recurrence Score (RS) risk categories were defined as: low (SSF 23 code 0-17 plus code 200), intermediate (codes 18-30 + 300) and high (codes 31-100 + 400).

Results

SSF22 was available for 12.1% of female BCa cases diagnosed in 2010-2012 (Table 1). The majority of the tests were Oncotype DX (93.5%), 2.8% had MammaPrint, 2.6% were other tests and in 1.1% with a test performed no specific test name was reported. Among cases that met the NCCN guidelines criteria, 27.4% had the testing, ranging from 23.2% in 2010 to 30.2% in 2012 (Table 2). Few of the cases among those that did not meet the guideline criteria had the test. Table 2 lists categories of cases outside guidelines that had the test. The largest proportion was in lymph node positive (LN+) BCa.
Out of 25,719 Oncotype Dx tested cases 80-83% were performed in accordance with clinical oncology practice guidelines, and 17-20% were not (Table 3). Concerning BC subtypes, 89.8% were HR+/HER2- (as guidelines recommend), 3.2% were HR+/HER2+, 1.7% were triple negative, 0.4% were HER2+/HR- and in 4.9% the subtype was unknown.
The overall distribution of Recurrence Score (RS) risk categories was: 56.7%, 31.0% and 12.3% in the low, intermediate and high risk groups. RS risk categories did not differ in LN- and LN+ cases (Figure 1) and according to tumor size (data not shown) but tumor grade was varying significantly with well and moderately differentiated cancers having low risk RS and poorly and undifferentiated cancer more likely to have high risk RS (Figure 3).
Table 4 shows discrepancies between SSF 22 and SSF 23 (in red). Eighty four percent of the Oncotype Dx test was reported with the actual recurrence score, 10% with risk categories and the rest did not have test results. The latter reflects the laboratory practice of not generating/reporting results in HR-, HER2+ cancers or when the tissue sample is not analyzable.

Discussion and Conclusion

- The availability of prognostic and predictive markers in cancer registry data should always be examined in the light of oncology guidelines and standard of care.
- The majority of BCa Oncotype Dx testing met the criteria for testing set in clinical guidelines but there are significant uses of the testing outside the guidelines in the data.
- Smaller proportion of cases with Oncotype Dx testing was in the high risk group compared to published literature reflecting differences between the population and clinical trials participants and demonstrating the importance of cancer population level data.
- The quality of manually collected data appears good though completeness cannot be ascertained from this data. SEER just completed a linkage of Oncotype Dx provided by the laboratory that performs the test and will be able to assess quality and completeness of manually collected data and the feasibility of automated collection in much detail in the near future.

Results: Tables and Figures

Table 1. Distribution of breast cancer cases by Site Specific Factor (SSF) 22 and year of diagnosis

SSF 22 code	Code description	Dx year 2010 N (%)	Dx year 2011 N (%)	Dx year 2012 N (%)	Total N (%)
10	Oncotype Dx	6,921 (9.5%)	8,722 (11.5%)	10,076 (13.1%)	25,719 (11.4%)
20	MammaPrint	166 (0.2%)	204 (0.3%)	396 (0.5%)	766 (0.3%)
30	Other	169 (0.2%)	267 (0.4%)	266 (0.3%)	702 (0.3%)
40	Test performed; name unknown	162 (0.2%)	93 (0.1%)	42 (0.1%)	297 (0.1%)
998	Test not done	41,251 (56.4%)	37,036 (48.8%)	36,935 (48%)	115,222 (51%)
999	Unknown	24,475 (33.5%)	29,521 (38.9%)	29,206 (38%)	83,202 (36.8%)
Total		73,144 (100%)	75,843 (100%)	76,921 (100%)	225,908 (100%)

Table 3. Number and proportion of Oncotype Dx tests performed per guidelines and outside guidelines

	2010 cases N (%)	2011 cases N (%)	2012 cases N (%)	2010-2012 cases N (%)
All Oncotype Dx tests in female BCa cases	6,921	8,722	10,076	25,719
Testing per guideline				
Met NCCN guideline for testing*	5,468 (79.0)	6,931 (79.5)	8,059 (80.0)	20,458 (79.5)
Loosely met NCCN guideline criteria**	5,793 (83.7)	7,286 (83.5)	8,404 (83.4)	21,483 (83.5)
Met 2007 ASCO guideline(LN-, ER+, stage I-II)	5,688 (82.2)	7,093 (81.3)	8,077 (80.2)	20,858 (81.1)
Not meeting the guidelines for testing:				
Positive Lymph nodes	641 (9.3)	831 (9.5)	975 (9.7)	2,447 (9.5)
Metastatic disease	40 (0.6)	28 (0.3)	45 (0.4)	113 (0.4)
HR negative	104 (1.5)	119 (1.4)	121 (1.2)	344 (1.3)
HER2 positive	261 (3.8)	279 (3.2)	253 (2.5)	793 (3.1)
In situ	62 (0.9)	125 (1.4)	253 (2.5)	440 (1.7)

* Lymph nodes (LN) pN0 or pN1mi, Hormone receptor (HR) positive, HER2 negative, tumor stage T1, T2 or T3 and tumor size > 0.5cm,

** LN N0, N1mi or unknown, HR+, borderline or unknown, HER2- or unknown

Table 2. Oncotype DX in breast cancer cases that met and did not meet the clinical practice guidelines for testing

	Cases dx 2010		Cases dx 2011		Cases dx 2012		Cases dx 2010-2012	
	N	OncotypeDX N (%)	N	OncotypeDX N (%)	N	OncotypeDX N (%)	N	OncotypeDX N (%)
All female BC cases	73,144	6,921 (9.5)	75,843	8,722 (11.5)	76,921	10,076 (13.1)	225,908	25,719 (11.4)
Testing per guideline								
Met NCCN guideline for testing*	23,584	5,468 (23.2)	25,270	6,931 (27.4)	26,723	8,059 (30.2)	75,577	20,458 (27.1)
Loosely met NCCN guideline criteria**	31,365	5,793 (18.5)	33,057	7,286 (22.0)	34,074	8,404 (24.7)	98,496	21,483 (21.8)
Met 2007 ASCO guideline (LN-, ER+, stage I-II)	29,669	5,688 (19.2)	31,309	7,093 (22.7)	32,779	8,077 (24.6)	93,748	20,858 (22.2)
Not meeting the guidelines for testing								
Positive lymph nodes	17,784	641 (3.6)	17,996	831 (4.6)	17,902	975 (5.4)	53,682	2,447 (4.6)
Metastatic disease	4,978	40 (0.8)	4,954	28 (0.6)	4,859	45 (0.9)	14,791	113 (0.8)
HR negative	10,725	104 (1.0)	11,119	119 (1.1)	10,814	121 (1.1)	32,658	344 (1.1)
HER2 positive	8,243	261 (3.2)	8,391	279 (3.3)	8,887	253 (2.8)	25,521	793 (3.1)
In situ	14578	62 (0.4)	15,135	125 (0.8)	15,187	253 (1.7)	44,900	440 (1.0)

* Lymph nodes (LN) N0 or N1mi, Hormone receptor (HR) positive, HER2 negative, tumor stage T1, T2 or T3 and tumor size > 0.5cm,

** LN N0, N1mi or unknown, HR+, borderline or unknown, HER2- or unknown

Table 4. Discrepancies between SSF22 and SSF23 (in red)

SSF22		SSF 23 Test Results					
Code	Code description	Score (Codes 0-100)	Risk Category (codes 200-400)	Test ordered; results not in chart (code 997)	Test not done (code 998)	Unknown (code 999)	Total
10	OncotypeDx	21,659	2,569	1,076	0	415	25,719
20	MammaPrint	37	648	56	0	25	766
30	Other	170	366	75	0	91	702
40	Test done; type unknown	27	33	185	0	52	297
998	Test not done	0	0	0	115,222	0	115,222
999	Unknown	74	27	56	0	83,045	83,202
Total		21,967	3,643	1,448	115,222	83,628	225,908

Figure 1. Distribution of Recurrance Score risk categories in LN+ and LN- cases

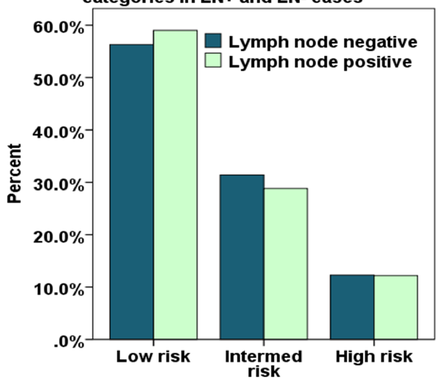
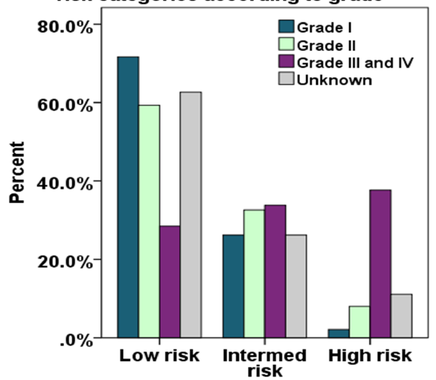


Figure 2. Distribution of Recurrance Score risk categories according to grade



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