Impact of the Breast Cancer Index for Extended Endocrine Decision-Making: First Results of the Prospective BCI Registry Study

Tara B. Sanft, MD[1]; Jenna Wong, MS[2]; Brandon O'Neal, MS[2]; Natalia Siuliukina, PhD[2]; Rachel C. Jankowitz, MD[3]; Mark D. Pegram, MD[4]; Jenny R. Fox, MD[5]; Yi Zhang, PhD[2]; Kai Treuner, PhD[2]; and Joyce A. O'Shaughnessy, MD[6]

ABSTRACT

Background: The Breast Cancer Index (BCI) test assay provides an individualized risk of late distant recurrence (5–10 years) and predicts the likelihood of benefitting from extended endocrine therapy (EET) in hormone receptor–positive early-stage breast cancer. This analysis aimed to assess the impact of BCI on EET decision-making in current clinical practice. **Methods:** The BCI Registry study evaluates long-term outcomes, decision impact, and medication adherence in patients receiving BCI testing as part of routine clinical care. Physicians and patients completed pre-BCI and post-BCI test questionnaires to assess a range of questions, including physician decision-making and confidence regarding EET; patient preferences and concerns about the cost, side effects, drug safety, and benefit of EET; and patient satisfaction regarding treatment recommendations. Pre-BCI and post-BCI test responses were compared using McNemar's test and Wilcoxon signed rank test. **Results:** Pre-BCI and post-BCI questionnaires were completed for 843 physicians and 823 patients. The mean age at enrollment was 65 years, and 88.4% of patients were postmenopausal. Of the tumors, 74.7% were T1, 53.4% were grade 2, 76.0% were N0, and 13.8% were HER2-positive. Following BCI testing, physicians changed EET recommendations in 40.1% of patients ($P<.0001$), and 45.1% of patients changed their preferences for EET ($P<.0001$). In addition, 38.8% of physicians felt more confident in their recommendation ($P<.0001$), and 41.4% of patients felt more comfortable with their EET decision ($P<.0001$). Compared with baseline, significantly more patients were less concerned about the cost (20.9%; $P<.0001$), drug safety (25.4%; $P=.0014$), and benefit of EET (29.3%; $P=.0002$). **Conclusions:** This analysis in a large patient cohort of the BCI Registry confirms and extends previous findings on the significant decision-making impact of BCI on EET. Incorporating BCI into clinical practice resulted in changes in physician recommendations, increased physician confidence, improved patient satisfaction, and reduced patient concerns regarding the cost, drug safety, and benefit of EET.

J Natl Compr Canc Netw 2024;22(2):99–107
doi:10.6004/jnccn.2023.7087

[1]Yale School of Medicine, New Haven, CT; [2]Biotheranostics, A Hologic Company, San Diego, CA; [3]University of Pennsylvania, Philadelphia, PA; [4]Stanford Comprehensive Cancer Institute, Palo Alto, CA; [5]Rocky Mountain Cancer Center, US Oncology, Boulder, CO; and [6]Baylor University Medical Center, Texas Oncology, US Oncology, Dallas, TX.

Background

For women with early-stage hormone receptor (HR)–positive breast cancer, >50% of all recurrences occur after 5 years from diagnosis.[1,2] Because of this persistent risk of recurrence, multiple clinical trials have investigated the benefit of extended endocrine therapy (EET).[3–16] These trials have demonstrated that patients with HR-positive breast cancer who received EET had a modest 1% to 5% risk reduction in recurrence but experienced increased adverse cevents, such as bone and cardiovascular toxicities, endometrial cancer, and other side effects that impair quality of life.[3,4,10,14,17] In addition, 30% to 50% of HR-positive tumors are endocrine-resistant.[18] Previous findings further revealed that standard clinical prognostic factors are not predictive of benefit from EET.[13,16,19] Thus, there is a critical need for clinically validated biomarkers to provide personalized information to guide patient selection for EET.

The Breast Cancer Index (BCI) is a validated gene expression–based assay consisting of 2 components: the 5-gene Molecular Grade Index (MGI) and the 2-gene ratio HOXB13:IL17BR (H/I) that assess proliferative and estrogen signaling pathways in breast cancer, respectively. The BCI test report provides both a prognostic and predictive result. The BCI prognostic score is an algorithmic combination of MGI and H/I and reports the risk of overall (0–10 years) and late (5–10 years) distant recurrence. The predictive component is based on the H/I ratio, which has been shown to predict EET benefit across different adjuvant endocrine treatment regimens, including tamoxifen monotherapy, aromatase inhibitor (AI) monotherapy, and sequenced tamoxifen-AI.[19–24]

The BCI Registry study is an ongoing, prospective, large-scale, multicenter study investigating long-term clinical outcomes, decision impact, and medication adherence in patients with HR-positive early-stage breast cancer receiving BCI testing as part of routine clinical care. This study aimed to assess the impact of BCI on

Supplementary material is published online at https://doi.org/10.6004/jnccn.2023.7087

clinical decision-making regarding EET based on the first 1,000 patients enrolled in the BCI Registry study out of an enrollment goal of 3,000.

Methods

Patients and Study Design

Patients eligible for inclusion in the BCI Registry are women diagnosed with stage I–III HR-positive breast cancer with available pretreatment tumor specimens who completed 4 to 7 years of primary adjuvant endocrine therapy and remained recurrence-free. Patients with noninvasive breast tumors or with tumors that have spread to the chest wall and/or skin are ineligible. Enrollment started in April 2021 and will continue until at least 3,000 patients have been recruited. The study protocol was amended in 2023 to include blood collection from patients at enrollment and during annual follow-up visits.

To assess the impact of BCI on physician decision-making and overall patient satisfaction, both physicians and patients completed pre-BCI and post-BCI decision-impact questionnaires. The physician questionnaire assessed physician treatment recommendations regarding EET and physician confidence levels with decision-making. The patient questionnaire assessed patient preferences for EET; patient concerns about the cost, side effects, drug safety, and benefit of EET; and patient comfort levels regarding the treatment recommendation.

All clinical information and questionnaire responses were recorded and entered into an electronic data capture system. BCI testing was performed following receipt of the tumor specimen and test requisition form. The BCI results were discussed with the patient prior to completing the posttest questionnaire. This study was approved by the US Oncology Institutional Review Board, and all patients were required to provide written informed consent.

BCI Testing

BCI gene expression analysis by quantitative reverse transcription PCR was performed on formalin-fixed, paraffin-embedded tumor specimens in a CLIA-certified, College of American Pathologists–accredited laboratory (Biotheranostics) as previously described.[20,21] Briefly, macrodissection was performed on formalin-fixed, paraffin-embedded sections to enrich tumor content before RNA extraction. Total RNA was reverse-transcribed, and the cDNA was preamplified by PCR using the PreAmp Master Mix Kit (Thermo Fisher Scientific) before TaqMan PCR analysis. Calculation of BCI, MGI, and H/I was performed using prespecified cut-points as described previously.[20,21] The BCI test report includes 2 separate components: BCI Prognostic provides an individual risk of late (5–10 years) distant recurrence and a categorical risk group of either BCI low risk or high risk, and BCI Predictive reports a categorical prediction of BCI (H/I)-high versus BCI (H/I)-low likelihood of benefit from EET. The categorical risk cutoff for either low or high risk corresponds with a 4.9% risk of late distant recurrence for N0 disease and an 8.5% risk of late distant recurrence for N1 disease.

Statistical Analyses

Primary outcomes include a comparison of all decision-impact questionnaire items before and after BCI testing. Descriptive statistics were used to summarize and display the distribution of pre-BCI and post-BCI responses. McNemar's test was used to analyze changes in physician treatment recommendations. The Wilcoxon signed rank test was used to compare pre-physician and post-physician confidence, patient preferences, patient concerns, and patient comfort levels regarding the treatment recommendation. Because the amount of missing data was considered negligible (<4% for each questionnaire item), missing values were excluded from statistical analysis.

Results

Patient Characteristics

A total of 1,186 patients with HR-positive early-stage breast cancer were enrolled in the BCI Registry study from April 2020 through May 2021 (see Figure S1 in the supplementary material, available online with this article). BCI testing was completed for 1,156 patients with available clinical information. After excluding 83 patients due to pending data verification, 1,073 were included in this decision-impact analysis. The final analyzable cohort consisted of 843 patients with completed pre-BCI and post-BCI physician questionnaires and 823 patients with completed pre-BCI and post-BCI patient questionnaires.

Clinicopathologic characteristics for the BCI Registry cohort are presented in Table 1. Of the 1,156 patients, most were postmenopausal (88.4%; n=1,022), with mostly T1 tumors (74.7%; n=863) of grade 2 (53.4%; n=617) and negative nodal status (76.0%; n=878). Most patients had tumors with ductal histology (83.8%; n=969) and did not receive (neo)adjuvant chemotherapy (62.3%; n=720). All but 4 (99.7%; n=1,152) patients had estrogen receptor–positive cancers, 88.6% (n=1,024) had progesterone receptor–positive cancers, and 13.8% (n=159) had HER2-positive cancers. Regarding adjuvant endocrine therapy, 14.5% (n=168) received 5 years of tamoxifen monotherapy, 73.4% (n=849) received 5 years of AI monotherapy, and 11.7% (n=135) received sequential tamoxifen-AI therapy. Clinicopathologic characteristics for the 843 patients with completed physician questionnaires and 823 patients with completed patient questionnaires are similar (Table 1).

Table 1. Clinicopathologic Characteristics of BCI Registry Cohort and the Subsets With Completed Questionnaires

	Registry Cohort n (%)	Physician Response n (%)	Patient Response n (%)
Total, n	1,156	843	823
Age at enrollment			
<40 y	13 (1.1)	10 (1.2)	10 (1.2)
40–49 y	87 (7.5)	62 (7.4)	57 (6.9)
50–59 y	241 (20.8)	165 (19.6)	162 (19.7)
60–74 y	585 (50.6)	431 (51.1)	421 (51.2)
≥75 y	230 (19.9)	175 (20.8)	173 (21.0)
Menopausal status at enrollment			
Perimenopausal	22 (1.9)	18 (2.1)	18 (2.2)
Postmenopausal	1,022 (88.4)	742 (88.0)	727 (88.3)
Premenopausal	112 (9.7)	83 (9.8)	78 (9.5)
T stage			
T1	863 (74.7)	641 (76.0)	629 (76.4)
T2	268 (23.2)	189 (22.4)	181 (22.0)
T3	19 (1.6)	9 (1.1)	9 (1.1)
Unknown	6 (0.5)	4 (0.5)	4 (0.5)
Grade			
1	313 (27.1)	251 (29.8)	245 (29.8)
2	617 (53.4)	440 (52.2)	436 (53.0)
3	221 (19.1)	151 (17.9)	141 (17.1)
Unknown	5 (0.4)	1 (0.1)	1 (0.1)
Nodal status			
N0	878 (76.0)	680 (80.7)	663 (80.6)
N1	276 (23.9)	163 (19.3)	160 (19.4)
Unknown	2 (0.2)	0 (0.0)	0 (0.0)
ER status			
Negative	4 (0.3)	3 (0.4)	3 (0.4)
Positive	1,152 (99.7)	840 (99.6)	820 (99.6)
PR status			
Negative	131 (11.3)	85 (10.1)	80 (9.7)
Positive	1,024 (88.6)	758 (89.9)	743 (90.3)
Unknown	1 (0.1)	0 (0.0)	0 (0.0)
HER2 status			
Negative	980 (84.8)	721 (85.5)	702 (85.3)
Positive	159 (13.8)	110 (13.0)	107 (13.0)
Uncertain	17 (1.5)	12 (1.4)	14 (1.7)
Histologic type			
Ductal	969 (83.8)	702 (83.3)	684 (83.1)
Lobular	148 (12.8)	111 (13.2)	109 (13.2)
Other	39 (3.4)	30 (3.6)	30 (3.6)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)

(*continued on next page*)

Table 1. Clinicopathologic Characteristics of BCI Registry Cohort and the Subsets With Completed Questionnaires (cont.)

	Registry Cohort n (%)	Physician Response n (%)	Patient Response n (%)
Race			
White	847 (73.3)	618 (73.3)	603 (73.3)
Black	79 (6.8)	50 (5.9)	50 (6.1)
Hispanic	48 (4.2)	35 (4.2)	33 (4.3)
Asian	16 (1.4)	10 (1.2)	10 (1.2)
Other	162 (14.0)	127 (15.1)	122 (14.8)
Unknown	4 (0.3)	3 (0.4)	3 (0.4)
BMI			
Underweight/Normal	276 (23.9)	197 (23.4)	190 (23.1)
Overweight	384 (33.2)	283 (33.6)	276 (33.5)
Obese	481 (41.6)	356 (42.2)	350 (42.5)
Unknown	15 (1.3)	7 (0.8)	7 (0.9)
Surgery			
Lumpectomy	717 (62.0)	535 (63.5)	520 (63.2)
Mastectomy	438 (37.9)	307 (36.4)	302 (36.7)
Unknown	1 (0.1)	1 (0.1)	1 (0.1)
Ki-67 proliferation index			
<20	489 (42.3)	369 (43.8)	358 (43.5)
≥20	384 (33.2)	276 (32.7)	268 (32.6)
Unknown	283 (24.5)	198 (23.5)	197 (23.9)
Chemotherapy			
Adjuvant	308 (26.6)	212 (25.1)	210 (25.5)
Neoadjuvant	124 (10.7)	74 (8.8)	73 (8.9)
Both	3 (0.3)	3 (0.4)	3 (0.4)
None	720 (62.3)	553 (65.6)	536 (65.1)
Unknown	1 (0.1)	1 (0.1)	1 (0.1)
Radiation			
Yes	733 (63.4)	528 (62.6)	515 (62.6)
No	423 (36.6)	315 (37.4)	308 (37.4)
Prior adjuvant endocrine therapy			
Tamoxifen	168 (14.5)	118 (14.0)	111 (13.5)
AI	849 (73.4)	620 (73.5)	608 (73.9)
Sequential	135 (11.7)	101 (12.0)	101 (12.3)
Other	3 (0.3)	3 (0.4)	2 (0.2)
Unknown	1 (0.1)	1 (0.1)	1 (0.1)

Abbreviations: AI, aromatase inhibitor; BCI, Breast Cancer Index; BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor.

Classification by BCI

Of the 1,073 patients with reported BCI results, 658 (61.3%) were classified as BCI (H/I)-low and 415 (38.7%) as BCI (H/I)-high likelihood of EET benefit. Among patients with N0 disease, 450 (52.1%) were classified as low risk for late distant recurrence (5–10 years) and 414 (47.9%) as high risk. Among patients with N1 disease, 55 (26.3%) were classified as low-risk for late distant recurrence (5–10 years) and 154 (73.7%) as high risk. Combining patients with N0 and N+ disease, 505 (47.1%) were classified as low risk and 568 (52.9%) as high risk of distant recurrence.

When combining both prognostic and predictive results, 412 (38.4%) patients were classified as low risk/low likelihood to benefit, 93 (8.7%) as low risk/high likelihood to benefit, 246 (22.9%) as high risk/low likelihood to benefit, and 322 (30.0%) as high risk/high likelihood to benefit.

Physician Treatment Recommendations for EET by BCI Status

In patients classified as BCI (H/I)-high (n=317), 91.2% (n=289) were recommended to receive EET after BCI testing compared with 62.1% (n=197) before BCI testing. In contrast, only 18.3% (n=96) of patients classified as BCI (H/I)-low (n=526) were recommended for EET after BCI testing, compared with 53.6% (n=282) before BCI testing. A similar percentage of patients classified as high risk (n=427) was recommended for EET before (66.3%; n=283) and after BCI testing (65.8%; n=281). However, only 25.0% (n=104) of patients classified as low risk (n=416) were recommended for EET after BCI testing compared with 47.1% (n=196) before BCI testing. Overall, the percentage of patients recommended for EET decreased from 56.8% (n=479) before BCI testing to 45.7% (n=385) after BCI testing, whereas the percentage of patients not recommended for EET increased from 42.5% (n=358) before BCI testing to 53.5% (n=451) after BCI testing ($P<.0001$) (Table 2).

Changes in Physician Treatment Recommendations After BCI Testing

Prior to BCI testing, 479 of the 843 patients (56.8%) were recommended to receive EET by the physician. Following BCI testing, physicians changed treatment recommendations in 40.1% (n=338) of patients ($P<.0001$; Figure 1). Of these cases, 63.3% (n=214) of patients changed their recommendation from "yes EET" to "no EET," and 36.7% (n=124) changed their recommendation from "no EET" to "yes EET." In the cases with a recommendation change from "yes EET" to "no EET" (n=214), 130 (60.7%) patients were low risk/low likelihood to benefit, 74 (34.6%) were high risk/low likelihood to benefit, 6 (2.8%) were low risk/high likelihood to benefit, and 4 (1.9%) were high risk/high likelihood to benefit (Table 3). Of these cases, 98.1% (n=210) of patients were low risk and/or low likelihood to benefit. In the cases with a recommendation change from "no EET" to "yes EET" (n=124), 75 (60.5%) patients were high risk/high likelihood to benefit, 30 (24.2%) were low risk/high likelihood to benefit, 16 (12.9%) were low risk/low likelihood to benefit, and 3 (2.4%) were high risk/low likelihood to benefit. Of these cases, 87.1% (n=108) of patients were high risk and/or high likelihood to benefit.

Furthermore, BCI results corroborated the physician's initial EET recommendation in the remaining approximately 60% of patients (Table 3). In the cases with both an initial and final recommendation not to extend endocrine therapy (n=233), 160 (68.7%) patients were low risk/low likelihood to benefit, 59 (25.3%) were high risk/low likelihood to benefit, 8 (3.4%) were low risk/high likelihood to benefit, and 6 (2.6%) were high risk/high likelihood to benefit. Of these cases, 97.4% (n=227) of patients were low risk and/or low likelihood to benefit. In the cases with both an initial and final recommendation to extend endocrine therapy (n=259), 151 (58.3%) patients were high risk/high likelihood to benefit, 51 (19.7%) were high risk/low likelihood to benefit, 32 (12.4%) were low risk/high likelihood to benefit, and 25 (9.7%) were low risk/low likelihood to benefit. Of these cases, 90.3% (n=234) of patients were high risk and/or high likelihood to benefit.

Physician Confidence in EET Decision-Making

Following BCI testing, 38.8% (n=327) of physicians felt more confident in their recommendation for EET ($P<.0001$). The percentage of physicians having high confidence levels (confident or strongly confident) increased from 58.2% (n=490) before BCI testing to 80.5% (n=679) after BCI testing (Figure 2A). The percentage of physicians having low confidence levels (not at all confident, not confident, or ambivalent) decreased from 39.1% (n=330) before BCI testing to 18.8% (n=158) after BCI testing.

Impact of BCI on Patient Comfort Levels, Preferences, and Concerns

After BCI testing, 341 of 823 patients (41.4%) felt more comfortable with their EET decision ($P<.0001$) (Figure 2B).

Table 2. Pre- Versus Post-BCI Physician Treatment Recommendations for EET

		Pre-BCI Recommendation			Post-BCI Recommendation		
	All Patients (n=843) n (%)	No EET (n=358) n (%)	Yes EET (n=479) n (%)	Not Answered (n=6) n	No EET (n=451) n (%)	Yes EET (n=385) n (%)	Not Answered (n=7) n
Low risk/low likelihood to benefit	339 (40.2)	177 (49.4)	157 (32.8)	5	294 (65.2)	42 (10.9)	3
Low risk/high likelihood to benefit	77 (9.1)	38 (10.6)	39 (8.1)	0	14 (3.1)	62 (16.1)	1
High risk/low likelihood to benefit	187 (22.2)	62 (17.3)	125 (26.1)	0	133 (29.5)	54 (14.0)	0
High risk/high likelihood to benefit	240 (28.5)	81 (22.6)	158 (33.0)	1	10 (2.2)	227 (59.0)	3

Abbreviations: BCI, Breast Cancer Index; EET, extended endocrine therapy.

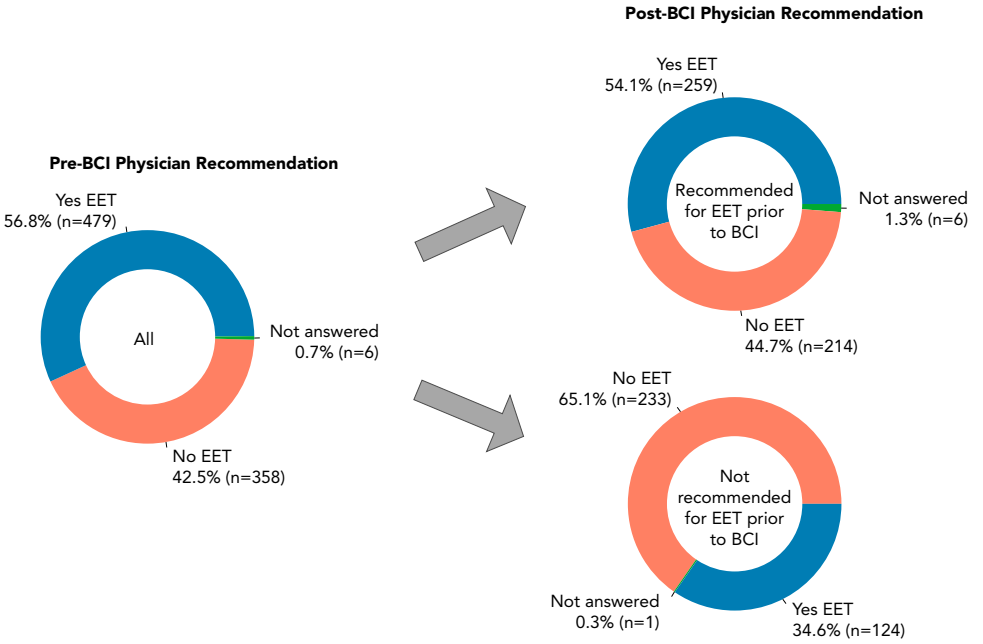

Figure 1. Physician pre-BCI and post-BCI test recommendation for EET.
Abbreviations: BCI, Breast Cancer Index; EET, extended endocrine therapy.

High comfort levels (comfortable, strongly comfortable) increased from 70.8% (n=582) to 84.0% (n=691), whereas low comfort levels (not at all comfortable, not comfortable, ambivalent) decreased from 28.9% (n=237) to 15.6% (n=128). Importantly, BCI results led to a 19.9% increase in patients feeling strongly comfortable with their EET decision.

After receiving BCI results, 45.1% (n=371) of patients changed their preferences for EET (see Supplementary Table S1). Of these cases, 70.9% (n=263) indicated a decreased preference for EET, and 29.1% (n=108) showed an increased preference for EET. Notably, changes in patient preferences for EET correlated with BCI test results. In BCI (H/I)-low patients, 46.9% (241/514) showed a decreased preference for EET ($P<.0001$), whereas in BCI (H/I)-high patients, 28.2% (87/309) showed an increased preference for EET ($P<.0001$). A total of 166 (63.1%) patients with a decreased preference for EET (n=263) were classified as low risk/low likelihood to benefit, 75 (28.5%) as high risk/low likelihood to benefit, 14 (5.3%) as high risk/high likelihood to benefit, and 8 (3.0%) as low risk/high likelihood to benefit. Conversely, 72 (66.7%) of patients with an increased preference for EET (n=108) were classified as high risk/high likelihood to benefit, 15 (13.9%) as low risk/high likelihood to benefit, 14 (13.0%) as high risk/low likelihood to benefit, and 7 (6.5%) as low risk/low likelihood to benefit.

Lastly, significantly more patients were less concerned about cost (20.9%; $P<.0001$), drug safety (25.4%; $P=.0014$), and the benefit of EET (29.3%; $P=.0002$; see Supplementary Figure S2). No significant change in concern regarding side effects was observed ($P=.1486$).

Table 3. BCI Prognostic and Predictive Categories by Pre-BCI to Post-BCI Treatment Recommendations for EET

		Pre-BCI to Post-BCI Recommendation for EET				
	All Patients (n=843) n (%)	**No to No (n=233) n (%)**	**No to Yes (n=124) n (%)**	**Yes to No (n=214) n (%)**	**Yes to Yes (n=259) n (%)**	**Not Answered (n=13) n**
Low risk/low likelihood to benefit	339 (40.2)	160 (68.7)	16 (12.9)	130 (60.7)	25 (9.7)	8
Low risk/high likelihood to benefit	77 (9.1)	8 (3.4)	30 (24.2)	6 (2.8)	32 (12.4)	1
High risk/low likelihood to benefit	187 (22.2)	59 (25.3)	3 (2.4)	74 (34.6)	51 (19.7)	0
High risk/high likelihood to benefit	240 (28.5)	6 (2.6)	75 (60.5)	4 (1.9)	151 (58.3)	4

Abbreviations: BCI, Breast Cancer Index; EET, extended endocrine therapy.

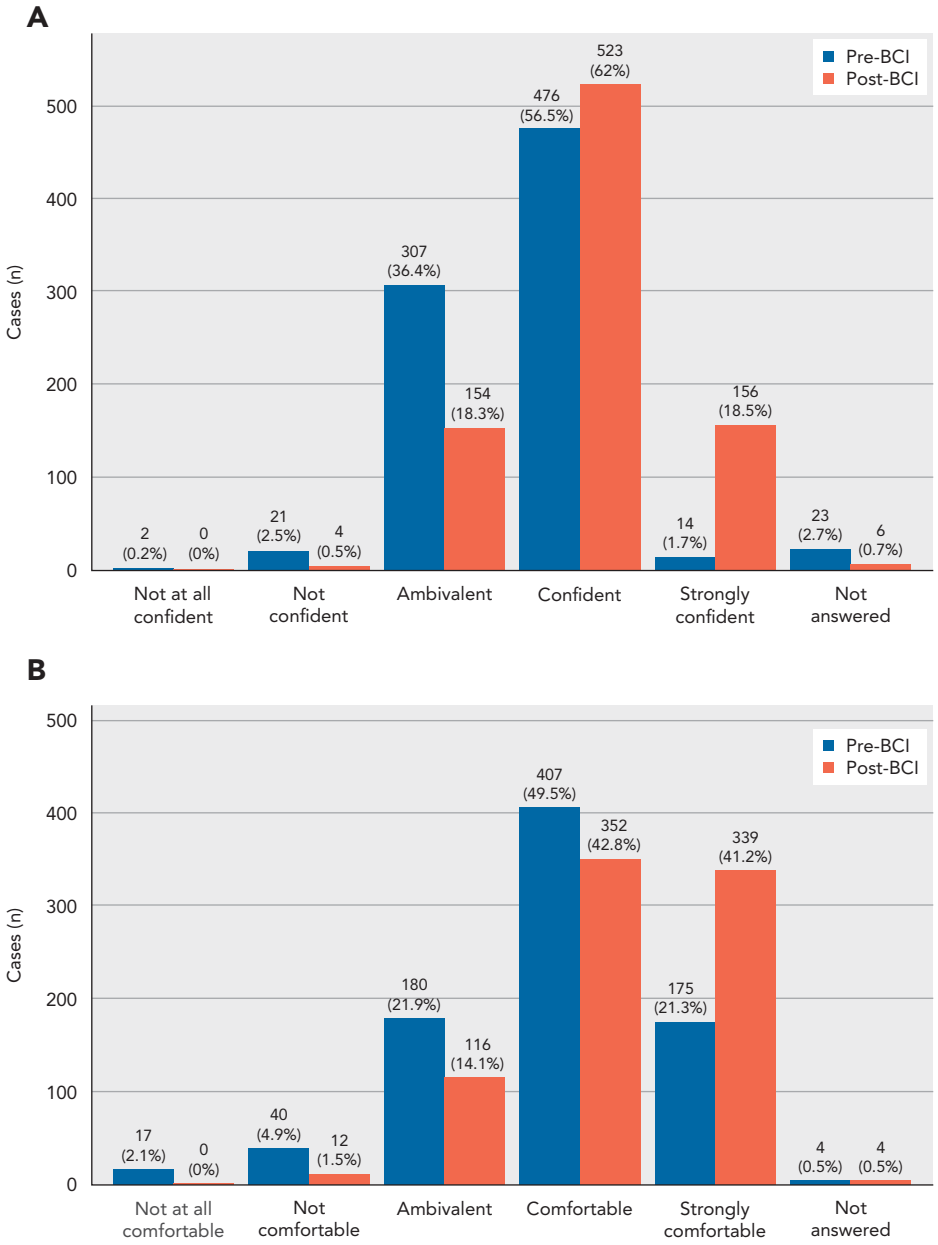

Figure 2. **(A)** Physician confidence levels pre-BCI and post-BCI test about EET decision. **(B)** Patient comfort levels pre-BCI and post-BCI test about EET decision.
Abbreviations: BCI, Breast Cancer Index; EET, extended endocrine therapy.

Discussion

This analysis of the prospective BCI Registry study assessed the impact of BCI on EET decision-making in current clinical practice. The results further substantiate that the use of BCI led to significant changes in physician treatment recommendations and patient preferences for EET, increased physician confidence, improved patient satisfaction regarding the treatment decision, and reduced patient concerns about the cost, drug safety, and benefit of EET. Notably, the results revealed that treatment recommendations by physicians for EET changed in >40% of patients informed by BCI. Most of the recommendation changes comprised patients who were recommended to stop EET after being considered for EET prior to BCI testing. Knowledge of the BCI results likely spared these patients from overtreatment and potentially serious adverse effects. BCI might also have been useful for the group of patients recommended to continue EET due to BCI predicting EET benefit after being initially considered to forgo EET. The net change in treatment decisions resulted in

46% of patients getting recommended for EET after BCI testing, compared with 57% of patients before BCI testing. Findings from this analysis further suggest that BCI not only informed physician EET decision-making in patients with a recommendation change but also supported decisions to remain on a course of treatment. Finally, >45% of patients changed their treatment preferences for EET. These results confirm that BCI testing meaningfully impacted both physician decision-making and patient preferences for EET.

The results from this analysis expand the findings of 2 previous BCI decision-impact studies. In these studies, treatment recommendations changed in 26% and 30% of patients, respectively.[25,26] Although these results were statistically significant, the decision-impact rate of 40% in this large BCI Registry study is meaningfully higher than previously reported. Additionally, in cases recommended for EET before BCI, 45% were not recommended to receive EET after BCI testing in the current study compared with 31% and 33% in previous studies. In cases not recommended for EET prior to BCI, 35% were recommended to receive EET, compared with 12% and 25% in the previous studies. In all 3 studies, physicians consistently reported being more confident about their treatment decision after knowing the BCI results. All 3 studies had cohorts with similar clinicopathologic characteristics, such as grade, stage, and nodal status.

BCI also had a favorable impact on patient perceptions regarding EET. Compared with baseline, a significant proportion of patients were less concerned about the cost, drug safety, and benefit of EET. Therefore, BCI could potentially improve medication adherence to EET in patients that decide to extend endocrine therapy. An analysis of medication adherence was incorporated into the BCI Registry, which may provide further insights. Although no significant change in patient concerns regarding side effects was seen, more patients were comfortable with their decision regarding EET.

These data underscore the importance of using both the prognostic and predictive BCI results to optimize endocrine therapy duration. As previous BCI validation studies indicate, the benefit of EET might not necessarily be proportional to the level of recurrence risk.[20,22,23] For example, in the IDEAL study, BCI (H/I) predicted the benefit of EET irrespective of traditional clinical risk factors, such as T stage and grade.[23] Although treatment recommendations are personalized, this analysis shows that physicians were more likely to prioritize the predictive results over the prognostic results when making treatment decisions. This is reflected in the percentage of patients with a final EET recommendation in each BCI category. Following BCI testing, 81% of patients with a low risk of recurrence and high likelihood of benefit were recommended to receive EET, compared with 95% of patients classified as high risk and high likelihood of benefit. In contrast, 29% of patients with a high risk of recurrence and low likelihood of benefit were recommended to receive EET, compared with only 12% of patients with a low risk of recurrence and low likelihood of benefit. The clinical implications of these findings are that BCI Predictive is distinctly impactful and that both BCI Prognostic and BCI Predictive results are informative in guiding treatment decisions for EET. This study further highlights the impact and use of BCI in clinical practice, which leading oncology guidelines such as those from NCCN and ASCO recognize as the only predictive genomic assay for making EET decisions.[27,28]

Our study has both strengths and limitations. The BCI Registry is a prospective, multi-institutional study and the largest study to evaluate the impact of BCI on physician decision-making around EET. Hence, these results more accurately demonstrate the use of BCI and its impact in current clinical practice than in previous studies. Some misreporting could be present because the decision-impact questionnaires were self-reported assessments. In addition, there were some missing data in each of the analyzed questionnaire items. Although it was a small proportion, it could produce biased estimates of the results.

Conclusions

Our findings support the use of BCI as an important clinical tool to select patients for EET based on an individualized risk/benefit analysis. Although both BCI Predictive and BCI Prognostic results were used to inform EET decision-making and patient preferences for EET, patient selection for EET was largely determined by the likelihood of benefit from EET rather than prognostic risk alone.

Submitted July 6, 2023; final revision received September 11, 2023; accepted for publication September 12, 2023. Published online March 4, 2024.

Author contributions: *Conceptualization:* Sanft, Jankowitz, Pegram, Fox, O'Shaughnessy. *Data analysis:* Wong, O'Neal, Siuliukina, Zhang, Treuner. *Methodology:* Zhang, Treuner. *Supervision:* Sanft, Jankowitz, Pegram, Fox, Zhang, Treuner, O'Shaughnessy. *Project administration:* Zhang, Treuner. *Visualization:* Wong, O'Neal, Siuliukina. *Writing—original draft:* Wong, O'Neal, Siuliukina, Zhang, Treuner. *Writing—review & editing:* Sanft, Jankowitz, Pegram, Fox, O'Shaughnessy.

Disclosures: J. Wong has disclosed owning stock or having ownership interest in Hologic. B. O'Neal has disclosed participating in research for, being employed by, and owning stock or having ownership interest in Biotheranostics. R.C. Jankowitz has disclosed serving as a scientific advisor for Biotheranostics; and serving on a BCI steering committee for Biotheranostics. M.D. Pegram has disclosed serving as a consultant for Biotheranostics. Y. Zhang has disclosed owning stock or having ownership interest in Hologic. K. Treuner has disclosed owning stock or having ownership interest in Hologic. J.A. O'Shaughnessy has disclosed serving as a scientific advisor for Agendia, Aptitude Health, AstraZeneca, Daiichi Sankyo, Eisai, GI Therapeutics, Genentech, Eli Lilly and Company, Novartis, Ontada, Pfizer Inc., Pierre Fabre Pharmaceuticals, Roche, Samsung Bioepis, Sanofi, Seagen, and Stemline Therapeutics; and serving as a consultant for Agendia, Aptitude Health, AstraZeneca, Daiichi Sankyo, Eisai, GI Therapeutics, Genentech, Eli Lilly and Company, Novartis, Ontada, Pfizer Inc., Pierre Fabre Pharmaceuticals, Roche, Samsung Bioepis, Sanofi, Seagen, and Stemline Therapeutics. The remaining authors have disclosed that they

have not received any financial consideration from any person or organization to support the preparation, analysis, results, or discussion of this article.

Supplementary material: Supplementary material associated with this article is available online at https://doi.org/10.6004/jnccn.2023.7087. The supplementary material has been supplied by the author(s) and appears in its originally submitted form. It has not been edited or vetted by *JNCCN*. All contents and opinions are solely those of the author. Any comments or questions related to the supplementary materials should be directed to the corresponding author.

Correspondence: Tara B. Sanft, MD, Survivorship Clinic, Yale School of Medicine, 333 Cedar Street, New Haven, CT 06520.
Email: tara.sanft@yale.edu

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