Original Article

Perceptions of Patients With Early Stage Breast Cancer Toward Research Biopsies

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BACKGROUND: The objective of this study was to describe the perspective of patients with early breast cancer toward research biopsies. The authors hypothesized that more patients at academic sites than at community-based sites would be willing to consider these procedures. **METHODS:** In total, 198 patients with early stage breast cancer were recruited from 3 academic centers (n = 102) and from 1 community oncology practice (n = 96). The primary objective was to compare the proportion of patients willing to consider donating excess tissue biospecimens from surgery, from a clinically indicated breast biopsy, or from a research purposes-only biopsy (RPOB) between practice types. **RESULTS:** Most patients (93% at academic sites, 94% at the community oncology site) said they would consider donating excess tissue from surgery for research. One-half of patients from academic or community sites would consider donating tissue from a clinically indicated breast biopsy. On univariate analysis, significantly fewer patients from academic sites would consider an RPOB (22% at academic sites, 42% at the community site; $P = .003$); however, this difference was no longer significant on multivariate analysis ($P = .96$). Longer transportation times and unfavorable prior experiences were associated with less willingness to consider an RPOB on multivariate analysis. Significantly fewer patients from academic sites (14%) than from the community site (35%) would consider a research biopsy in a clinical trial ($P = .04$). Contributing to scientific knowledge, return of results, and a personal request by their physician were the strongest factors influencing patients' willingness to undergo research biopsies. **CONCLUSIONS:** The current results rejected the hypothesis that more patients with early breast cancer at academic sites would be willing to donate tissue biospecimens for research compared with those at community oncology sites. These findings identify modifiable factors to consider in biobanking studies and clinical trials. ***Cancer* 2021;127:1208-1219**.

KEYWORDS: biospecimen ethics, breast cancer, patient perspectives, research biopsy, survey study.

INTRODUCTION

There is a growing effort to correlate findings on a percutaneous biopsy, both initially and on-treatment, with clinical outcomes to maximize tradeoffs between efficacy and toxicity and to increase our understanding of therapeutic resistance. Although diagnostic percutaneous biopsies are clinically indicated to confirm the presence of cancer and directly influence clinical management, research biopsies often involve the collection of tissue with no intent to use the information for clinical care.[1] Although the rate of serious adverse events after percutaneous breast biopsies is low, the procedures do involve risks to the patient.[1-4] Research biopsy tissue specimens can be obtained as part of a standalone procedure, referred to as a *research purposes-only biopsy* (RPOB), or as additional passes as part of a clinically indicated biopsy (*additional biopsy* [AB]).[5]

In our prior survey of 160 patients with metastatic breast cancer, 72% of participants indicated that they would consider having ABs, and 51% reported that they would consider having RPOBs.[5] We also surveyed medical oncologists and found that, in the context of breast cancer, medical oncologists indicated a high level of comfort in asking patients

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to provide RPOBs (78%) and ABs (93%) of the breast. However, they were less comfortable asking for RPOBs (50%) and ABs (70%) of the liver, which are considered more invasive.[6]

Several other survey-based studies have assessed the willingness of patients with breast cancer to consider research biopsies. One study queried whether patients with localized or recurrent breast cancer would consider undergoing 6 different research biopsy procedures of increasing invasiveness, discomfort, and inconvenience. In order from the most to the least invasive procedure, in the adjuvant group, 64% to 71% of participants would undergo a research biopsy as a requirement to participate in a clinical trial, and 54% to 87% would have undergo a biopsy purely for research purposes.[7] Another study assessed the willingness of patients with suspected or diagnosed breast cancer to consent to an AB or RPOB. Overall, 57% of respondents stated a willingness to undergo a research biopsy at 1 or both time points.[8] An additional survey study of patients with localized or metastatic breast cancer revealed that 46% were willing to consider undergoing a research biopsy.[9]

The major conclusion from most of the prior survey-based studies was that the inclusion of optional or mandatory percutaneous breast biopsies for research purposes would not be a significant barrier to clinical trial participation. However, despite the apparent willingness of oncologists to discuss research biopsies and of patients to consider them, a study from The University of Texas MD Anderson Cancer Center revealed that only 4.4% of patients with cancer elected to undergo an optional biopsy during a phase 1 clinical trial.[4] Understanding the attitudes of patients with breast cancer, particularly in the early stages, toward research biopsies may provide insights into how the inclusion of mandatory biopsies might affect clinical trial enrollment and prospective biobanking efforts and may identify modifiable factors to increase participation in such studies.

We investigated the perspectives toward research blood collections, donation of excess breast tissue from surgery, and percutaneous breast biopsies for research purposes among women recently diagnosed with early stage breast cancer who were pursuing treatment at academic centers or at a community oncology practice. Our primary hypothesis was that more patients at academic sites than at community sites would be willing to consider donating biospecimens for research purposes. This hypothesis was driven by the assumption that patients who are interested in research studies and clinical trials may preferentially seek out academic centers for care.

MATERIALS AND METHODS

Participants

Consecutive patients with newly diagnosed early stage breast cancer were approached for participation by a clinical research coordinator during a routine office visit. Participants were at aged ≥18 years with the ability to understand written English. The study was approved by the institutional review boards of each of the participating sites before initiation of study procedures. A cover letter explained the study, including reassurance regarding the anonymity of responses and that the choice to participate or not participate would not affect patient care. Participants were given a $5 gift card upon survey completion.

Participants were identified from the practices of 3 academic sites (Dana-Farber Cancer Institute [DFCI], Brigham and Women's Hospital, and Beth Israel Deaconess Medical Center) and 1 community site (Cancer Care of Maine). Eligibility criteria included a recent diagnosis (within 6 months) of stage I through III invasive breast cancer.

Survey

A survey was developed with input from patient advocates, radiologists, and medical oncologists, and then was piloted in a group of 30 patients with newly diagnosed breast cancer. Based on input from the pilot study, the survey was further refined. The final survey comprised 34 items (see Supporting Materials).

The survey sought to assess the attitude of patients toward undergoing elective procedures, including donation of blood, donation of excess breast tissue obtained at surgery, AB, RPOB, and research biopsy in the context of a clinical trial. Patients were asked to rate whether they would consider undergoing an RPOB or AB on a 5-point Linkert scale (definitely, probably, maybe, probably not, or definitely not). The surveys also collected information on age, race, education, marital status, employment status, prior clinical trial participation, number of prior biopsies, type of insurance, mode of transportation, and travel time to the clinic.

Statistical Methods

The primary objective was to determine the proportion of patients in academic and community practice settings who would be willing to undergo procedures, including

TABLE 1. Patient Characteristics

Characteristic, N = 198	No. of Patients (%)		*P*
	Academic Center, n = 102	Community Center, n = 96	
Age, y			
Mean ± SD	49.09 ± 11.50	59.92 ± 11.36	<.01
Median [range]	48.97 [25.85-77.88]	59.64 [34.14-82.15]	
No. missing data	6	2	
Race			
American Indian	0 (0.0)	3 (3.1)	<.01
Asian	6 (5.9)	1 (1.0)	
Black	4 (3.9)	0 (0.0)	
Native Hawaiian	0 (0.0)	0 (0.0)	
White	84 (82.4)	91 (94.8)	
Other	3 (2.9)	0 (0.0)	
Missing	5 (4.9)	1 (1.0)	
Ethnicity			
Non-Hispanic	93 (91.2)	91 (94.8)	.62
Hispanic	3 (2.9)	1 (1.0)	
Missing	6 (5.9)	4 (4.2)	
Education			
Trade school	0 (0.0)	1 (1.0)	<.01
Some high school	0 (0.0)	6 (6.3)	
High school graduate	9 (8.8)	25 (26.0)	
Some college	8 (7.8)	24 (25.0)	
2-Year college	6 (5.9)	11 (11.5)	
4-Year college	36 (35.3)	17 (17.7)	
Postgraduate school	39 (38.2)	9 (9.4)	
Missing	4 (3.9)	3 (3.1)	
Marital status			
Single	19 (18.6)	11 (11.5)	.03
Married/long-term partner	68 (66.7)	60 (62.5)	
Divorced	9 (8.8)	14 (14.6)	
Separated	1 (1.0)	0 (0.0)	
Widowed	2 (2.0)	10 (10.4)	
Missing	3 (2.9)	1 (1.0)	
Employment status			
Not employed	31 (30.4)	50 (52.1)	<.01
Employed	65 (63.7)	44 (45.8)	
Missing	6 (4.9)	2 (2.1)	
Type of insurance			
MassHealth[a]	5 (4.9)	5 (5.2)	<.01
Private insurance	85 (81.4)	44 (45.8)	
Medicare	4 (3.9)	30 (31.3)	
No insurance	0 (0.0)	3 (3.1)	
Missing	8 (7.8)	14 (14.6)	
Prior clinical trial participation			
No	79 (77.5)	89 (92.7)	.015
Yes	18 (17.6)	6 (6.3)	
Missing	5 (4.9)	1 (1.0)	
No. of prior breast biopsies			
Mean ± SD	1.9 ± 1.2	1.6 ± 1.0	.08
Median [range]	2 [1-7]	1 [0-6]	
No. missing data	1	0	
Transportation time to appointment, min			
Mean ± SD	71.3 ± 33.8	49.6 ± 37.7	<.01
Median [range]	65.0 [10.0-150.0]	45.0 [1.0-180.0]	
<45	20 (19.6)	46 (47.9)	
≥45	79 (77.5)	49 (51.0)	
No. missing data	3 (2.9)	1 (1.0)	
Transportation mode			
Car	91 (89.2)	90 (93.8)	.84
Foot	1 (1.0)	1 (1.0)	
Public transportation	4 (3.9)	2 (2.1)	
Missing	6 (5.9)	3 (3.1)	

[a]MassHealth is Massachusetts' combined Medicaid and Children's Health Insurance Program.

TABLE 2. Multivariate Analysis of Patients' Willingness to Undergo a Blood Test for Research Purposes Alone

Characteristic	No. of Patients (%)				OR [95% CI]	*P*
	All Patients	Would Consider, n = 161	Would Not Consider, n = 34	Unknown, n = 3		
Type of practice						
Academic	102 (51.5)	82 (80.4)	19 (18.6)	1 (1.0)	Ref	.37
Community	96 (48.5)	79 (82.3)	15 (15.6)	2 (2.1)	0.5 [0.1-2.1]	
Age, y						
Mean ± SD	54.4 ± 12.6	54.9 ± 12.6	52.5 ± 12.8	53.1 ± 10.5	1.0 [0.96-1.1]	.78
Median [range]	52.9 [25.8-82.2]	53.1 [25.8-82.2]	52.8 [28.8-76.6]	52.2 [43.1-64.1]		
No. missing data	8	7	1	0		
Race						
White	175 (88.4)	148 (84.6)	24 (13.7)	3 (1.7)	Ref	.01
Black/African American	4 (2.0)	1 (25.0)	3 (75.0)	0 (0.0)	0.1 [0.02-0.6]	
Other	13 (6.6)	7 (53.8)	6 (46.2)	0 (0.0)		
Missing	6 (3.0)	5 (83.3)	1 (16.7)	0 (0.0)		
Ethnicity						
Non-Hispanic	184 (92.9)	151 (82.1)	30 (16.3)	3 (1.6)	Ref	.57
Hispanic	4 (2.0)	2 (50.0)	2 (50.0)	0 (0.0)	0.4 [0.02-16.8]	
Missing	10 (5.1)	8 (80.0)	2 (20.0)	0 (0.0)		
Education						
No/some high school	7 (3.0)	4 (57.1)	3 (42.9)	0 (0.0)	0.1 [0.01-1.9]	.63
High school graduate	34 (17.2)	26 (76.5)	6 (17.6)	2 (5.9)	0.3 [0.04-2.1]	
Some college	32 (16.2)	27 (84.4)	5 (15.6)	0 (0.0)	0.8 [0.1-6.5]	
2-Year college	17 (8.6)	14 (82.4)	3 (17.6)	0 (0.0)	0.6 [0.1-4.5]	
4-Year college	53 (26.8)	47 (88.7)	6 (11.3)	0 (0.0)	0.9 [0.2-4.4]	
Postgraduate school	48 (24.2)	38 (79.2)	9 (18.8)	1 (2.1)	Ref	
Missing	7 (3.5)	5 (71.4)	2 (28.6)	0 (0.0)		
Marital status						
Married/long-term partner	128 (64.6)	104 (81.2)	22 (17.2)	2 (1.6)	Ref	.76
Single	30 (15.2)	21 (70.0)	8 (26.7)	1 (3.3)	0.8 [0.3-2.7]	
Separated/divorced	24 (12.1)	22 (91.7)	2 (8.3)	0 (0.0)		
Widowed	12 (6.1)	11 (91.7)	1 (8.3)	0 (0.0)		
Missing	4 (2.0)	3 (75.0)	1 (25.0)	0 (0.0)		
Employment status						
Not employed	81 (40.9)	68 (84.0)	12 (14.8)	1 (1.2)	Ref	.58
Employed	109 (55.1)	87 (79.8)	20 (18.3)	2 (1.8)	0.7 [0.2-2.6]	
Missing	8 (4.0)	6 (75.0)	2 (25.0)	0 (0.0)		
Type of insurance						
Private insurance	129 (65.2)	106 (82.2)	22 (17.1)	1 (0.8)	Ref	.59
MassHealth[a]	10 (5.1)	8 (80.0)	0 (0.0)	2 (20.0)	0.7 [0.1-3.1]	
Medicare	34 (17.2)	27 (79.4)	7 (20.6)	0 (0.0)		
No insurance	3 (1.5)	1 (33.3)	2 (66.7)	0 (0.0)		
Missing	22 (11.1)	19 (86.4)	3 (13.6)	0 (0.0)		
Prior clinical trial participation						
No	168 (84.8)	135 (80.4)	30 (17.9)	3 (1.8)	Ref	.96
Yes	24 (12.1)	21 (87.5)	3 (12.5)	0 (0.0)	1.0 [0.2-6.0]	
Missing	6 (3,0)	5 (83.3)	1 (16.7)	0 (0.0)		
Transportation time to appointment, min						
Mean ± SD	60.7 ± 37.3	60.1 ± 38.2	63.9 ± 34.3	55.0 ± 31.2		
Median [range]	60 [1-180]	60 [1-180]	60 [15-150]	45 [30-90]		
<45	66 (33.3)	57 (86.4)	8 (12.1)	1 (1.5)	Ref	.02
≥45	128 (64.6)	101 (78.9)	25 (19.5)	2 (1.6)	0.2 [0.03-0.7]	
No. missing data	4 (2.0)	3 (75.0)	1 (25.0)	0 (0.0)		
Transportation mode						
Car	181 (91.4)	151 (83.4)	28 (15.5)	2 (1.1)	Ref	.19
Foot	2 (1.0)	2 (100)	0 (0.0)	0 (0.0)	0.3 [0.03-2.1]	
Public transportation	6 (3.0)	2 (33.3)	3 (50.0)	1 (16.7)		
Missing	9 (4.5)	6 (66.7)	3 (33.3)	0 (0.0)		
No. of prior breast biopsies						
Mean ± SD	1.7 ± 1.1	1.7 ± 1.0	1.8 ± 1.3	2.0 ± 1.4	0.7 [0.4-1.1]	.10
Median [range]	1 [0-7]	1 [0-6]	1 [1-7]	2 [1-3]		
Overall experience with previous biopsies						

TABLE 2. *Continued*

Characteristic	No. of Patients (%)					
	All Patients	Would Consider, n = 161	Would Not Consider, n = 34	Unknown, n = 3	OR [95% CI]	*P*
Much better than expected	79 (39.9)	65 (82.3)	14 (17.7)	0 (0.0)	Ref	.19
Little better than expected	24 (12.1)	21 (87.5)	1 (4.2)	2 (8.3)		
Average, as expected	51 (25.8)	43 (84.3)	8 (15.7)	0 (0.0)	1.1 [0.3-4.5]	
Little worse than expected	13 (6.6)	10 (76.9)	3 (23.1)	0 (0.0)	0.3 [0.1-1.3]	
Much worse than expected	14 (7.1)	11 (78.6)	3 (21.4)	0 (0.0)		
Missing	17 (8.6)	11 (64.7)	5 (29.4)	1 (5.9)		

Abbreviations: OR, odds ratio; Ref, reference category.
[a]MassHealth is Massachusetts' combined Medicaid and Children's Health Insurance Program.

donation of excess breast tissue from surgery, AB, and RPOB. The sample size of 202 patients (101 per site) was chosen to provide 80% power to detect a 20% difference between site type, using a 2-sided .05-level test for 2 proportions. Each procedure was considered separately for the power calculation.

Wilcoxon rank-sum tests were used to compare continuous characteristics, and Fisher exact tests were used to compare categorical characteristics. The primary analysis collapsed the 5 responses of the Linkert scale into a dichotomous variable (*definitely/probably* vs *maybe/probably not/definitely not*). Patients were considered to be willing to undergo a research biopsy if they answered *definitely* or *probably*. The individual items on each survey were considered as separate outcomes and were analyzed separately. Patients with unknown outcomes or unknown characteristics were treated as missing and were excluded from analyses. For each outcome, proportions in each cohort were estimated and compared using 2-sided Fisher exact tests at the .05 level. Logistic regression models were used to estimate odds ratios (OR) for both univariate and multivariate analyses. All analyses were conducted in R version 3.6.1 (R Foundation for Statistical Computing).

RESULTS

Response Rate and Final Study Cohort

Among 211 eligible patients who were approached, 198 enrolled, for a response rate of 94%. One hundred eleven patients (52.6%) were from DFCI, Brigham and Women's Hospital, and Beth Israel Deaconess Medical Center (academic sites), and 100 patients (47.4%) were from the Maine Cancer Care Center (community site). In total, 102 patients from DFCI and 96 patients from the Maine site were included in the final analysis. Patient characteristics are reported in Table 1. On average, patients at academic sites were younger, had completed a higher level of education, and were more likely to have participated in a prior clinical trial. Although racial diversity was slightly greater at academic sites, most participants in the study (88%) were White. Travel time was significantly longer for patients at academic sites.

Research Blood Collection and Collection of Excess Breast Tissue at the Time of Surgery

Overall, 80% of patients from academic sites and 82% from the community site reported that they would consider a blood test for research purposes alone (see Supporting Table 1). On multivariate analysis, we observed that non-White patients were significantly less likely than White patients to consider undergoing a research blood test (OR, 0.1; 95% CI, 0.02-0.6; $P = .01$) (Table 2). However, because non-White patients made up <12% of the study population, this finding must be interpreted with caution. Longer transportation time (>45 minutes) to an appointment was also significantly associated with less willingness to donate a blood sample for research (OR, 0.2; 95% CI, 0.03-0.7; $P = .02$). Practice type was not significantly associated with willingness to consider research blood donation.

Overall, 93% of patients from academic sites and 94% from the community site would consider donating excess breast tissue from surgery for research. Practice type was not significantly associated with willingness to donate excess tissue from surgery (see Supporting Table 2).

Research Specimens Obtained as Part of a Clinically Indicated Biopsy Procedure

Approximately one-half of patients (51% from academic sites and 52% from the community site) would consider undergoing an AB for research purposes (see Supporting Table 3). On multivariable analysis, a negative experience with a prior biopsy was strongly associated with less willingness to consider an AB ($P < .001$) (Table 3). There was a

TABLE 3. Multivariate Analysis of Patients' Willingness to Undergo an Additional Biopsy for Research Purposes Alone at the Time of a Clinically Indicated Biopsy

Characteristic	All Patients	No. of Patients (%)			OR [95% CI]	*P*
		Would Consider, n = 102	Would Not Consider, n = 91	Unknown, n = 5		
Type of practice						
Academic	102 (51.5)	52 (51.0)	48 (47.1)	2 (2.0)	Ref	.60
Community	96 (48.5)	50 (52.1)	43 (44.8)	3 (3.1)	0.8 [0.3-2.1]	
Age, y						
Mean ± SD	54.4 ± 12.6	54.3 ± 12.4	54.2 ± 12.8	61.7 ±14.4	1.0 [0.99-1.1]	.17
Median [range]	52.9 [25.8-82.2]	53.6 [25.8-82.2]	52.8 [27.8-78.2]	57.5 [50.8-81.2]		
No. missing data	8	3	4	1		
Race						
White	175 (88.4)	94 (53.7)	77 (44.0)	4 (2.3)	Ref	.45
Black/African American	4 (2.0)	0 (0.0)	4 (100)	0 (0.0)	0.6 [0.1-2.5]	
Other	13 (6.6)	5 (38.5)	8 (61.5)	0 (0.0)		
Missing	6 (3.0)	3 (50.0)	2 (33.3)	1 (16.7)		
Ethnicity						
Non-Hispanic	184 (92.9)	96 (52.2)	84 (45.7)	4 (2.2)	Ref	.40
Hispanic	4 (2.0)	1 (25.0)	3 (75.0)	0 (0.0)	0.3 [0.01-4.5]	
Missing	10 (5.1)	5 (50.0)	4 (40.0)	1 (10.0)		
Education						
No/some high school	7 (3.5)	2 (28.6)	5 (71.4)	0 (0.0)	0.4 [0.1-1.4]	.17
High school graduate	34 (17.2)	14 (41.2)	18 (52.9)	2 (5.9)		
Some college	32 (16.2)	19 (59.4)	13 (40.6)	0 (0.0)	1.2 [0.3-5.0]	
2-Year college	17 (8.6)	9 (52.9)	8 (47.1)	0 (0.0)	1.0 [0.2-5.1]	
4-Year college	53 (26.8)	32 (60.4)	21 (39.6)	0 (0.0)	1.6 [0.5-4.9]	
Postgraduate school	48 (24.2)	23 (47.9)	23 (47.9)	2 (4.2)	Ref	
Missing	7 (3.5)	3 (42.9)	3 (42.9)	1 (14.3)		
Marital status						
Married/long-term partner	128 (64.6)	65 (50.8)	60 (46.9)	3 (2.3)	Ref	.79
Single	30 (15.2)	15 (50.0)	15 (50.0)	0 (0.0)	0.9 [0.4-4.9]	
Separated/divorced	24 (12.1)	17 (70.8)	7 (29.2)	0 (0.0)		
Widowed	12 (6.1)	4 (33.3)	7 (58.3)	1 (8.3)		
Missing	4 (2.0)	1 (25.0)	2 (50.0)	1 (25.0)		
Employment status						
Not employed	81 (40.9)	38 (46.9)	41 (50.6)	2 (2.5)	Ref	.26
Employed	109 (55.1)	60 (55.0)	47 (43.1)	2 (1.8)	1.7 [0.7-4.4]	
Missing	8 (4.0)	4 (50.0)	3 (37.5)	1 (12.5)		
Type of insurance						
Private insurance	129 (65.2)	71 (55.0)	56 (43.4)	2 (1.6)	Ref	.18
MassHealth[a]	10 (5.1)	5 (50.0)	4 (40.0)	1 (10.0)	0.5 [0.1-1.4]	
Medicare	34 (17.2)	15 (44.1)	19 (55.9)	0 (0.0)		
No insurance	3 (1.5)	0 (0.0)	3 (100)	0 (0.0)		
Missing	22 (11.1)	11 (50.0)	9 (40.9)	2 (9.1)		
Prior clinical trial participation						
No	168 (84.8)	85 (50.6)	79 (47.0)	4 (2.4)	Ref	.07
Yes	24 (12.1)	16 (66.7)	8 (33.3)	0 (0.0)	3.0 [0.9-10.7]	
Missing	6 (3.0)	1 (16.7)	4 (66.7)	1 (16.7)		
Transportation time to appointment, min						
Mean ± SD	60.7 ± 37.3	64.1 ± 39.4	56.6 ± 34.9	67.5 ± 35.7		
Median [range]	60.0 [1.0-180.0]	60.0 [5.0-180.0]	55.0 [1.0-150.0]	52.5 [45.0-120.0]		
<45 min	66 (33.3)	36 (54.5)	30 (45.5)	0 (0.0)	Ref	.64
≥45 min	128 (64.6)	65 (50.8)	59 (46.1)	4 (3.1)	0.8 [0.3-1.9]	
No. missing data	4 (2.0)	1 (25.0)	2 (50.0)	1 (25.0)		
Transportation mode						
Car	181 (91.4)	98 (54.1)	80 (44.2)	3 (1.7)	Ref	.28
Foot	2 (1.0)	0 (0.0)	2 (100)	0 (0.0)	0.3 [0.01-2.1]	
Public transportation	6 (3.0)	1 (16.7)	4 (66.7)	1 (16.7)		
Missing	9 (4.5)	3 (33.3)	5 (55.6)	1 (11.1)		
No. of prior breast biopsies						
Mean ± SD	1.7 ± 1.1	1.8 ± 1.2	1.6 ± 1.0	2.8 ± 0.8	1.0 [0.7-1.6]	.92
Median [range]	1 [0-7]	1 [0-6]	1 [1-7]	3 [2-4]		
Overall experience with previous biopsies						

TABLE 3. *Continued*

Characteristic	All Patients	No. of Patients (%)			OR [95% CI]	*P*
		Would Consider, n = 102	Would Not Consider, n = 91	Unknown, n = 5		
Much better than expected	79 (39.9)	52 (65.8)	26 (32.9)	1 (1.3)	Ref	<.001
Little better than expected	24 (12.1)	10 (41.7)	11 (45.8)	3 (12.5)		
Average, as expected	51 (25.8)	25 (49.0)	26 (51.0)	0 (0.0)	0.4 [0.2-1.1]	
Little worse than expected	13 (6.6)	6 (46.2)	6 (46.2)	1 (7.7)	0.1 [0.03-0.3]	
Much worse than expected	14 (7.1)	1 (7.1)	13 (92.9)	0 (0.0)		
Missing	17 (8.6)	8 (47.1)	9 (52.9)	0 (0.0)		

Abbreviations: OR, odds ratio; Ref, reference category.
[a]MassHealth is Massachusetts' combined Medicaid and Children's Health Insurance Program.

trend toward greater willingness to consider an AB among patients who had previously participated in a clinical trial (OR, 3.0; 95% CI, 0.9-10.7; $P = .07$). Practice type was not significantly associated with willingness to consider an AB.

Research Purposes-Only Biopsy Procedures

Overall, 22% of patients from academic sites and 42% of patients from the community site reported that they would consider an RPOB ($P = .003$) (see Supporting Table 4). On multivariate analysis (Table 4), the difference in patient willingness by practice type was no longer significant ($P = .96$). Instead, transportation time >45 minutes (OR, 0.3; 95% CI, 0.1-0.7; $P = .01$) and worse experience with prior biopsies ($P < .001$) remained significant predictors of willingness to consider RPOB. There were also trends toward greater willingness to consider RPOB among patients who had participated in a clinical trial ($P = .07$) and among White patients compared with non-White patients ($P = .08$).

When queried about willingness to consider a research biopsy in the context of a hypothetical clinical trial, 14% of patients from academic sites and 35% of patients from the community site responded that they would definitely or probably consider it ($P < .001$) (see Supporting Table 5). Upon multivariate analysis, patients at the community site remained more likely than patients at academic sites to consider participating in a clinical trial that included a mandatory research biopsy ($P = .04$). Older age ($P = .03$) and positive experiences with prior biopsy procedures ($P = .02$) were also associated with willingness to consider undergoing a research biopsy in the context of a clinical trial (see Supporting Table 6).

Patient-Reported Factors Associated With Attitudes Toward Research Biopsies

As indicated in Supporting Table 7, the most frequently cited barrier to consideration of an AB was concern about pain or discomfort of a biopsy (26.3%). Patients were also worried about the risks associated with having more biopsy specimens obtained than would be needed for clinical reasons (21.2%). For RPOB, concern about the pain or discomfort of a biopsy was also the most frequently cited concern (see Supporting Table 8). Notably, concerns about possible side effects of a drug (43.4% of patients listed this as 1 of their top 2 reasons) or lack of benefit of the study medication (25.8% listed this as 1 of their top 2 reasons) were the most frequent reasons patients might not participate in a clinical trial requiring a research biopsy (see Supporting Table 9).

In terms of factors motivating patients to consider research biopsies, 76.5% of patients at academic sites and 79.2% of patients at the community site cited the possibility that information gleaned from a research biopsy could contribute to scientific knowledge that might help future patients with breast cancer ($P = .31$) (Table 5). Other highly salient factors included learning about overall study results (66.7% of patients at both academic and community sites); learning about results of research tests on the biopsy sample, although they would not directly affect their care (61.8% and 65.5% of patients at academic and community sites, respectively; $P = .20$); a personal request by their physician (57.8% and 56.3%, respectively; $P = .64$); and learning more about the risks of a biopsy (43.1% and 47.9%, respectively; $P = .13$). Compared with patients from academic sites, patients from the community site were more often influenced by informational brochures about research biopsies (34.3% vs 41.7%, respectively; $P = .03$) and by talking to patients who had already undergone a research biopsy (29.4% vs 42.7%, respectively; $P = .004$).

Anxiety Regarding Hypothetical Donation of Research Biospecimens

Patients were asked to indicate their likely level of anxiety or distress if they were approached to donate blood or excess breast tissue from surgery or to undergo a

TABLE 4. Multivariate Analysis of Patients' Willingness to Undergo a Biopsy for Research Purposes Only

Characteristic	All Patients	No. of Patients (%)			OR [95% CI]	*P*
		Would Consider, n = 62	Would Not Consider, n = 131	Unknown, n = 5		
Type of practice						
Academic	102 (51.5)	22 (21.6)	77 (75.5)	3 (2.9)	Ref	.96
Community	96 (48.5)	40 (41.7)	54 (56.2)	2 (2.1)	1.0 [0.3-3.4]	
Age, y						
Mean ± SD	54.4 ± 12.6	57.2 ± 12.7	52.8 ± 12.2	64.8 ± 13.0	1.0 [0.98-1.1]	.21
Median [range]	52.9 [25.8-82.2]	57.4 [25.8-82.2]	51.8 [27.8-78.2]	63.6 [50.8-81.2]		
No. missing data	8	2	5	1		
Race						
White	175 (88.4)	59 (33.7)	112 (64.0)	4 (2.3)	Ref	.08
Black/African American	4 (2.0)	0 (0.0)	4 (100)	0 (0.0)	0.1 [0.005-0.9]	
Other	13 (6.6)	3 (23.1)	10 (76.9)	0 (0.0)		
Missing	6 (3.0)	0 (0.0)	5 (83.3)	1 (16.7)		
Ethnicity						
Non-Hispanic	184 (92.9)	59 (32.1)	122 (66.3)	3 (1.6)	Not included	
Hispanic	4 (2.0)	0 (0.0)	4 (100)	0 (0.0)		
Missing	10 (5.1)	3 (30.0)	5 (50.0)	2 (20.0)		
Education						
No/some high school	7 (3.5)	2 (28.6)	5 (71.4)	0 (0.0)	0.6 [0.1-3.6]	.10
High school graduate	34 (17.2)	10 (29.4)	23 (67.6)	1 (2.9)		
Some college	32 (16.2)	14 (43.8)	18 (56.2)	0 (0.0)	2.9 [0.6-15.1]	
2-Year college	17 (8.6)	8 (47.1)	8 (47.1)	1 (5.9)		
4-Year college	53 (26.8)	16 (30.2)	37 (69.8)	0 (0.0)	1.8 [0.5-8.3]	
Postgraduate school	48 (24.2)	10 (20.8)	36 (75.0)	2 (4.2)	Ref	
Missing	7 (3.5)	2 (28.6)	4 (57.1)	1 (14.3)		
Marital status						
Married/long-term partner	128 (64.6)	36 (28.1)	90 (70.3)	2 (1.6)	Ref	.37
Single	30 (15.2)	10 (33.3)	20 (66.7)	0 (0.0)	1.6 [0.6-4.1]	
Separated/divorced	24 (12.1)	12 (50.0)	11 (45.8)	1 (4.2)		
Widowed	12 (6.1)	4 (33.3)	7 (58.3)	1 (8.3)		
Missing	4 (2.0)	0 (0.0)	3 (75.0)	1 (25.0)		
Employment status						
Not employed	81 (40.9)	29 (35.8)	51 (63.0)	1 (1.2)	Ref	.71
Employed	109 (55.1)	30 (27.5)	76 (69.7)	3 (2.8)	0.8 [0.3-2.5]	
Missing	8 (3.5)	3 (37.5)	4 (50.0)	1 (12.5)		
Type of insurance						
Private insurance	129 (65.2)	37 (28.7)	90 (69.8)	2 (1.6)	Ref	.10
MassHealth[a]	10 (5.1)	4 (40.0)	6 (60.0)	0 (0.0)	0.4 [0.1-1.2]	
Medicare	34 (17.2)	12 (35.3)	21 (61.8)	1 (2.9)		
No insurance	3 (1.5)	0 (0.0)	3 (100)	0 (0.0)		
Missing	22 (11.1)	9 (40.9)	11 (50.0)	2 (9.1)		
Prior clinical trial participation						
No	168 (84.8)	55 (32.7)	109 (64.9)	4 (2.4)	Ref	.07
Yes	24 (12.1)	7 (29.2)	17 (70.8)	0 (0.0)	3.5 [0.9-14.3]	
Missing	6 (3.0)	0 (0.0)	5 (83.3)	1 (16.7)		
Transportation time to appointment, min						
Mean ± SD	60.7 ± 37.3	57.5 ± 42.4	62.1 ± 35.2	63.8 ± 18.9		
Median [range]	60 [1-180]	45 [10-180]	60 [1-150]	60 [45-90]		
<45	66 (33.3)	30 (45.5)	36 (54.5)	0 (0.0)	Ref	.01
≥45	128 (64.6)	32 (25.0)	92 (71.9)	4 (3.1)	0.3 [0.1-0.7]	
No. missing data	4 (2.0)	0 (0.0)	3 (75.0)	1 (25.0)		
Transportation mode						
Car	181 (91.4)	59 (32.6)	118 (65.2)	4 (2.2)	Ref	.89
Foot	2 (1.0)	0 (0.0)	2 (100)	0 (0.0)	1.2 [0.1-10.9]	
Public transportation	6 (3.0)	1 (16.7)	5 (83.3)	0 (0.0)		
Missing	9 (4.5.0)	2 (22.2)	6 (66.7)	1 (11.1)		
No. of prior breast biopsies						
Mean ± SD	1.7 ± 1.1	1.7 ± 1.1	1.7 ± 1.1	2.2 ± 0.4	0.8 [0.5-1.3]	.46
Median [range]	1 [0-7]	2 [0-6]	1 [1-7]	2 [2-3]		
Overall experience with previous biopsies						

TABLE 4. *Continued*

Characteristic	All Patients	No. of Patients (%)			OR [95% CI]	*P*
		Would Consider, n = 62	Would Not Consider, n = 131	Unknown, n = 5		
Much better than expected	79 (39.9)	40 (50.6)	37 (46.8)	2 (2.5)	Ref	<.001
Little better than expected	24 (12.1)	6 (25.0)	16 (66.7)	2 (8.3)		
Average, as expected	51 (25.8)	10 (19.6)	40 (78.4)	1 (2.0)	0.2 [0.05-0.6]	
A little worse than expected	13 (6.6)	1 (7.7)	12 (92.3)	0 (0.0)	0.02 [0.001-0.2]	
Much worse than expected	14 (7.1)	0 (0.0)	14 (100)	0 (0.0)		
Missing	17 (8.6)	5 (29.4)	12 (70.6)	0 (0.0)		

Abbreviations: OR, odds ratio; Ref, reference category.
[a]MassHealth is Massachusetts' combined Medicaid and Children's Health Insurance Program.

breast biopsy for research purposes. Very few patients indicated that they would be very anxious or distressed if approached to undergo a blood test for research purposes (3.5%) or to donate excess breast tissue (5.6%). However, a significant minority of patients would be very anxious or distressed if asked to undergo an additional breast biopsy (15.2%), an RPOB (19.7%), or a breast biopsy of either type as part of a clinical trial (19.7%), and approximately one-third of patients indicated that they would be somewhat anxious or distressed (see Supporting Table 10).

DISCUSSION

Patients are increasingly asked to consider donating biospecimens in the context of clinical trials and banking or cohort studies. Previous survey-based studies have indicated that patients with cancer experience anxiety before a biopsy.[10] Despite this, the inclusion of mandatory research biopsies is not consistently reported as a major barrier to clinical trial participation for women with breast cancer.[9,11] We conducted a survey to investigate the willingness of patients with early stage breast cancer to consider research blood collection and research biopsies.

Contrary to our primary hypothesis, we observed that patients from academic versus community oncology sites did not differ in their willingness to donate blood or excess tissue for research, or in their willingness to undergo AB or RPOB, once additional factors, including transportation time, were taken into account. Indeed, on multivariable analysis accounting for potential explanatory factors, we found that transportation time >45 minutes was significantly associated with less willingness to consider multiple types of research collections, including research blood tests, RPOB, and donation of excess tissue at time of surgery. Notably, we conducted our survey before the coronavirus 2019 disease pandemic, and we suspect that longer transportation time may be an even stronger deterrent now and into the future. In most cases, even as telehealth expands, and there is more flexibility regarding the site of standard-of-care treatments and procedures on clinical trials, collection of research samples typically can still only be performed at select clinical trial/study sites. Moving forward, academic centers and study sponsors could consider partnering with patients and community oncology sites on a more routine basis to allow for research collections in patients' local communities.[12] Furthermore, the finding that >80% of patients at both academic and community sites would be willing to donate research-only blood specimens underscores the importance of continued development of less invasive methods, such as assays of circulating biomarkers.

In agreement with prior studies in patients with breast cancer,[5,7,9] we observed that willingness to consider donating biospecimens varied by perceived level of invasiveness of the collection procedure. Most patients (80% from academic sites and 82% from the community site) were willing to consider undergoing blood tests for research purposes. Greater than 90% of patients from both types of sites indicated a willingness to donate excess breast tissue from surgery. In contrast, only one-half of patients (51% from academic sites and 52% from the community site) would be willing to undergo a research breast biopsy if it was part of a clinically indicated procedure in which AB specimens were obtained; even fewer were willing to consider a breast biopsy purely for research purposes (RPOB) (42% from the community site and 22% from academic sites).

We also noted a strong association between negative prior biopsy experiences and willingness to consider AB, RPOB, or breast biopsy in the context of a clinical trial. Reassuringly, more than one-half of patients reported that their overall experience with breast

TABLE 5. Factors Influencing Patients' Interest in Research Biopsies

Factor	No. of Patients (%)		*P*
	Academic Center, n = 102	Community-Based Center, n = 96	
Contributing to scientific knowledge that may help other people in the future	78 (76.5)	76 (79.2)	.31
Learning about overall results of the study	68 (66.7)	64 (66.7)	.62
Learning the results of the research tests on your biopsy sample, although the results would not directly affect your care	63 (61.8)	63 (65.6)	.20
Personal request by your physician	59 (57.8)	54 (56.3)	.64
Time taken away from work or home to come into the hospital	52 (51.0)	39 (40.6)	.65
Learning more about the risks of a biopsy	44 (43.1)	46 (47.9)	.13
Informational brochure about research biopsies	35 (34.3)	40 (41.7)	.03
Costs associated with coming into the hospital	37 (36.3)	35 (36.5)	.44
Talking to another patient who has undergone a research biopsy	30 (29.4)	41 (42.7)	.004

biopsies was better than they had expected; however, 14% of patients reported that their prior biopsies were worse than expected. In the study by Naim et al,[8] patients who had prior breast biopsy experience were significantly more likely to consider a research biopsy at the time of a clinically indicated biopsy (AB) than patients with no prior breast biopsy experience. However, there was no significant difference between the 2 groups regarding willingness to undergo a research biopsy at a later date (RPOB). Although that study did not report on the nature of the patients' prior biopsy experience (positive vs negative), the findings do suggest that prior biopsy experience can dispel some of the anxiety associated with anticipation of the procedure. Overall, these findings underscore the salience that every clinical encounter has in influencing patient perceptions, including future research participation.

Patients reported that the potential for contributing to breast cancer research that might help other patients in the future, learning about overall study results, and receiving results of research testing on their biospecimens were the most important motivating factors to consider research biopsies. Other important factors included a personal request from the physician and learning more about research biopsies, in the form of informational brochures, opportunities to talk with other patients who had undergone research biopsies, or receiving more information about biopsy risks. The main deterrents to research biopsies were worry about pain and discomfort as well as the potential harms from a biopsy. We believe our findings provide actionable data on modifiable factors to encourage participation in biospecimen collection efforts for research. Particular emphasis should be placed on continually improving preprocedure counseling and consent discussions to ensure that patients understand the true risks of pain and discomfort of the procedure as well as the valuable contribution of research biopsies to therapeutic clinical trials. Effective, open communication by clinicians could help to minimize preprocedure anxiety in patients considering research biopsies.

Our study has several limitations. We included only 3 academic sites and 1 community site, which may affect the generalizability of our results. Patients were approached by a research coordinator and then provided responses to hypothetical scenarios in a written survey. We are unable to determine how well patient responses to these written scenarios reflect what patients would have chosen to do if actually offered participation in such collection efforts. More than one-half of patients in both academic and community sites indicated that a personal request from their physician would increase their interest in undergoing a research biopsy. This emphasizes the essential role of medical oncologists in providing accurate information to their patients about the nature of research biopsy procedures and the importance of the tissue thus obtained for advancing breast cancer research. In light of this, our written survey, which stressed the hypothetical nature of the scenarios, might underestimate patient willingness to donate biospecimens for research compared with a face-to-face discussion with their treating oncologist.

However, it is important to note the study from The University of Texas MD Anderson Cancer Center, which demonstrated that only 40 of 911 phase 1 clinical trial participants (4.4%) underwent a research biopsy on an optional basis. In contrast, 86.6% of patients enrolled in trials requiring mandatory biopsies underwent the procedure. The success rate in obtaining tissue from mandatory biopsies was 100% in industry-sponsored trials with minimal flexibility, compared with 57.8% in nonindustry-sponsored trials with protocol flexibility for medical or logistical reasons. Interestingly, the most common reason for not carrying out *mandatory* biopsies on more flexible protocols was lack of funding. This finding suggests that

financial constraints might also play a role in the failure to obtain tissue from research biopsies performed on an optional basis.[4] Finally, our survey did not include questions explicitly asking about privacy, data sharing, or biospecimen concerns. In retrospect, inclusion of such items would have provided further important information on the salience of these concerns from a patient perspective.

Unfortunately, our study included few minority participants; thus our ability to draw conclusions by racial or ethnic background is limited. Despite this limitation, it is concerning that non-White participants generally indicated less willingness to consider research blood draws and biopsy procedures than White participants, a finding that has been previously reported.[9] This pattern speaks to the need for dedicated and culturally sensitive efforts to overcome mistrust in the medical system and other barriers that may stem from historic and ongoing injustices.[13-15] Replicating our survey in a more diverse patient population may provide additional actionable insights.

Finally, this study was not designed to address the ethical implications of collecting patient tissue samples for research, particularly in the context of mandatory research biopsies within clinical trials.[2,3] The study was limited to patients and did not include surveys of institutional review board members, ethics researchers, or members of the general public. Ethical frameworks for the inclusion of research biopsies in oncology clinical trials have been proposed by several groups, including the American Society of Clinical Oncology. The willingness of many patients to undergo invasive procedures for research purposes does not negate our responsibility to ensure appropriate scientific rationale and informed consent. Furthermore, our results highlight the importance patients place on contributions to scientific knowledge that their participation in research has enabled and their desire to learn about the scientific advances their participation has generated.[3]

Conclusions

In summary, findings from this study suggest that most patients with early stage breast cancer would be willing to consider donating blood samples or excess tissue collected at the time of clinically indicated surgery for research purposes. Approximately one-half would consider undergoing ABs for research purposes at the time of a clinically indicated biopsy, and some would consider RPOBs. However, there are still significant barriers to participation. Efforts to reduce the specific barriers to participating in biospecimen research efforts in patients with early stage breast cancer are warranted.

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AUTHOR CONTRIBUTIONS

Davinia S. Seah: Conceptualization, methodology, data curation, writing–original draft, and writing–review and editing. **Jose Pablo Leone:** Conceptualization, methodology, data curation, formal analysis, writing–original draft, and writing–review and editing. **Thomas H. Openshaw:** Conceptualization, methodology, and writing–review and editing. **Sarah M. Scott:** Conceptualization, methodology, writing–original draft, and writing–review and editing. **Nabihah Tayob:** Data curation, formal analysis, writing–original draft, and writing–review and editing. **Jiani Hu:** Data curation, formal analysis, writing–original draft, and writing–review and editing. **Ruth I. Lederman:** Data curation, writing–original draft, and writing–review and editing. **Elizabeth S. Frank:** Conceptualization, methodology, writing–original draft, and writing–review and editing. **Jessica J. Sohl:** Conceptualization, methodology, data curation, and writing–review and editing. **Zsofia K. Stadler:** Conceptualization, methodology, and writing–review and editing. **Timothy K. Erick:** Formal analysis, writing–original draft, and writing–review and editing. **Stuart G. Silverman:** Conceptualization, methodology, writing–original draft, and writing–review and editing. **Jeffrey M. Peppercorn:** Conceptualization, methodology, formal analysis, and writing–review and editing. **Eric P. Winer:** Conceptualization, methodology, and writing–review and editing. **Steven E. Come:** Conceptualization, methodology, writing–original draft, and writing–review and editing. **Nancy U. Lin:** Conceptualization, methodology, writing–original draft, and writing–review and editing.

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