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## Characteristics associated with requests by pathologists for second opinions on breast biopsies

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### Abstract

**Aims**—Second opinions in pathology improve patient safety by reducing diagnostic errors, leading to more appropriate clinical treatment decisions. Little objective data are available regarding the factors triggering a request for second opinion despite second opinion consultations

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**Competing interests** None declared.

**Ethics approval** The Institutional Review Boards of Dartmouth College, the Fred Hutchinson Cancer Research Center, Providence Health & Services of Oregon, the University of Vermont, and the University of Washington approved all study procedures. All participating pathologists signed an informed consent form.

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being part of the diagnostic system of pathology. Therefore we sought to assess breast biopsy cases and interpreting pathologists characteristics associated with second opinion requests.

**Methods**—Collected pathologist surveys and their interpretations of 60 test set cases were used to explore the relationships between case characteristics, pathologist characteristics and case perceptions, and requests for second opinions. Data were evaluated by logistic regression and generalised estimating equations.

**Results**—115 pathologists provided 6900 assessments; pathologists requested second opinions on 70% (4827/6900) of their assessments 36% (1731/4827) of these would not have been required by policy. All associations between case characteristics and requesting second opinions were statistically significant, including diagnostic category, breast density, biopsy type, and number of diagnoses noted per case. Exclusive of institutional policies, pathologists wanted second opinions most frequently for atypia (66%) and least frequently for invasive cancer (20%). Second opinion rates were higher when the pathologist had lower assessment confidence, in cases with higher perceived difficulty, and cases with borderline diagnoses.

**Conclusions**—Pathologists request second opinions for challenging cases, particularly those with atypia, high breast density, core needle biopsies, or many co-existing diagnoses. Further studies should evaluate whether the case characteristics identified in this study could be used as clinical criteria to prompt system-level strategies for mandating second opinions.

## BACKGROUND

Second opinions in pathology improve patient safety by reducing diagnostic errors, leading to more appropriate clinical treatment decisions.<sup>12</sup> Pathologists frequently request second opinions for pathological interpretations of breast specimens, particularly for new cancer diagnoses and when surgery is performed at referral hospitals.<sup>3–7</sup> In a recent survey of US pathologists participating in the Breast Pathology Study (B-Path), 81% of respondents reported obtaining second opinions in their clinical practice on at least some breast pathology cases that did not require second opinions due to mandated institutional policies.<sup>8</sup> The vast majority of surveyed pathologists also agreed that second opinions improve their diagnostic accuracy and protect them from malpractice suits. Few objective data are available regarding the factors triggering a request for second opinion despite second opinion consultations being part of the diagnostic system of pathology.<sup>9</sup> Additional data from practicing pathologists may inform system-level future policy.

The purpose of this study was to determine whether specific characteristics of breast biopsy cases were associated with requesting second opinions, and how these associations varied by specific diagnoses. In addition, we explored the relationship between requesting a second opinion and pathologists' perceptions of the case, including confidence in their assessment, whether they considered a case difficult, and whether they considered a case borderline between two diagnoses. Finally, we compared the association between these variables and whether the request for second opinion was based on institutional policy or desired for diagnostic reasons regardless of policy.

## METHODS

This observational cross-sectional study is part of the larger B-Path Study,<sup>10–12</sup> which was designed to evaluate diagnostic variation in the interpretation of breast biopsies among practicing pathologists. Two hundred and forty breast specimens were randomly selected from two state pathology registries (NH, VT) that are part of the National Cancer Institute sponsored Breast Cancer Surveillance Consortium.<sup>13</sup> Selection was stratified by age (49% age 40–49 years, 51% age ≥ 50 years), breast density (51% with heterogeneously or extremely dense breast tissue based on mammography), and biopsy type (58% core needle, 42% excisional). The cases were divided into four test sets of 60 cases as described in a previous publication.<sup>10</sup> Each case was represented by one glass slide, which was carefully checked for quality. Participants were instructed to assume that the single slide demonstrated the best diagnostic features of the case.

### Participating pathologists

Pathologists from eight US states (Alaska, Maine, Minnesota, New Hampshire, New Mexico, Oregon, Vermont and Washington) were invited to participate. Details of their identification and recruitment have been described elsewhere.<sup>10,14</sup> Participating pathologists completed a web-based survey followed by interpreting their assigned test set of 60 cases.

### Physician survey

Pathologists self-reported demographic and clinical practice characteristics, including age, gender, expertise in breast pathology, professional and academic affiliations, fellowship training in surgical and breast pathology, number of years interpreting breast pathology, and proportion of caseload devoted to breast specimens.

### Diagnostic histology data collection

Participants completed an online histology data collection form<sup>10</sup> for each case, and were asked to interpret the cases using the same diagnostic criteria they would use in regular clinical practice. We categorised their interpretations on each case into one of four primary diagnostic categories (benign without atypia, atypia (atypical ductal hyperplasia (ADH) or ADH in a papilloma), ductal carcinoma in situ (DCIS), and invasive carcinoma) as detailed elsewhere.<sup>10</sup> There were 14 unique possible diagnoses comprising the four primary diagnostic categories; we calculated the sum of total unique diagnoses used for each case to create a cumulative diagnosis value as a surrogate measure of case complexity. The histology form also asked pathologists if they considered the case borderline between two diagnoses. Pathologists rated their perceived levels of diagnostic challenge and their confidence in their diagnosis for each test case. A six-point Likert scale ranging from 1 ('very easy') to 6 ('very challenging') was provided for the question 'Rate your opinion of the level of diagnostic difficulty of this case', and a six-point Likert scale from 1 ('very confident') to 6 ('not confident at all') was used to rate confidence in their assessment. Likert responses were collapsed into binary outcomes: 'low degree of challenge' (Likert 1, 2, 3) versus 'high degree of challenge' (Likert 4, 5, 6); and 'high confidence' (Likert 1, 2, 3) versus 'low confidence' (Likert 4, 5, 6).

Finally, pathologists recorded whether they would have asked for a second pathologist's opinion of the case before finalising the report if they were interpreting the case in clinical practice. They could choose from the following responses: (1) Yes, I would want a second pathologist's opinion for diagnostic reasons; (2) Yes, because it is our policy to get a second opinion in cases with this diagnosis; (3) Yes, I would want a second pathologist's opinion for diagnostic reasons and yes, because it is our policy to get a second opinion in cases with this diagnosis (ie, both response 1 and 2 were checked); and (4) No, I do not want a second opinion.

### Case characteristics

The woman's age at the time of biopsy and biopsy type were available to the pathologists for each case. The registry provided patient age, while biopsy type was determined by review of the original case slides and pathology report. Radiologists provided mammographic breast density according to the BIRADS mammographic density classifications. For analysis, we dichotomised mammographic density to high (very dense or heterogeneously dense) and low (scattered fibroglandular densities or almost entirely fat).

### Statistical analysis

Frequencies and percentages for each of four response categories for second opinions were calculated. Associations between the dependent variable, request for second opinion, and pathologist and case characteristics (including diagnostic category) as single covariates were tested using repeated measures logistic regression with and without adjustment under PROC GENMOD in SAS software. To assess the impact these characteristics had on the dependent variable, responses to the request for a second opinion were dichotomised by grouping all three affirmative responses together as 'Yes' compared with 'No, I do not want a second opinion'. Second opinion rates were calculated using a generalised estimating equation (GEE) with a binomial distribution and independent correlation structure, accounting for clustered responses within each participant. Estimates and SEs of least square (LS) means were computed and transformed back to the original response scale via the inverse-link function to provide rates of second opinion and their 95% CIs. An additional sensitivity analysis was conducted for the dichotomous outcome of requesting a second opinion after removing second opinion requests that were based on policy alone. Wald-based p values and 95% CIs were computed using a two-sided significance level of 0.05. Statistical analyses were performed using SAS software V.9.4 for the Windows Operating System (SAS Institute Inc, Cary, North Carolina, USA).

## RESULTS

One hundred and fifteen pathologists completed the survey and each reviewed 60 breast biopsy cases that included more cases of ADH and DCIS than in clinical practice. Among the 6900 independent case assessments, pathologists reported that they would request a second opinion (either as required by policy and/or desired by the pathologist) for 70% (4827/6900). Of cases for which the pathologists requested a second opinion, just over one-third (36%; 1731/4827) would *not* have been required by laboratory policies in their clinical practices (table 1).

Only two pathologists' characteristics were statistically significantly associated with requesting second opinions. Requesting second opinions occurred less frequently for pathologists with academic medical centre affiliations (60% vs 73%,  $p = 0.021$ ) and among pathologists considered experts in breast pathology by their peers (56% vs 74%,  $p = 0.003$ ) compared with pathologists without these characteristics (table 1).

All of the case characteristics evaluated were significantly associated with whether or not a second opinion was requested (table 2).

Cases in which women had high versus low mammographic breast density (72% vs 68%;  $p = 0.001$ ) were more likely to have a second opinion requested. Cases from core needle biopsies compared with excisional biopsies (72% vs 67%;  $p = 0.006$ ), and cases with increasing cumulative unique diagnoses as indicated by the pathologists who interpreted the cases (<4 (64%), 4–7 (70%) and 8 (74%);  $p = 0.001$ ) were also associated with more frequent requests for second opinions.

Pathologists were more likely to request second opinions for cases they considered challenging (94%), had low confidence in their assessments (94%), or considered borderline (95%), regardless of whether their decisions were based on policy and/ or for diagnostic reasons (all  $p = 0.001$ ) (table 2). Pathologists requested a second opinion for diagnostic reasons alone for 50% of the cases when they considered them challenging or when confidence in their assessment was low, and 53% when they considered the case borderline between two diagnoses.

Figure 1 shows the reasons pathologists requested second opinions for each of the cases interpreted, according to the diagnosis that they indicated for the case. The most frequent request for a second opinion for either policy and/or diagnostic reasons was for cases of atypia; pathologists requested a second opinion on 88% of all cases that they interpreted as atypia. Atypia was the most frequent diagnosis for which a second opinion was desired for personal diagnostic reasons (66% of all cases interpreted as atypia). In contrast, pathologists were least likely to request a second opinion for diagnostic reasons for cases of invasive carcinoma (20% of all invasive cases). However, as expected, invasive carcinoma was the most common diagnostic category for which pathologists noted that a second opinion would be required by policy in their own practices (60% of all invasive cases).

To better understand how perceptions of a case and diagnostic categories were related to the second opinion requests for diagnostic reasons (and not for policy reasons) we used a comparison group combining the responses 'No, I don't want a second opinion' and 'Yes, I want a second opinion because it is a policy' (left side of figure 2 and see online supplementary table S1). Pathologists' perception of a case mattered when they checked off whether or not they desired a second opinion for diagnostic reasons. Pathologists were significantly more likely to want a second opinion when they had low confidence in their assessment, when the case was perceived as challenging, or when it was considered borderline ( $p < 0.001$ ). These statistically significant differences were noted regardless of the pathologists' diagnosis of the case. The atypia diagnosis category was distinct from the other three diagnostic categories; pathologists desired a second opinion for more than 50% of the

cases they interpreted as atypia even when the pathologist was confident, ranked the case a low degree of challenge, and did not consider it borderline. The most frequent request for a second opinion for diagnostic reasons was for invasive cancer that was considered borderline (82%, CI 69% to 90%); the most frequent alternative diagnoses selected for these borderline cases were DCIS (60%), sclerosing adenosis (19%) and radial scar (17%). The least frequent request for a second opinion was for invasive cases in which the case was ranked low in degree of challenge (12%, CI 8% to 17%).

When comparing interpretations for which a second opinion was desired for diagnostic reasons with those for which a second opinion was not desired (excluding from the analysis second opinions indicated only due to policy), comparison of rates of second opinions was statistically significantly associated only with cases considered borderline across all diagnostic categories (right side of figure 2;  $p = 0.005$ ). When the pathologists' confidence in the assessment was low, pathologists desired a second opinion most frequently for the diagnosis of atypia (96%, CI 92% to 98%) and invasive cancer (96%, CI 77% to 99%) (see online supplementary table S2). However, pathologists desired second opinions for over 67% of cases (data not shown) of atypia despite feeling confident in their diagnoses, indicating the case was easy, and noting that the case was not borderline.

## DISCUSSION

In this study of interpretations of breast biopsy cases, pathologists indicated frequent requests for second opinions when they were less confident in their assessments, found the case challenging, and identified the case as borderline, even when their laboratory policies did not require second opinions. As expected, pathologists affiliated with academic medical centres or considered experts in breast pathology by their peers were less likely to request second opinions than pathologists without these characteristics. However, characteristics of the case, rather than the pathologist, were more often associated with requests for second opinions.

The diagnosis of breast epithelial atypia (ADH and ADH in a papilloma) had the highest rate of second opinion requests by the participating pathologist within the four diagnostic categories evaluated. Notably, these requests were observed regardless of the pathologists' confidence in assessment, diagnostic challenge of the case, or presence of borderline diagnostic features. When we excluded cases where the pathologist indicated the only reason for a second opinion was a laboratory policy, the rates for second opinion requests increased in all diagnostic categories. As expected, rates were high (86–96%) when pathologists indicated they were not confident in the diagnosis, the case was challenging, or the case was borderline between two categories. In contrast to the other diagnostic categories, cases with atypia had high rates of second opinion requests (67–78%) even when pathologists indicated they were confident, the case was easier, and the case did not have borderline features.

These findings suggest that pathologists frequently desire and likely obtain second opinions in clinical practice, particularly for cases with atypia. Considering the low diagnostic agreement rates for atypia that have been reported,<sup>10</sup> diagnostic accuracy might be improved if second opinions were obtained for all cases with atypia. More widespread adoption of



second opinion policies and guidelines may improve diagnostic accuracy and provide the support that practicing pathologists seem to want.

A decade ago, an external review of the UK National Health Service Breast Screening Programme (NHSBSP) reported several areas in breast pathology that could be improved but concluded that the diagnosis of atypical hyperplasia, which they found to have very poor concordance, cannot be improved.<sup>15</sup> In the evaluation of the NHSBSP they noted that the diagnostic criteria for atypical hyperplasia, which at that time had been recently updated, did not improve the diagnosis and they did not recommend any other avenues for improvement. However, others have suggested that obtaining second opinions on these challenging cases might improve accuracy.<sup>16</sup>

Increased mammographic breast density was associated with higher rates of requests for second opinions in the present study, as well as with lower diagnostic agreement among pathologists in a prior B-Path Study.<sup>10</sup> Breast density is primarily attributable to fibrous tissue of the breast.<sup>17–19</sup> However, breast fibrosis is not a factor considered in the diagnosis of epithelial proliferations pathologically. To further explore the potential effect of density, we also evaluated whether the spectrum of epithelial proliferation present in a case might be associated with increased requests for second opinion and noted that requests increased for cases with higher cumulative unique diagnoses attributed to the case by the multiple pathologists who independently interpreted the case. Thus, we hypothesise that epithelial breast complexity, by inference, is associated with breast density.

This work presents new findings of the B-Path Study, which was originally designed to evaluate diagnostic variation in the interpretation of breast biopsies among practicing pathologists by collecting data related to diagnostic accuracy. The present study describes in detail pathologists' desires for second opinion when interpreting breast biopsy cases and evaluates whether intrinsic features of the breast biopsy specimen and characteristics of pathologists were associated with pathologists' requests for consultative second opinions. To our knowledge, this is the first study to examine these associations of case and pathologists' characteristics with obtaining second opinions. Most studies examining the use of second opinions focus on changes in histological diagnoses<sup>3–720</sup> and do not report the pathologists' underlying perceptions of the case or characteristics associated with cases where they desire second opinions. Although some studies have reported case characteristics, such as diagnoses and oestrogen-progesterone receptors and HER2 status, none have related them to the use of second opinion.<sup>1520</sup>

The strengths of this study include the participation of a large number of practicing pathologists ( $N=115$ ) from across the US, each interpreting 60 cases and providing independent diagnostic assessments and their perceptions regarding challenges in interpreting these cases. These data were then linked to pathologist demographic and clinical practice characteristics and case characteristics. The results of this study could guide educational interventions for practicing pathologists and trainees, as well as inform policy changes to improve diagnostic systems by establishing system-level strategies for when second opinions should be obtained.

There are several limitations to this study. While this study used a single slide to improve efficiency and enhance participation of practicing pathologists, it does not replicate clinical practice, where the initial pathologist evaluating a case may have access to additional slides or special stains and the option to consult with other pathologists. Interpreting cases in this situation, especially when the cases included more atypia and DCIS than typically observed in clinical practice, may also alter interpretive performance. This may have led to more assessments rated as challenging.

## CONCLUSIONS

In conclusion, breast biopsies are challenging to interpret<sup>10</sup> and likely lead to frequent second opinions in clinical practice regardless of institutional policy.<sup>8</sup> Clinical systems may need to be optimised to support pathologists and their desires for the use of second opinions. In addition, broader reimbursement may be needed for second opinion if future research shows that second opinions lead to improvements in clinical care. We identified breast biopsy case characteristics that are strongly associated with whether practicing pathologists desire second opinions. Pathologists frequently request second opinions for challenging cases, particularly for cases with atypia, high breast density, core needle biopsies, or many co-existing diagnoses. Further studies should evaluate whether the case characteristics identified in this study could be used as clinical criteria to prompt second opinions. The ultimate goal of these efforts is to improve support for practicing pathologists, laboratory efficiency, and outcomes for patients.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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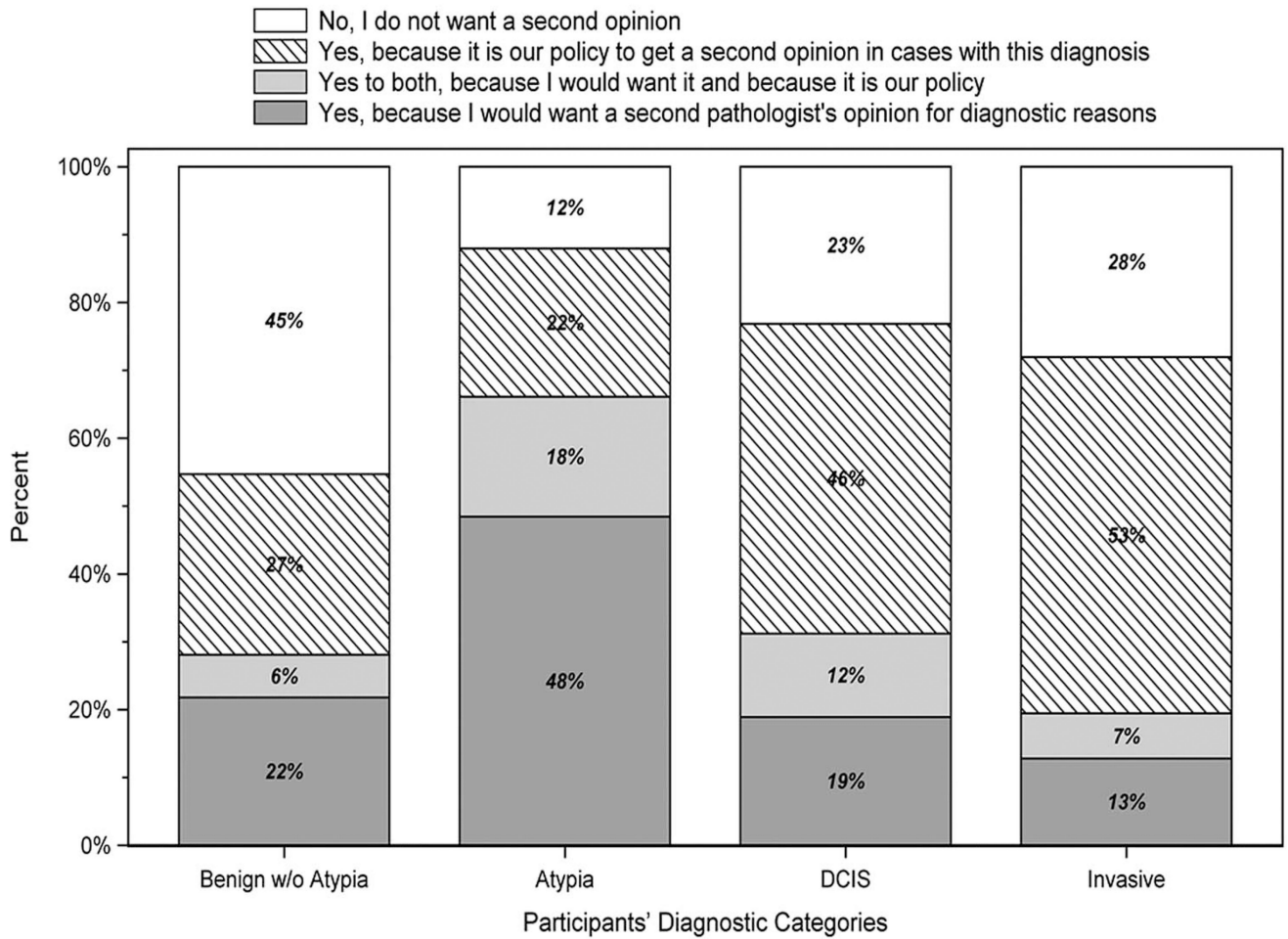


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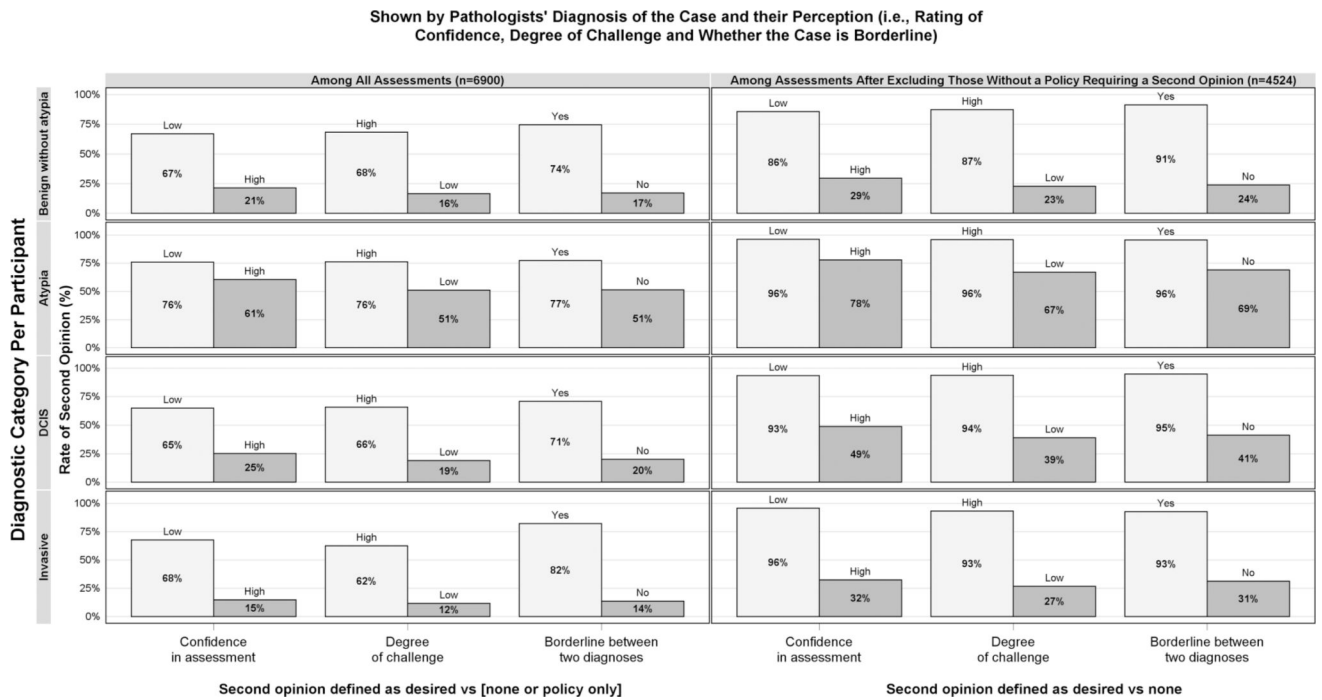
**Take home messages**

- ▶ Breast biopsy case characteristics such as patient age, core needle biopsy and dense mammographic breast tissue were significantly associated with requests for a second opinion.
- ▶ Pathologists frequently requested second opinions when they were less confident in their assessments, found the case challenging, and/or identified the case as borderline between two diagnostic categories, even when their laboratory policies did not require second opinions.
- ▶ Second opinions were most frequently requested for diagnoses of atypical ductal hyperplasia.
- ▶ Adoption of broader second opinion guidelines and policies may improve diagnostic accuracy and provide the support that practicing pathologists seem to desire.

Would you ask for a second pathologist's opinion of this case before finalizing the report?:



**Figure 1.** Requests for second opinion by participating pathologists' diagnostic categories.



**Figure 2.** Proportion of second opinions requested for the test set cases by case-level pathologists' perceptions and their diagnostic categories.

Demographic and clinical experience of pathologists by second opinion during the independent assessment of breast biopsy cases (N = 115 participants, 6900 independent assessments)

Table 1

Pathologist characteristics *	Number of pathologists	Number of independent assessments	Rate of second opinion †	P Value ‡	Response options		
					Combined yes responses rate (95% CI)	N (%)	N (%)
<b>Would you ask for a second pathologist's opinion of this case before finalising the report? (Assume a pathologist is available)</b>							
Total	115	6900	70 (65 to 75)	-	1731 (25)	2376 (34)	2073 (30)
<i>Demographics</i>							
Age at survey (years)							
33-39	16	960	77 (65 to 89)	0.69	164 (17)	381 (40)	220 (23)
40-49	41	2460	68 (59 to 76)		589 (24)	916 (37)	790 (32)
50-59	42	2520	69 (61 to 77)		775 (31)	704 (28)	781 (31)
60+	16	960	71 (57 to 85)		203 (21)	375 (39)	282 (29)
Gender							
Female	46	2760	74 (67 to 81)	0.19	812 (29)	951 (34)	724 (26)
Male	69	4140	67 (61 to 74)		919 (22)	1425 (34)	1349 (33)
<i>Clinical practice and breast pathology expertise</i>							
Have you received fellowship training in breast pathology?							
No	109	6540	71 (66 to 75)	0.36	1696 (26)	2256 (34)	1923 (29)
Yes	6	360	58 (31 to 86)		35 (10)	120 (33)	150 (42)
Affiliation with academic medical centre							
No	87	5220	73 (68 to 78)	0.021	1324 (25)	1895 (36)	1399 (27)
Yes	28	1680	60 (49 to 70)		407 (24)	481 (29)	674 (40)
Do your colleagues consider you an expert in breast pathology?							
No	90	5400	74 (69 to 79)	0.003	1411 (26)	1916 (35)	1408 (26)
Yes	25	1500	56 (44 to 67)		320 (21)	460 (31)	665 (44)
How many years have you been interpreting breast pathology cases (not including residency/fellowship training)?							

**Would you ask for a second pathologist's opinion of this case before finalising the report? (Assume a pathologist is available)**

Pathologist characteristics *	Number of pathologists	Number of independent assessments	Rate of second opinion †	p Value ‡	Response options			
					Yes, because I would want a second pathologist's opinion for diagnostic reasons	Yes, because it is our policy to get a second opinion in cases with this diagnosis	No, I do not want a second opinion	
<5	22	1320	75 (65 to 85)	0.47	252 (19)	548 (42)	193 (15)	327 (25)
5-9	23	1380	74 (65 to 82)		363 (26)	480 (35)	176 (13)	361 (26)
10-19	34	2040	65 (55 to 76)		488 (24)	661 (32)	187 (9)	704 (35)
20	36	2160	68 (60 to 77)		628 (29)	687 (32)	164 (8)	681 (32)
What percentage of your caseload includes interpreting breast specimens?								
<10%	59	3540	70 (63 to 77)	0.34	953 (27)	1093 (31)	434 (12)	1060 (30)
10-24%	45	2700	73 (66 to 79)		683 (25)	1000 (37)	283 (10)	734 (27)
25%	11	660	58 (37 to 78)		95 (14)	283 (43)	3 (0)	279 (42)
Estimate the number of breast cases you interpret during an average week								
<5	31	1860	71 (62 to 80)	0.58	579 (31)	494 (27)	253 (14)	534 (29)
5-9	44	2640	72 (64 to 79)		645 (24)	935 (35)	314 (12)	746 (28)
10-19	31	1860	71 (62 to 79)		463 (25)	716 (38)	134 (7)	547 (29)
20	9	540	54 (30 to 79)		44 (8)	231 (43)	19 (4)	246 (46)

Row percentages might not add up to 100 due to rounding.

\* By self-report on baseline survey.

† Binary variable created from all three affirmative responses where 1=yes, 0=no. LS means and CIs estimated on logit scale and back transformed on the scale of the mean using the inverse link function.

‡ Probability >  $\chi^2$ , Wald statistics for type 3 GEE analysis.

GEE, generalised estimating equation; LS, least square.



Characteristics of test set cases by whether a participant pathologist would request a second opinion ( $N = 115$  participants, 6900 independent assessments)

**Table 2**

Would you ask for a second pathologist's opinion of this case before finalising the report? (Assume a pathologist is available.)								
Case characteristics*	Number of cases	Number of assessments	Rate of second opinion for combined responses <sup>†</sup>	Response options				
				Combined yes response rate (95% CI)	Yes, because I would want a second pathologist's opinion for diagnostic reasons	Yes, because it is our policy to get a second opinion in cases with this diagnosis	Yes to both, because I would want it and because it is our policy	No, I do not want a second opinion
Total	240	6900	70 (65 to 75)	–	1731 (25)	2376 (34)	720 (10)	2073 (30)
<i>Patient characteristics for breast biopsy cases</i>								
Patient age (years) <sup>§</sup>								
40–49	118	3391	71 (66 to 76)	0.038	856 (25)	1188 (35)	356 (10)	991 (29)
50–59	67	1924	70 (65 to 75)		495 (26)	663 (34)	195 (10)	571 (30)
60–69	29	833	67 (60 to 73)		171 (21)	295 (35)	88 (11)	279 (33)
70+	26	752	69 (63 to 75)		209 (28)	230 (31)	81 (11)	232 (31)
Breast density <sup>§</sup>								
Low density	118	3391	68 (63 to 73)	<0.001	786 (23)	1184 (35)	340 (10)	1081 (32)
High density	122	3509	72 (67 to 77)		945 (27)	1192 (34)	380 (11)	992 (28)
Biopsy type <sup>§,¶</sup>								
Core needle biopsy	138	3953	72 (67 to 77)	0.006	969 (25)	1415 (36)	459 (12)	1110 (28)
Excisional biopsy	102	2947	67 (62 to 73)		762 (26)	961 (33)	261 (9)	963 (33)
<i>Case characteristics assessed by participant pathologists</i>								
Cumulative number of unique sub-diagnoses given to a case**								
<4	50	1436	64 (58 to 71)	<0.001	141 (10)	702 (49)	80 (6)	513 (36)
4–7	137	3938	70 (66 to 75)		1090 (28)	1240 (31)	445 (11)	1163 (30)
8	53	1526	74 (69 to 79)		500 (33)	434 (28)	195 (13)	397 (26)
Degree of challenge								
Low	–	4829	59 (53 to 66)	<0.001	701 (15)	1879 (39)	292 (6)	1957 (41)
High	–	2071	94 (92 to 97)		1030 (50)	497 (24)	428 (21)	116 (6)
Confidence in assessment								

**Would you ask for a second pathologist's opinion of this case before finalising the report? (Assume a pathologist is available.)**

Case characteristics*	Number of cases	Number of assessments	Rate of second opinion for combined responses <sup>†</sup>	p Value <sup>‡</sup>	Response options			
					Combined yes response rate (95% CI)	Yes, because I would want a second pathologist's opinion for diagnostic reasons	Yes, because it is our policy to get a second opinion in cases with this diagnosis	Yes to both, because I would want it and because it is our policy
High Confidence	–	5640	65 (59 to 70)	<0.001	1107 (20)	2071 (37)	464 (8)	1998 (35)
Low confidence	–	1260	94 (91 to 97)		624 (50)	305 (24)	256 (20)	75 (6)
Case considered borderline								
Yes	–	1803	95 (93 to 97)	<0.001	954 (53)	366 (20)	398 (22)	85 (5)
No	–	5097	61 (55 to 67)		777 (15)	2010 (39)	322 (6)	1988 (39)
Participant diagnosis								
Benign w/o atypia	–	2658	55 (49 to 61)	<0.001	579 (22)	708 (27)	167 (6)	1204 (45)
Atypia	–	1336	88 (83 to 93)		647 (48)	292 (22)	236 (18)	161 (12)
DCIS	–	2186	77 (71 to 83)		413 (19)	998 (46)	269 (12)	506 (23)
Invasive	–	720	72 (65 to 79)		92 (13)	378 (53)	48 (7)	202 (28)

\* By self-report on baseline survey.

† Row percentages might not add up to 100 due to rounding.

‡ Binary variable created from all three affirmative responses where 1=yes, 0=no. LS means and CIs estimated on logit scale and back transformed on the scale of the mean using the inverse link function.

§ Probability >  $\chi^2$ , Wald statistics for type 3 GEE analysis.

¶ Women's age and biopsy type were provided to participants during specimen assessment; breast density was not provided.

¶¶ Low density (< 50 fibroglandular; BIRADS category 1 and 2) and high density (> 51% fibroglandular; BIRADS category 3 and 4; breast density was not provided to participants during specimen assessment).

¶¶¶ Number of unique diagnostic subtypes at the level of each case as determined by participants.

¶¶¶ DCIS, ductal carcinoma in situ; GEE, generalised estimating equation; LS, least square.