Published in final edited form as:

Ann Surg Oncol. 2015 December ; 22(0 3): 470–475. doi:10.1245/s10434-015-4698-6.

Do the ACOSOG Z0011 Criteria Affect the Number of Sentinel Lymph Nodes Removed?

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Abstract

Introduction—In this study we sought to determine if adoption of the Z0011 criteria was associated with removal of more SLNs.

Methods—In a retrospective review of a prospective database of breast cancer patients treated at our institution between 2006–2013, we identified 5213 eligible patients who elected to undergo breast-conserving surgery; 2372 were treated pre-Z0011 and 2841 post-Z0011. Clinicopathologic factors were collected, and univariate and multivariate models were fit to identify variables associated with number of SLNs removed.

Results—Median patient age, 60 years, did not differ between groups. Median tumor size was similar in both groups—1.1 (0.05–5.0cm) in the pre-Z0011 group and 1.2 (0.1–5.2cm) in the post-Z0011 group. The mean number of SLNs excised in the pre-Z0011 patients was 2.8 compared to 2.9 in post-Z0011 patients ($p=0.01$). 3 lymph nodes were removed in 1771 (75%) pre-Z0011 patients compared to 2006 (71%) post-Z0011 patients ($p=0.01$). Factors associated with the removal of more SLNs on multivariate analysis included adoption of ACOSOG Z0011 criteria ($p=0.03$), young age ($p=0.0001$), and large tumor size ($p=0.0005$). ALND was performed in 379 (16%) patients pre-Z0011 compared to 68 (2%) node-positive post-Z0011 patients ($p<0.0001$).

Conclusion—Since the adoption of Z0011 criteria, we found significantly fewer patients undergoing ALND for positive SLNs. We noted a significant, slight shift in the removal of 4 SLNs. The Z0011 criteria were not associated with a clinically significant increase in the number of SLNs removed.

INTRODUCTION

Sentinel lymph node biopsy (SLNB) is the standard of care for axillary staging in clinically node-negative breast cancer patients. The ability of SLNB to accurately predict the status of other axillary nodes as been validated in several studies.¹ The NSABP B32 trial showed that

SLNB was equal to axillary lymph node dissection (ALND) in the ability to accurately stage the axilla in clinically node-negative patients. Veronesi et al showed that the overall survival (OS) was similar between node-negative patients who had a SLNB alone compared to those who had an ALND.² The 10-year follow-up results of this randomized control study confirmed no difference in survival between the group that had SLNB alone and the group that had ALND, thus confirming that ALND could be avoided in patients with a negative SLNB.³ Since the incorporation of SLNB into axillary staging, ALND is reserved for those patients with clinically palpable nodes or in whom a SLNB is positive.

Management of a positive sentinel lymph node (SLN) changed with the ACOSOG Z0011 trial.⁴ This prospective, phase III, non-inferiority trial was first presented at the American Society of Clinical Oncology meeting in June 2010 and subsequently published in February 2011. It randomized patients with T1-2, clinically node-negative cancers who had a positive SLNB to completion ALND versus no ALND. Eligible patients had to undergo breast-conservation therapy (BCT), whole-breast irradiation, and systemic therapy. Over a 5-year period, 445 patients were randomized to ALND and 446 to no ALND. At a median follow up of 6.3 years there was no difference between groups with respect to nodal or in-breast recurrence and disease-free survival (DFS) or OS. In early-stage, clinically node-negative patients undergoing BCT, the need for ALND is now determined by the number of positive SLNs in patients who meet the ACOSOG Z0011 criteria.⁴

SLNB removes an average of 2 lymph nodes in most studies.⁵ However, several recent studies have identified factors associated with the removal of additional nodes at the time of SLNB.^{6,7,8} Chagpar et al found that large tumor size and surgeon inexperience with SLNB were associated with the removal of more sentinel nodes.⁶ Young patient age and large tumor size were cited by Port et al as factors that biased surgeons to remove extra lymph nodes.⁷ Recently, the ACOSOG Z0011 trial has been examined as a potential bias for removing additional sentinel nodes. Robinson et al found no statistical difference in the median number of SLNs removed before or after publication and presentation of the ACOSOG Z0011 trial, and a significant decrease in completion axillary node dissection.⁹

One of the benefits of SLNB is the reduction of lymphedema often associated with an ALND, but if a greater number of sentinel nodes are being removed, then this may ultimately contribute to a reduction in this benefit.

Here we examined whether the adoption of the ACOSOG Z011 criteria at our institution has affected the number of sentinel nodes removed and its effect on rate of ALNDs performed.

METHODS

A retrospective review of a prospectively maintained database was performed in 5213 patients who were eligible for and elected to undergo BCT at a single institution between January 2006 and December 2013. The ACOSOG Z0011 criteria were institutionally adopted in August 2010. Our study group consisted of 2372 patients in the pre-Z0011 cohort (January 2006–December 2009.) and 2841 patients in the post-Z0011 cohort (August 2010–December 2013). Fifteen surgeons performed SLNB using dual tracer mapping with Tc-99

labeled sulfur colloid and/or isosulfan blue dye. The Memorial Sloan Kettering Cancer Center technique for SLNB has been previously described.¹⁰ All nodes that were blue, “hot”, or palpable were considered SLNs and removed.

Patient, tumor, and treatment variables were collected for both cohorts to determine factors associated with the number of SLNs removed. Pre-Z0011 and post-Z0011 cohorts were compared using Chi-square and Wilcoxon rank sum tests. Univariate linear regression, controlling for surgeon using a random effect, was performed to identify variables associated with number of SLNs removed. Multivariate linear regression was used to assess the association between the adoption of ACOSOG Z0011 and the number of SLNs removed after adjusting for known confounders. All analysis was performed in SAS 9.4 (SAS Institute, Cary, NC), and p-values less than 0.05 were considered significant.

RESULTS

A total of 5213 patients were included for analysis. Patients who had a sentinel node procedure but no nodes identified on pathologic examination were excluded (n=14). The clinical pathologic features for the pre- and post-Z0011 cohorts are summarized in Table 1. The median patient age was 60 years in both groups (pre-Z0011, range 24–91; post-Z0011, range 20–92). The median tumor size was similar in both groups: 1.1 cm (0.05–5.0 cm) in the pre-Z0011 cohort and 1.2 cm (0.1–5.2 cm) in the post-Z0011 cohort. Ductal histology was the most common subtype of invasive cancer, comprising 1963 (82.8%) patients in the pre-Z0011 cohort, compared to 2453 (86.3%) in the post-Z0011 cohort. Multifocality was not present in 1989 (84.5%) of tumors in the pre-Z0011 cohort, compared to 2339 (83.0%) in the post-Z0011 cohort. 1965 (84.3%) patients were estrogen receptor positive in the pre-Z0011 cohort, compared to 2479 (88.5%) patients in the post-Z0011 cohort ($p<0.0001$). 2040 (90%) of patients in the pre-Z0011 cohort were HER2 negative, compared with 2448 (89.4%) in the post-Z0011 cohort ($p=0.4$). Lymphovascular invasion was present in 439 pre-Z0011 tumors (20.1%) versus 689 post-Z0011 tumors (26.1%) ($p<0.0001$). 2278 (96.0%) tumors in the pre-Z0011 cohort were found to have no evidence of extracapsular extension (ECE), compared to 2745 (96.8%) in the post-Z0011 cohort, ($p=0.1$).

The mean number of SLNs excised in the pre-Z0011 patients was 2.8 compared to 2.9 in the post-Z0011 patients ($p=0.01$). Figure 1a shows the distribution of SLNs excised as a categorical variable of 1–3 SLNs vs 4 SLNs excised. Four or more SLNs were removed in 601 (25.3%) pre-Z0011 patients compared to 835 (29.4%) post-Z0011 patients ($p=0.01$). Figure 1b shows the distribution of the axillary procedure performed. In the pre-Z0011 cohort, 379 (16.0%) had a completion axillary lymph node dissection (cALND) compared to 68 (2.4%) patients in the post-Z0011 group ($p<0.0001$).

The univariate analysis is shown in Table 2. We found younger age ($p<0.0001$), larger tumor size ($p<0.0001$), the adoption of ACOSOG Z0011 criteria ($p=0.03$), and ECE 2 ($p<0.0001$) to be significantly associated with removal of additional sentinel nodes.

The multivariate analysis is shown in Table 3. Factors associated with the removal of additional SLNs on multivariate analysis remained young age ($p<0.0001$), large tumor size

($p<0.0001$) and ECE 2 ($p=0.001$). Adoption of the Z0011 criteria was also significantly associated with the removal of more SLNs ($p=0.03$), but the effect was not clinically significant (0.12 additional SLNs).

Figure 2a shows the mean number of SLNs removed stratified by age. An increasing number of SLNs was removed with decreasing age. In addition, in each age category, more SLNs were removed in the post-Z0011 cohort versus the pre-Z0011 cohort. Figure 2b shows the mean number of SLNs removed stratified by tumor size. An increasing number of SLNs was removed with increasing tumor size. In addition, for each tumor size, additional SLNs were removed in the post-Z0011 cohort versus the pre-Z0011 cohort.

DISCUSSION

The NSABP B32 trial showed that SLNB was equivalent in OS and DFS when compared to ALND.¹¹ Although the median number of SLNs described in the literature is between 2 and 3, the number of actual SLNs removed is affected by several factors, including technique, experience, clinical factors, and the surgeon's perceived risk of axillary metastasis.¹¹² Schrenk et al noted that the pathologic status of the axilla was accurately determined by the first and second SLNs in 99% of patients.⁸ In addition, the authors noted that removing more than 3 lymph nodes did not increase the chance of finding a positive node. Additionally, Yi et al reported that >99% of positive SLNs were found in the first 5 SLNs removed.¹²

Several studies have reported on factors associated with the number of nodes removed during SLNB. Chagpar et al found in a study of 4131 patients that palpable tumors ($p<0.001$), dermal injection of radiocolloid tracer ($p=0.001$), and surgeon inexperience ($p<0.007$) were independently associated with the removal of 4 SLNs on multivariate analysis.⁶ Schrenk et al evaluated whether variables, including tumor size, histologic characteristics, receptor status, age, and type of lymphatic mapping influenced the number of SLNs removed.⁸ This study found no association between the variables studied and the number of SLNs removed. Port et al identified age and large tumor size as significantly associated with removal of more sentinel nodes at our institution.⁷ In the 4103 patients undergoing SLNB, more lymph nodes were removed for patients ≤ 50 years of age versus > 50 years (4.6 nodes versus 4.2 nodes; $p=0.006$) and in those with larger tumors (6.3 nodes for T2 tumors versus 4.3 nodes for T1 tumors; $p<0.006$). Our study findings are consistent with this earlier report. Yi et al found that certain factors required increased SLN sampling to achieve 99% recovery of all positive SLNs. Patients with mixed ductal and lobular histology required 2 additional SLNs versus patients with pure ductal or lobular histology (7 SLNs versus 5 SLNs, $p<0.001$), Caucasian ethnicity required 2 additional SLNs versus non-Caucasian ethnicity (6 SLNs versus 4 SLNs, $p<0.001$), and inner quadrant tumors required 3 additional SLNs versus outer quadrant tumors (8 SLNs versus 5 SLNs, $p<0.001$).¹² We did not identify tumor histology, nuclear grade, multifocality, hormone status, or presence of lymphovascular invasion to be associated with the removal of additional lymph nodes in our study.

The influence of the ACOSOG Z0011 criteria on SLNB was recently reported by Robinson et al.⁹ They hypothesized that surgeons would either place less importance on axillary lymph nodes, resulting in fewer SLNs being removed, or more importance and thus potentially remove more SLNs, since cALND was no longer being performed unless 2 nodes were positive. In either scenario, the ACOSOG Z0011 trial could be a potential source of bias, either for under-sampling or over-sampling the clinically negative axilla. In their single-institution study of 923 patients undergoing BCT for T1-2, clinically node-negative breast cancer, they found that the mean and median numbers of SLNs removed for the entire cohort were 2.7 and 2, respectively. The authors looked at the number of SLNs removed before and after both presentation and publication of the Z0011 trial. The mean number of SLNs removed before presentation of the trial was 2.7 (95% confidence interval [CI] 2.6–2.8) compared with 2.6 (95% CI 2.4–2.7) after presentation ($p=0.19$). Similarly, the mean number of SLNs removed before trial publication was 2.7 (95% CI 2.6–2.8) compared with 2.5 (95% CI 2.4–2.7) after trial publication ($p=0.10$). In addition, the authors found no difference in SLNs removed before or after Z0011 implementation when patients were divided into three age groups (50, 60, and 70 years). In contrast to the study by Robinson et al, we found that as age decreased, the mean number of SLNs removed increased in the post-Z0011 cohort ($p<0.0001$).

In a prior study from our institution, the impact of ECE on the burden of axillary disease was evaluated in 11,730 patients meeting Z0011 criteria.¹³ Patients with ECE were older (57 versus 54 years of age, $p=0.001$), had larger tumors (2.0 vs 1.7 cm; $p<0.0001$), multifocal tumors ($p=0.006$), hormone positive tumors ($p=0.016$), and lymphovascular invasion ($p<0.0001$). On multivariate analysis, 2 mm of ECE was the strongest predictor of 4 positive nodes on cALND (odds ratio [OR] 14.2), indicating that the presence and amount of ECE is an important indicator of nodal disease burden. In a study by Dengel et al, the presence of ECE, involvement of 3 SLNs, and matted nodes identified patients at high risk of nodal disease in ACOSOG Z0011-eligible patients, and represented a subset of patients who were appropriately treated with cALND.¹⁴ Similarly, Stitzenberg et al found that ECE was highly predictive of non-SLN involvement on multivariate analysis (OR 6.04, 95% CI 1.5–24.2, $p=0.01$).¹⁵ ECE was associated with the removal of more SLNs in our study ($p=0.001$). While the presence of ECE is not known at the time of SLN, the presence of 2 mm of ECE predicts a possibility for greater tumor burden in the axilla and may serve as an indication for cALND, even if <3 SLNs are positive at the time of SLNB.

The National Comprehensive Cancer Network guidelines were updated in 2011 to include results of the Z0011 trial as standard of care. Several studies have assessed the impact of the trial on clinical practice. Wright et al found that ALND ($p<0.001$) and intraoperative SLN analysis ($p<0.001$) declined after implementation of Z0011 criteria at their institution.¹⁶ The authors found that patients with ECE (OR 12.8, 95% CI 2.5–67.1) or those patients undergoing reoperative surgery (OR 10.8, 95% CI 2.6–44.4) were more likely to undergo ALND. Robinson et al found their rate of completion ALND after trial publication decreased from 83% to 62% ($p<0.01$).⁹ Caudle et al found that the rate of ALND decreased after implementation of Z0011 from 85% to 24% ($p<0.001$).¹⁷ The authors noted that surgeons were more likely to perform ALND in patients with larger tumors (2.2 versus 1.5 cm, $p=0.09$), lobular histology ($p=0.001$), fewer SLNs harvested (1 vs. 3, $p=0.09$), larger

SLN metastasis size (4 versus 2.5 mm, $p=0.19$), ECE (20 versus 6%, $p=0.16$), and in patients with a higher probability of positive non-sentinel lymph nodes ($p=0.03$). At our institution, Dengel et al prospectively assessed a cohort of patients undergoing BCT who met ACOSOG Z0011 criteria and found that 84% of patients had ALND omitted since implementation of the trial.¹⁴ In our current study, the rate of ALND decreased from 16.0% to 2.4%, indicating that implementation of the Z0011 criteria has been successfully adopted into our clinical practice. To our knowledge, our study is the largest examining the impact of the Z0011 criteria on SLNB. The rate of ALND decreased in the post-Z0011 cohort, in keeping with our institutional acceptance of Z0011 criteria. We noted a slightly higher proportion of patients who had 4 SLNs harvested in the post-Z0011 cohort compared with the pre-Z0011 cohort. This may be a reflection of a bias for removal of all potential SLNs as no completion ALND is to be performed in patients who met Z0011 criteria.

Conclusion

Consistent with our prior study, we found young age and large tumor size to be associated with a greater number of SLNs removed at SLNB. Since adoption of the ACOSOG Z0011 trial criteria, we found the mean number of SLNs removed changed very little (2.8 before, 2.9 after), with significantly fewer patients undergoing ALND for 2 positive SLNs. We noted a slight shift in the removal of 4 SLNs in the post-Z0011 cohort, possibly representing an additional bias to remove all potential SLNs during the SLNB. Surgeons should be aware of factors that may potentially influence the removal of a greater number of sentinel nodes.

Acknowledgments

Funding: This study was supported in part by NIH/NCI Cancer Center Support Grant No. P30 CA008748.

REFERENCES

1. Giuliano AE, Kirgan DM, Guenther JM, et al. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann Surg.* 1994; 220(3):391–8. discussion 8-401. [PubMed: 8092905]
2. Veronesi U, Paganelli G, Viale G, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. *N Engl J Med.* 2003; 349(6):546–53. [PubMed: 12904519]
3. Veronesi U, Viale G, Paganelli G, et al. Sentinel lymph node biopsy in breast cancer: ten-year results of a randomized controlled study. *Ann Surg.* 2010; 251(4):595–600. [PubMed: 20195151]
4. Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. *Jama.* 2011; 305(6):569–75. [PubMed: 21304082]
5. Cody HS 3rd. Clinical aspects of sentinel node biopsy. *Breast Cancer Res.* 2001; 3(2):104–8. [PubMed: 11250755]
6. Chagpar AB, Carlson DJ, Laidley AL, et al. Factors influencing the number of sentinel lymph nodes identified in patients with breast cancer. *Am J Surg.* 2007; 194(6):860–4. [PubMed: 18005785]
7. Port ER, Patil S, Stempel M, et al. Number of lymph nodes removed in sentinel lymph node-negative breast cancer patients is significantly related to patient age and tumor size: a new source of bias in morbidity assessment? *Cancer.* 2010; 116(8):1987–91. [PubMed: 20151427]
8. Schrenk P, Rehberger W, Shamiyeh A, et al. Sentinel node biopsy for breast cancer: does the number of sentinel nodes removed have an impact on the accuracy of finding a positive node? *J Surg Oncol.* 2002; 80(3):130–6. [PubMed: 12115795]

9. Robinson KA, Pockaj BA, Wasif N, et al. Have the American College of Surgeons Oncology Group Z0011 trial results influenced the number of lymph nodes removed during sentinel lymph node dissection? *Am J Surg.* 2014; 208(6):1060–4. discussion 3–4. [PubMed: 25312842]
10. Cody HS 3rd, Borgen PI. State-of-the-art approaches to sentinel node biopsy for breast cancer: study design, patient selection, technique, and quality control at Memorial Sloan-Kettering Cancer Center. *Surg Oncol.* 1999; 8(2):85–91. [PubMed: 10732960]
11. Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer--a multicenter validation study. *N Engl J Med.* 1998; 339(14):941–6. [PubMed: 9753708]
12. Yi M, Meric-Bernstam F, Ross MI, et al. How many sentinel lymph nodes are enough during sentinel lymph node dissection for breast cancer? *Cancer.* 2008; 113(1):30–7. [PubMed: 18457326]
13. Gooch J, King TA, Eaton A, et al. The extent of extracapsular extension may influence the need for axillary lymph node dissection in patients with T1-T2 breast cancer. *Ann Surg Oncol.* 2014; 21(9):2897–903. [PubMed: 24777858]
14. Dengel LT, Van Zee KJ, King TA, et al. Axillary dissection can be avoided in the majority of clinically node-negative patients undergoing breast-conserving therapy. *Ann Surg Oncol.* 2014; 21(1):22–7. [PubMed: 23975314]
15. Stitzenberg KB, Meyer AA, Stern SL, et al. Extracapsular extension of the sentinel lymph node metastasis: a predictor of nonsentinel node tumor burden. *Ann Surg.* 2003; 237(5):607–12. discussion 12–3. [PubMed: 12724626]
16. Wright GP, Mater ME, Sobel HL, et al. Measuring the impact of the American College of Surgeons Oncology Group Z0011 trial on breast cancer surgery in a community health system. *Am J Surg.* 2015; 209(2):240–5. [PubMed: 25236187]
17. Caudle AS, Hunt KK, Tucker SL, et al. American College of Surgeons Oncology Group (ACOSOG) Z0011: impact on surgeon practice patterns. *Ann Surg Oncol.* 2012; 19(10):3144–51. [PubMed: 22847123]

Synopsis

The number of SLNs removed before and after ACOSOG Z0011 was similar. A shift in the removal of 4 SLNs in the post-Z0011 cohort was seen, representing a bias to remove all potential SLNs during the SLNB.

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Fig 1.

(a) Number of sentinel lymph nodes removed, pre-Z0011 vs post-Z0011; (b) axillary procedure performed, pre-Z0011 vs post-Z0011

SLN, sentinel lymph nodes; ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy

Fig 2.

(a) Mean number of SLN Removed by Age Pre vs Post Z0011 (b) Mean Number of SLN Removed by Tumor Size Pre vs Post Z0011
SLN, sentinel lymph nodes

Table 1

Summary of clinical pathologic features for the pre- and post-Z0011 cohorts.

		Pre-Z0011 (N=2372)		Post-Z0011 (N=2841)		
Variable		N	%	N	%	p-value
Surgery date range		1/2006–12/2009		8/2010–12/2013		
Age (years) median (range)		60 (24–91)		60 (20–92)		0.7
Tumor size (cm) median (range)		1.1 (0.05–5.0)		1.2 (0.1–5.2)		0.01
Excised SLN mean		2.8		2.9		0.01
Excised SLN median (range)		2 (1–16)		2 (1–18)		
Excised SLN	1–3 SLNs	1771	74.7%	2006	70.6%	0.01
	4 SLNs	601	25.3%	835	29.4%	
Final axillary procedure	SLNB converted to ALND	379	16.0%	68	2.4%	<0.0001
	SLNB only	1993	84.0%	2773	97.6%	
Histology	DCIS-microinvasion	98	4.1%	2	0.1%	0.0001
	Ductal	1963	82.8 %	2453	86.3%	
	Lobular	239	10.1%	260	9.2%	
	Other	72	3.0%	126	4.4%	
Nuclear grade	1	96	5.0%	187	7.2%	0.0008
	2	1013	52.7%	1431	54.8%	
	3	575	30.0%	732	28.0%	
	Lobular	239	12.4%	260	10.0%	
	Unknown	449	--	231	--	
Multifocal	Yes	365	15.5%	480	17.0%	0.1
	No	1989	84.5%	2339	83.0%	
	Unknown	18	--	22	--	
Estrogen receptor status	Positive	1965	84.3%	2479	88.5%	<0.0001
	Negative	366	15.7%	321	11.5%	
	Unknown	41	--	41	--	
Progesterone receptor status	Positive	1601	68.7%	2224	79.8%	<0.0001
	Negative	731	31.3%	564	20.2%	
	Unknown	40	--	53	--	
HER2 status	Positive	225	10.0%	290	10.6%	0.4
	Negative	2040	90.0%	2448	89.4%	
	Unknown	107	--	103	--	
Lymphovascular invasion	Present	439	20.1%	689	26.1%	<0.0001
	Absent	1744	79.9%	1950	73.9%	
	Unknown	189	--	202	--	
Extracapsular extension	None or <2mm	2278	96.0%	2745	96.8%	0.1
	2mm	94	4.0%	89	3.1%	

		Pre-Z0011 (N=2372)		Post-Z0011 (N=2841)			
Variable		N	%	N	%	p-value	
	Unknown	1	--	6	--		

SLN, sentinel lymph node

Table 2

Univariate analysis of factors associated with number of SLN removed.

Variable	Coefficient	p-value
Post-Z0011 vs pre-Z0011	0.12	0.03
Age (per 10 years)	−0.21	<.0001
Age <50 years	0.52	<.0001
Tumor size	0.16	<.0001
Histology		0.8
Ductal or DCIS-M	Ref	
Lobular	0.06	
Other	0.00	
Nuclear grade		0.1
1	Ref	
2	0.16	
3	0.26	
Lobular	0.22	
Multifocal (yes vs no)	0.02	0.8
Lymphovascular invasion (yes vs no)	0.10	0.1
Estrogen receptor status (positive vs negative)	0.00	0.9
Progesterone receptor status (positive vs negative)	0.01	0.9
HER2 status (positive vs negative)	0.08	0.4
ECE (≥ 2mm vs <2mm)	0.53	<.0001

DCIS, ductal carcinoma in situ; ECE, extracapsular extension

Table 3

Multivariate analysis of factors associated with number of sentinel lymph nodes removed.

Variable	Coefficient	p-value
Post-Z0011 vs pre-Z0011	0.12	0.03
Age (per 10 years)	−0.21	<.0001
Tumor size	0.12	0.0005
Estrogen receptor status (positive vs negative)	0.06	0.4
ECE (≥2mm vs <2mm)	0.46	0.001

ECE, extracapsular extension