Utility and Costs of Routine Staging Scans in Early-Stage Breast Cancer

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Abstract

Background: In October 2013, the American Society of Clinical Oncology (ASCO) recommended avoiding routine staging in patients with newly diagnosed early-stage (clinical stage I/II) breast cancer as part of the Choosing Wisely initiative. Our study examines the impact of adopting ASCO imaging recommendations at an academic medical center in a retrospective cohort.

Methods: Patients diagnosed with breast cancer at the University of Vermont Cancer Center (UVMCC) between October 1, 2011, and September 30, 2013, were identified. For those who had undergone staging imaging, the indications, results, costs, and changes in management were assessed. Staging imaging was categorized as "indicated" if patients had signs or symptoms suggestive of metastases or "nonindicated" when none of these factors was present.

Results: During the study period, 683 women were diagnosed with breast cancer; 13.9% (95/683) underwent staging, of which 69.5% (66/95) had clinical stage I/II disease. Nonindicated staging was performed in only stage I/II patients and identified no cases of metastatic disease. For the entire cohort, indicated staging had significantly greater detection of metastatic disease (21.9% vs 0%; P <.001) and changes in patient management (21.9% vs 1.85%; P <.01). The false-positive rate of staging was higher in the nonindicated group but not significantly different (37% vs 20%; P = .07). The total cost of nonindicated staging imaging was $5720 per patient.

Conclusions: Adopting ASCO recommendations for imaging may improve patient care and lead to cost savings.

Implications for Practice: We have shown that changing practice to use the staging criteria proposed by ASCO's Choosing Wisely recommendations decreases the numbers of total imaging studies, false-positive scans, and imaging costs, without modifying the detection of asymptomatic metastases. Staging scans in patients with stage I/II breast cancer are unlikely to guide clinical decision, mainly due to the rarity of asymptomatic metastases. The use of criteria-based imaging saves nearly $6000 per patient. Recent studies suggest that despite ASCO's Choosing Wisely recommendations, women with early-stage breast cancer continue to receive unnecessary imaging evaluations, highlighting the need for ongoing educational efforts regarding these recommendations.

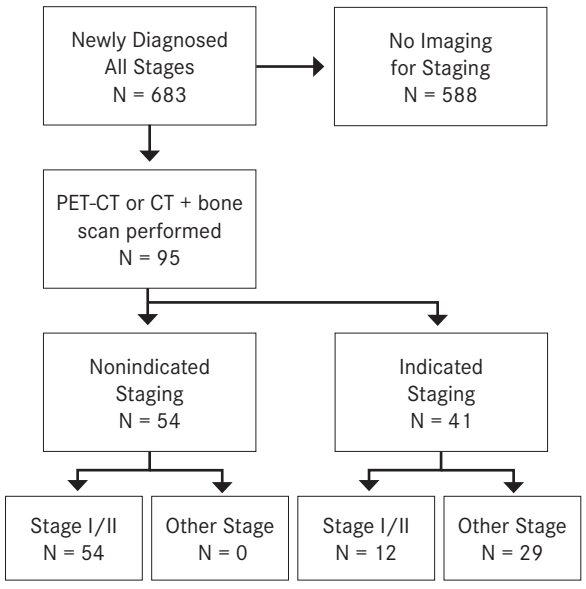
Key words: breast cancer, diagnostic imaging, cancer staging, cost-effectiveness analysis, evidence-based medicine, guideline adherence, sensitivity and specificity.

Introduction

Although breast cancer is the most common malignancy in women, with approximately 230,000 cases diagnosed yearly in the United States,[1] most patients are diagnosed with early-stage breast cancer (stage I/II). These patients have a high rate of cure with surgery and adjuvant therapies, such as radiation, chemotherapy, hormonal therapy, and biologic therapy.[2] Detection of metastatic disease allows patients who cannot be cured to proceed to systemic therapy and avoid morbidity of loco-regional surgical therapy. Thus, accurate staging of breast cancer provides prognostic information and guides treatment decisions.[3,4]

Clinical staging for breast cancer is based on history, physical examination, laboratory work, and breast imaging. Advanced radiology studies such as positron emission tomography (PET), computed tomography (CT), integrated PET with CT (PET-CT), or bone scan may be used to determine if disease is present outside of the breast and axilla (metastatic sites). National guidelines do not recommend routine staging scans for asymptomatic patients with clinical stage I or II breast cancer.[4,5] This recommendation is based on data from several studies demonstrating that asymptomatic but radiologically evident metastases are rare in this group of patients, with a median prevalence of 0.2% and 1.2% for stage I and stage II disease, respectively.[6-15] In addition, staging scans are expensive, CT scans result in additional radiation exposure, and false-positive scans are common.[9,11,16-18] False-positive scans are of special concern in patients with cancer

FIGURE 1. Patient population with distribution of indicated and nonindicated staging evaluations.



because they may cause significant emotional distress and treatment delays, and can harm patients by the invasive procedures necessary to investigate abnormalities.

The Choosing Wisely campaign is a national physician and patient-centered initiative from the American Board of Internal Medicine meant to reduce healthcare practices that offer limited benefit to patients. The American Society of Clinical Oncology (ASCO) has contributed several recommendations about cancer care to the Choosing Wisely campaign.[19] In 2013 ASCO officially recommended to "not perform PET, CT, and radionuclide bone scans in the staging of early breast cancer at low risk for metastasis" (ductal carcinoma in situ, clinical stage I or II) because the incidence of asymptomatic, radiologically evident metastatic cancer is low.[19] This recommendation is consistent with other national guidelines.[4] Clinical practice at the University of Vermont Cancer Center (UVMCC) had been to obtain routine staging scans for all patients with breast cancer who had clinical or pathologic nodal involvement, because patients with lymph node–positive disease have a higher likelihood of metastatic disease and, consequently, a very different prognosis and treatment options. We conducted the current study to evaluate the effect of changing current clinical practice to be consistent with ASCO recommendations. We examined the effect on identification of asymptomatic but radiologically apparent metastatic disease, clinical management, and cost.

Materials and Methods

This study was conducted at the UVMCC, located at the 450-

TABLE 1: Demographic data for patient population

	Registry: 683		Imaged Cohort: 95		
Characteristic	No	%	No	%	P value
Age					.05
Mean	59.8	(SD 12.3)	57.9	(SD 11.9)	
Range	26-92		34-78		
<35	16	2.3%	1	1.1%	
36-50	155	22.7%	32	33.7%	
>51	512	75.0%	62	65.3%	
Clinical Stage (preoperative)					<.001
0 (in situ)	138	20.2%	1	1.1%	
I	372	54.5%	22	23.2%	
IIA	77	11.3%	22	23.2%	
IIB	36	5.3%	22	23.2%	
III	31	4.5%	26	27.4%	
IV	18	2.6%	2	2.1%	
Unknown	11	1.6%	0	0.0%	
Histologic Grade					.01
I	118	17.3%	5	5.3%	
II	316	46.3%	46	48.8%	
III	217	31.8%	41	43.2%	
Unknown	32	4.7%	3	3.2%	
ER Status					.01
Positive	558	81.7%	72	75.8%	
Negative	110	16.1%	22	23.2%	
Unknown	15	2.2%	1	1.1%	
PR Status					.11
Positive	489	71.6%	60	63.2%	
Negative	178	26.1%	34	35.8%	
Unknown	16	2.3%	1	1.1%	
HER2 Status					<.001
Positive	81	11.9%	18	18.9%	
Negative	454	66.5%	74	77.9%	
Unknown	148	21.7%	3	3.2%	
Neoadjuvant Chemotherapy					<.001
Yes	56	8.2%	36	37.9%	
No	627	91.8%	59	62.1%	
Surgical Therapy					<.001
BCT	449	65.7%	14	14.7%	
Mastectomy	200	29.3%	71	74.7%	
None	34	5.0%	10	10.5%	
Radiation Therapy					.04
Yes	420	61.5%	69	72.6%	
No	263	38.5%	26	27.4%	

FIGURE 2. Imaging in patients with early-stage breast cancer.

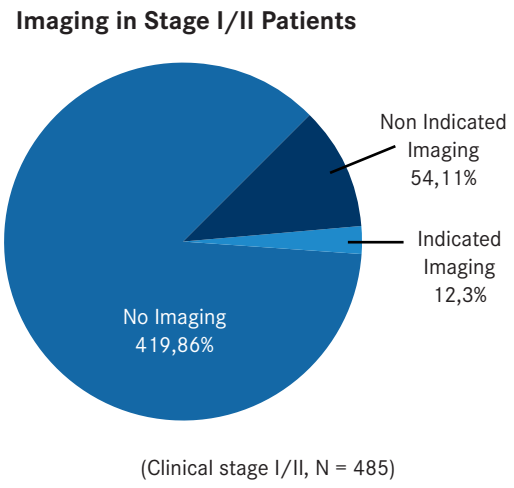


TABLE 2. Cost of Non-indicated Staging Imaging and Subsequent Costs of Follow-up Investigations

Non-indicated Staging			
Evaluation	No.	Charge (ea)	Cost
CT C/A + bone scan	32	$8,463.00	$139,199.42
CT C/A/P + bone scan	18	$12,062.25	$111,599.94
PET-CT	4	$7,022.00	$14,437.23
	Staging Subtotal		**$265,236.59**

Staging Follow-up			
Evaluation	No.	Charge (ea)	Cost
CT chest	1	$3,727.00	$1,915.68
CT abdomen	6	$2,696.00	$8,314.46
CT pelvis	3	$2,537.00	$3,912.05
PET-CT	4	$7,022.00	$14,437.23
US transvaginal	7	$818.00	$2,943.16
US abdominal	2	$1,005.44	$1,033.59
US Thyroid	2	$1,071.48	$1,101.48
CT head	1	$2,615.00	$1,344.11
MRI head	1	$7,848.00	$4,033.87
Thyroid biopsy	1	$3,135.48	$1,611.64
Lung biopsy	1	$5,932.10	$3,049.10
	Follow-up scan subtotal		**$43,696.38**
		Total cost	**$308,932.98**

bed tertiary care University of Vermont Medical Center in Burlington. The study was approved by the Institutional Review Board and the Protocol Review and Monitoring Committee of the UVMCC.

Patients: New cases of breast cancer diagnosed and treated at UVMCC between October 1, 2011, and September 30, 2013, were identified through the Vermont Cancer Registry. Patients who had undergone radionuclide bone scan, PET-CT, CT chest, CT abdomen, and CT pelvis during this time were identified from billing databases by Current Procedural Terminology codes. Patient charts were abstracted if scans were associated with an International Classification of Diseases-9 code for breast cancer. Patients were excluded from this cohort if they had undergone imaging during the study period but were diagnosed before October 1, 2011.

Data Sources: We obtained data from several sources: administrative billing, the Vermont Cancer Registry, and medical record abstractions. Medical records of imaged patients were reviewed by a physician to obtain the following variables: age, tumor/nodes/metastasis (TNM) clinical stage at presentation (American Joint Committee on Cancer, 7th edition), symptoms potentially attributable to cancer, radiology scans ordered with results, final pathologic stage, tumor characteristics, and breast cancer treatment changes secondary to staging imaging. Clinical stage was documented by the treating physician and confirmed by chart review.

CT scans were obtained with intravenous contrast on multidetector-row scanners with a reconstructed slice thickness of 3 mm. PET-CT scans were obtained with F18-fluorodexoyglucose and 3D time-of-flight PET imaging from skull vertex to feet with low-dose CT attenuation correction. Bone scans used Tc-99m with standard whole body bone images. Scan results were obtained by reviewing radiology reports signed by an attending radiologist. The staging scan was defined as the initial radiographic assessment obtained by each patient (PET-CT or bone scan with CT chest/abdomen ± pelvis) to assess a new diagnosis of breast cancer.

Definitions of "Indicated" and "Nonindicated" Scans

Staging scans were categorized as "indicated" or "nonindicated" **(Figure 1)**. The definitions for indicated and nonindicated scans were based on clinical stage in accordance with ASCO Choosing Wisely recommendations.[19] Thus, scans were considered "indicated" if patients had any of the following: clinical stage III or IV breast cancer, clinical stage 0/I/II with symptoms concerning for metastatic spread (bone pain, headache, abdominal pain, neurologic symptoms), abnormal serologic tests (liver function studies, complete blood count [CBC]), or findings suggestive of metastasis on routine preoperative studies. Scans in clinical stage 0/I/II patients were considered "indicated" if final pathology revealed stage III disease, thus prompting metastatic work-up. Scans were considered "nonindicated" if none of the above factors was present.

Outcomes

Staging scan results were categorized (based on findings outside of the breast and axilla) into 4 groups:

1. Normal/benign: defined as scan with no abnormalities or minor abnormalities that did not require further investigation for cancer care.

2. Positive for radiologic evidence of metastasis: defined as imaging with features suggestive of malignancy outside of the breast and axillae (upstaging to metastatic disease) that was confirmed on biopsy and/or by further imaging (PET-CT, MRI, and CT scan).

3. Positive for second primary cancer: defined as biopsy revealing cancer of nonbreast origin originally detected by a staging scan for breast cancer.

4. False-positive: defined as staging imaging for which further investigation was recommended by radiology, and that further investigation was either unremarkable or not obtained at the discretion of the treating oncologist with no evidence of metastatic disease in the area of concern after at least 1 year of clinical follow-up.

Changes in patient management resulting from staging imaging were identified by physician chart review. Changes in management included deferral of breast surgery because of discovery of metastasis, breast chemotherapy regimen change, and change in radiation therapy sites.

Cost Estimates

Costs of staging imaging and follow-up investigations of abnormal staging scans were determined by the cost-to-charge ratio method.[20] Charges for procedures and imaging studies were obtained from The University of Vermont Medical Center patient financial office. Charges were then corrected to costs by the 2013 institutional cost-to-charge ratio (0.514) as reported by the Centers for Medicare & Medicaid Services (CMS).[21] Additional physician visits or physician referrals were not incorporated into cost estimates.

Statistical Analysis

Demographic data are presented as totals and means, with ranges and standard deviations displayed where appropriate. Patient demographic proportions between the registry population and the cohort with imaging were compared using X^2 tests and alpha (α) = .05. We compared scan outcomes between indicated and nonindicated groups using a 2x2 contingency table with the Fisher exact test and two-tailed significance testing with α = .05. Analyses were performed in R (version 2.7.2, R Development Core Team).

Results

Patient Characteristics

During the study period, 683 patients received care at UVMCC for breast cancer (**Figure 1**). The mean patient age was 59.9 years

FIGURE 3. Outcomes of breast cancer staging scans according to nonindicated and indicated.

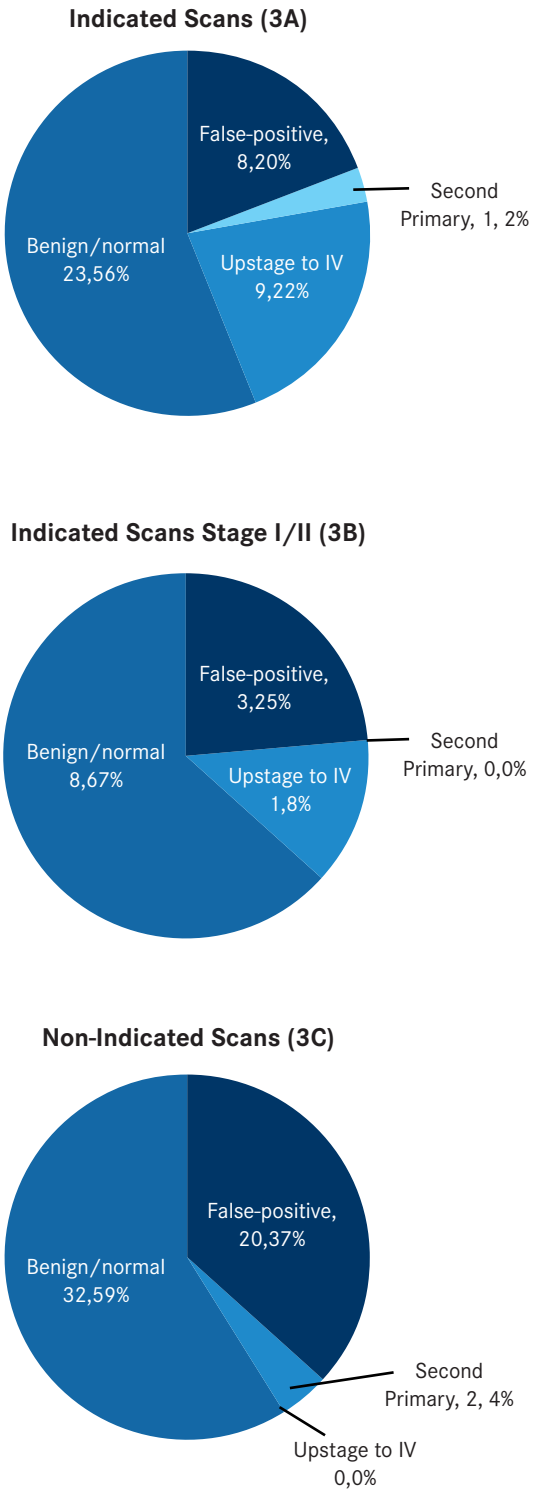


TABLE 3. Studies of imaging for early-stage breast cancer

Author, Year	Country	Stage	Imaging modalities used	% of patients with metastasis identified
Lee, 1981[10]	US	I/II	Bone scan	2%
Samant, 1999[15]	Canada	I/II	Liver ultrasound, bone scan	3%
Ravaioli, 2002[13]	Italy	I/II	Liver ultrasound, chest x-ray, bone scan	1.46%
Puglisi, 2005[12]	Italy	I/II	Bone scan	Stage I: 5.1% Stage II: 5.6%
Kim, 2011[22]	Korea	I/II	CT chest abdomen	Stage I: 0.2% Stage II: 0.0%
Tanaka, 2012[24]	Japan	I/II	CT chest/abdomen	Stage I: 0.0% Stage III:.9%
Simos, 2014[23]	Canada	I/II	Not stated	0%
Current study	US	I/II	PET, CT chest/abdomen, bone scan	0%

(range, 26-92 years). Patient characteristics are listed in **Table 1**. Women with stage I or stage II disease represented 71.0% (485) of the cohort. During the study period, 95 (13.9%) newly diagnosed patients underwent staging imaging with either PET-CT or bone scan with CT chest/abdomen ± pelvis. Sixty-six (69.5%) of the staging examinations were performed for women with clinical stage I or II disease (Figure 2). Patients who had staging imaging were noted to have more aggressive tumor characteristics compared with the registry population (Table 1). Staged patients had significantly higher tumor grade (P = .01) and were more likely to be HER2+ (P = .001). Patients with imaging were also more likely to undergo mastectomy (P <.001) and were more likely to receive neoadjuvant chemotherapy (P <.001).

Indicated Versus Nonindicated Staging Imaging

The study found that 43% (41/95) of all staging scans were determined to be indicated. These women had symptoms concerning for metastatic spread (bone pain, headache, abdominal pain, neurologic symptoms), abnormal serologic tests (liver function studies, CBC), or findings suggestive of metastases on routine preoperative studies. In this group, 70% (29/41) of scans were performed for clinical stage III or greater disease.

Indicated scans resulted in upstaging in 21.9 % (9/41) of patients and clinical management changes in 21.9% (9/41). Indicated scans detected second primary cancer in 2% (1/41). The false-positive rate for women who had indicated scans was 19.5% (8/41). Of those false-positives, 62.5% (5/8) underwent further imaging and/or biopsy and 37.5% (3/8) had unremarkable clinical follow-up at a mean of 2.1 years (Figure 3A). Evaluating findings in only stage I/II patients with indicated scans (Figure 3B) revealed a false-positive rate of 25% (3/12) and upstaging in 8% (1/12). No patients in this group were found to have second primary cancers.

During the study period, 56.8% (54/95) of staging scans were determined to be nonindicated (Figure 3C). No patient in this group was upstaged; however, 2 patients were found to have second primary cancers and clinical management was changed in 1 patient. The false-positive rate for this group was 37% (20/54): 8 (40%) patients had unremarkable further imaging and/or biopsy, while 12 (60%) were followed clinically for mean of 2.09 years.

Comparative Utility of Breast Cancer Staging Strategies

Indicated scans (9/41; 21.9%) had statistically greater detection of metastases than did nonindicated scans (0/54; P <.001). Indicated scans were also statistically more likely than nonindicated scans (21.9% vs 1.85%; P <.01) to result in changes in clinical management. The false-positive rates of nonindicated scans and indicated scans were not significantly different (37.0% vs 19.5%; P =.07).

Costs of Staging

The total cost of nonindicated staging was $308,932.98 over the study period, or $5720.98 per patient (**Table 2**). This total included costs for staging imaging, follow-up scans, and diagnostic interventions. The cost of nonindicated staging imaging during the study window was $256,236. The 9 patients with abnormal, nonindicated staging who underwent further evaluation at the discretion of the treating oncologists received 27 additional imaging studies and 2 invasive diagnostic procedures. The cost of these investigations was $43,696 over an average of 2.13 years of poststaging follow-up.

Incidence of Asymptomatic Metastasis for Clinical Stage 0-II Disease at UVM

Only 2 of 623 newly diagnosed clinical stage 0/II patients had asymptomatic, radiologically evident metastases at the time of presentation. One patient had clinical stage 0 (grade III, ER+/PR-/HER2+) and the other had clinical stage IIA (grade II, ER-/PR-/HER2+, cT2N0) disease. Thus, the incidence of metastasis in all patients with early-stage breast cancer (clinical stage 0/II) was 0.3% (2/623).

Discussion

To our knowledge, the current study represents the most recent cohort of US patients evaluated for the utility of staging for early breast cancer since Lee et al in 1981[10] and demonstrates that using current, more sophisticated imaging for staging does not enhance management of early-stage breast cancer. In our cohort, we had a very low rate of identification of metastatic disease in early-stage breast cancer. Our overall rate of identification of metastatic disease in clinical stage I/II breast cancer was 0.2% (1/485 women) with 0% (0/372) for stage I and 0.8% (1/113) for stage II. This is on the low end of published series, which have identified rates of 0.2% for stage I and 1.2% for stage II disease.[6-15]

Most women who had staging imaging in our cohort had risk factors for identification of asymptomatic metastases, such as lymph node involvement and aggressive tumor characteristics (grade III and HER2+). In our study, staging for all patients with lymph node–positive breast cancer did not upstage any patient and rarely resulted in clinical management changes. Thus, our analysis confirms that following ASCO recommendations promotes high-value breast cancer care and effectively identifies patients at increased risk of metastasis. As a result of this analysis, we have changed our practice to follow ASCO recommendations.

Indicated staging scans were associated with significantly greater detection of metastases (22%) and clinical management changes (22%), despite a high false-positive rate (19.5%). Non-indicated staging scans cost at least $5700 per patient and are associated with an even higher false-positive rate (37%). Use of the ASCO recommendations for imaging as outlined above could have avoided 54 staging scans. Our findings suggest that adoption of ASCO-recommended breast cancer staging practices may decrease imaging costs and reduce false-positive findings, especially in patients with lymph node involvement.

The low likelihood of radiologic upstaging that we observed in patients with early-stage breast cancer is supported by other studies (**Table 3**). Earlier studies were performed using liver ultrasound, chest x-ray, and bone scan, and identified metastatic disease in patients with asymptomatic stage I/II breast cancer in 1.4% to 5.6% of cases.[10,12,13,15] More recent studies used CT chest and abdomen scans for staging identified asymptomatic disease in fewer (0%-1.9%) patients with stage I/II breast cancer.[22-24] In these 3 studies, asymptomatic, radiologically evident metastases were observed in 0% to 0.2% of patients with stage I disease and in 0% to 1.9% of patients with stage II disease after CT chest/abdomen imaging. In a Canadian cohort published in 2014, most of those evaluations did not use CT-based imaging.[23]

Our study did not assess the emotional impact of nonindicated imaging, but additional testing provokes anxiety, especially when indeterminate or abnormal scans require further interventions.[25,26] The false-positive rate of 37% that we observed is greater than that reported by Kim et al (13.4%-14.4%) and by Tanaka et al (7.7%-9.5%), but similar to the 25% false-positivity reported for a CT-based staging approach in the United Kingdom and to the 21.9%-35.1% of stage I/II patients that had further confirmatory imaging in Canada.[22-24,27] The Choosing Wisely Campaign accurately describes the populations that should and should not be further staged; and patients with newly diagnosed stage I/II breast cancer should be spared the emotional, physical, and financial burdens of routine staging imaging.

Limitations

Our study has limitations. Our cohort is smaller than other non-US cohorts, even though our findings are in accord with those studies.[22,24] Second, our method of cost estimation may have wrongly estimated costs for breast cancer staging, since patient level charges are expected to vary as a result of negotiations by insurance providers and we did not include reimbursement for CMS part B or equivalent. Although claim reimbursement approaches provide cost estimates that more closely represent revenue, such approaches are labor-intensive, payments may not reflect the resources required to provide the service, and insurer-specific prices have been shown to correlate well with the charge-to-cost ratio.[28,29] Furthermore, our approach facilitated incorporation of downstream follow-up costs over several years, and our methodology is easily adaptable to cost structures at other institutions. Finally, the combination of bone scan and CT imaging used at our institution may complicate comparison to other studies, because the use of bone scan with CT for breast cancer staging does not appear to be common practice at other institutions.[22-24]

Conclusion

Using the staging criteria proposed by ASCO's Choosing Wisely recommendations decreases the number of total imaging studies, false-positive scans, and imaging costs, without modifying the detection of asymptomatic metastases. Staging scans in patients with stage I/II breast cancer are unlikely to guide clinical decision making because of the rarity of asymptomatic metastases. In addition, the use of criteria-based imaging saves almost $6000 per patient. Two recent studies suggest that despite ASCO's Choosing Wisely recommendations, women with early-stage breast cancer continue to receive unnecessary imaging evaluations, however,[30,31] highlighting the importance of ongoing ef-

forts to educate oncology providers.

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