A Comparison of Breast-Specific Gamma Imaging of Invasive Lobular Carcinomas and Ductal Carcinomas

The practice of preoperatively evaluating the breast tissue of patients with newly diagnosed breast cancer has evolved, with increased use of advanced imaging. The evaluation of breast tissue using functional breast-specific gamma imaging (BSGI) has proven to be a valuable method of imaging as an adjunct to mammography and ultrasonography for early detection of breast cancer. The use of BSGI specifically in imaging invasive lobular carcinomas (ILCs), which are known to be difficult to detect, has not been well characterized. We reviewed our experience with BSGI as an adjunct imaging method used specifically for detecting ILCs.

Methods | This is a retrospective review of a prospectively maintained imaging registry evaluating all patients who underwent BSGI during the period from 2006 to 2012 at our institution. It was approved by the institutional review board of the Breast Health Center at the Legacy Cancer Institute in Portland, Oregon. All data were deidentified. Any patient with a new, biopsy-proven diagnosis of breast cancer who underwent BSGI for a preoperative evaluation was included. Women underwent diagnostic mammography and a breast biopsy confirming the diagnosis of cancer. Lesions newly identified by use of BSGI were further assessed using ultrasonography and/or magnetic resonance imaging (MRI). Patients with invasive ductal carcinoma (IDC) and ductal carcinoma in situ were included in the IDC group, and this group was compared with the patients with ILC. Invasive mammary carcinomas and other lesions, which accounted for 7.6% of the carcinomas in our population, were not included in the analysis. Sensitivity and

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Table 2. Comparison of C Statistic By Procedure Between the Nationwide Inpatient Sample (NIS) and National Surgical Quality Improvement Program (NSQIP) Databases

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Complication</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NIS</td>
<td>NSQIP</td>
</tr>
<tr>
<td>Abdominal aortic aneurysm repair</td>
<td>0.5921</td>
<td>0.7130</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>0.7158</td>
<td>0.8231</td>
</tr>
<tr>
<td>Aortic valve replacement</td>
<td>0.6079</td>
<td>0.6613</td>
</tr>
<tr>
<td>Coronary artery bypass graft</td>
<td>0.6469</td>
<td>0.7422</td>
</tr>
<tr>
<td>Carotid endarterectomy</td>
<td>0.6496</td>
<td>0.7001</td>
</tr>
<tr>
<td>Laparoscopic cholecystectomy</td>
<td>0.6863</td>
<td>0.8321</td>
</tr>
<tr>
<td>Colectomy</td>
<td>0.6040</td>
<td>0.7338</td>
</tr>
<tr>
<td>Esophagectomy</td>
<td>0.5883</td>
<td>0.7215</td>
</tr>
<tr>
<td>Sleeve gastrectomy</td>
<td>0.8123</td>
<td>0.7628</td>
</tr>
<tr>
<td>Pancreatectomy</td>
<td>0.5742</td>
<td>0.6286</td>
</tr>
<tr>
<td>Ventral hernia repair</td>
<td>0.6473</td>
<td>0.7261</td>
</tr>
</tbody>
</table>

Authors:

Anna Weiss, MD
Jamie E. Anderson, MD, MPH
David C. Chang, PhD, MBA, MPH

Author Affiliations: Department of Surgery, University of California, San Diego (Weiss); Department of Surgery, University of California, Davis, Sacramento (Anderson); Department of Surgery, Massachusetts General Hospital, Boston (Chang).

Corresponding Author: Anna Weiss, MD, Department of Surgery, University of California, San Diego, 200 W Arbor Dr, 8402, San Diego, CA 92103 (a3weiss@ucsd.edu).

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Study concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Weiss, Anderson.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Anderson.

Administrative, technical, or material support: Weiss, Chang.

Study supervision: Weiss, Chang.

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specificity were calculated and compared between the ILC and IDC groups using the χ² test of proportions, with P < .05 considered statistically significant.

Results | A total of 699 patients with breast cancer underwent BSGI during the study period. The baseline patient and tumor characteristics are represented in Table 1. We identified 44 patients with ILC lesions, 4 of whom had bilateral breast disease. The ILC group tended to be older and have larger tumors and more nodal involvement. The known lesion was identified using BSGI in 40 of the 44 patients (90.9%) in the ILC group and in 485 of the 602 patients (80.6%) in the IDC group. In cases in which the known ILC was not visualized, the mean size of these lesions was 1.2 cm (range, 0.7-1.7 cm). New ipsilateral or contralateral cancers were identified using BSGI in 7 of the 44 patients (15.9%) in the ILC group and in 34 of the 602 patients (5.6%) in the IDC group.

The sensitivity and specificity of BSGI for all cancers was 85.4% and 81.3%, respectively (Table 2). The sensitivity of BSGI for ILCs was 88.9%, and the sensitivity of BSGI for IDCs was 85.1% (P = .64; 95% CI, 0.038-0.078). The specificity of BSGI for ILCs was 78.7%, and the specificity of BSGI for IDCs was 81.8% (P = .74; 95% CI, −0.101 to 0.163).

Discussion | To our knowledge, this appears to be the largest series of functional imaging of ILCs reported to date. Breast-specific gamma imaging has a slightly higher sensitivity for the detection of ILCs than for the detection of IDCs (88.9% vs 85.1%). The specificities of BSGI for ILCs and IDCs are comparable. Smaller series have reported a BSGI sensitivity for ILCs near 100%.2-4 In addition, with the use of BSGI, a greater proportion of additional ILC lesions (15.9%) were detected compared with IDC lesions (5.6%). This finding is clinically significant given that 20% of patients with ILC have contralateral breast cancers, and it suggests that this subgroup should routinely undergo advanced breast imaging.

In comparing advanced breast imaging tools, such as MRI, we found that BSGI is simple to interpret, better tolerated by patients, and far less costly. Furthermore, BSGI has a higher sensitivity for ILC than does MRI.5 The limitations of BSGI are increased radiation exposure and a lower sensitivity for subcentimeter lesions and axillary nodal metastasis.6 Unlike other breast imaging modalities, BSGI reporting is not yet standardized by the Breast Imaging-Reporting and Data System classification. In addition, very few patients with ILC in our study also underwent MRI, prohibiting any comparisons between BSGI and MRI.

Our subgroup of patients with ILC had a higher incidence of synchronous cancer and therefore should routinely be considered for advanced breast imaging. Breast-specific gamma imaging has a high sensitivity and specificity and is an excellent adjunctive imaging tool for patients with newly diagnosed ILCs.

Katherine A. Kelley, MD  
Jeffrey D. Crawford, MD  
Kari Thomas, MD  
Stuart K. Gardiner, PhD  
Nathalie G. Johnson, MD  

Author Affiliations: Department of Surgery, Oregon Health and Sciences University, Portland (Kelley, Crawford); Breast Health Center, Legacy Cancer Institute, Portland, Oregon (Thomas, Gardiner, Johnson).

Corresponding Author: Nathalie G. Johnson, MD, Breast Health Center, Legacy Cancer Institute, 1040 NW 22nd, Ste 560, Portland, OR 97210 (nemtipi@aol.com).

Letters
COMMENT & RESPONSE

Less Surgery, Improved Survival From Stage IV Colorectal Cancer?

To the Editor Hu et al1 report improved survival for patients with metastatic colorectal cancer over time and note that this corresponds to a decrease in the rate of surgery for the primary lesion. Based on the data, they suggest that resections for synchronous primary lesions may be overused. There are a number of concerns in making such a broad conclusion. Improved survival from metastatic colorectal cancer has occurred because of a combination of factors, including the improved use of systemic therapy and metastasectomy.2 Partly based on the advances in systemic therapy associated with significantly higher response rates, a review of the role of primary resection has occurred. Data were emerging that suggested that the risk of complications related to withholding resection of the primary lesion was no higher than the risk of having surgery prior to chemotherapy.3 This had led to more clinicians deferring resection of the primary lesion.

However, there is increasing evidence that for synchronous metastatic colorectal cancer, resection of the primary lesion may be associated with an overall survival benefit, and this is noted briefly by Hu et al.1 Importantly, the recently published pooled analysis of 810 patients from 4 randomized trials gives very strong evidence for this argument.4 The median overall survival was 19.2 months for patients who had a resection prior to chemotherapy and 13.3 months for patients who did not (hazard ratio, 0.54 [95% CI, 0.45-0.64]; P < .001). This pooled analysis4 also reported an association with improved progression-free survival. Importantly, multivariate analysis showed resection to be an independent predictor of overall survival. Why overall survival may be improved remains unclear, although prevention of colonic complications may play a role or, as others have hypothesized, a change in the angiogenesis environment may also be a factor.5

Several other developments are also worth noting. Improvements in surgical techniques, such as laparoscopic surgery, have decreased the potential morbidity associated with surgery. In addition, the increased risks of emergency surgery in the context of angiogenesis inhibitors such as bevacuzumab tend to favor initial resection. Moreover, the effect of surgery on quality of life has never been evaluated. Randomized trials are required to address the role of palliative surgery, but such studies have proved extremely difficult to perform. It is our view that the role of palliative resection of the primary tumor remains an open question in many cases, and this approach might in fact constitute optimal management. Arguably, primary tumor resection may not be overused but underused.

Timothy J. Price, MBBS, FRACP, DHSc
Niall Tebbutt, MBBS, FRACP, PhD
Amanda R. Townsend,MBBS, FRACP

Author Affiliations: The Queen Elizabeth Hospital and University of Adelaide, Woodville, South Australia, Australia (Price, Townsend); Olivia Newton-John Cancer and Wellness Centre, Austin Health, Melbourne, Victoria, Australia (Tebbutt).

Corresponding Author: Timothy J. Price, MBBS, FRACP, DHSc, The Queen Elizabeth Hospital and University of Adelaide, 28 Woodville Rd, Woodville, South Australia, Australia 5011 (timothy.price@health.sa.gov.au).

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To the Editor We were surprised at the conclusions reached by Hu et al1 in their analysis of rates of primary tumor resection (PTR) and of survival of patients with metastatic colorectal cancer (MCRC) over time. Specifically, they have concluded that decreasing rates of PTR have directly contributed to the observed improvement in overall survival for patients with MCRC over a 22-year period, despite not providing an explanation as

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Study concept and design: Crawford. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Kelley, Johnson.

Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Kelley, Gardiner. Administrative, technical, or material support: Crawford, Johnson.

Study supervision: Thomas.

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