BSGI in Clinical Use: A Summary of Potential Utility, Impact on Early Cancer Detection and Cost Savings

Breast Specific Gamma Imaging (BSGI) is scintimammography performed with breast optimized detectors and has been found to be a cost-effective, highly sensitive and specific breast imaging procedure. Therefore, several authors have proposed various applications for this modality as an adjunctive procedure to mammography and other applications (1,2). The purpose of this summary is to propose the indications for this technique in diagnosis and therapy planning.

In several studies, BSGI or scintimammography has demonstrated comparable sensitivity to that of MRI with an equivalent or significantly higher specificity (3,4). This higher specificity can greatly reduce the number of false positives and result in fewer benign biopsies when compared to MRI (5,67). Additionally, BSGI can be conducted at a fraction of the cost of MRI thereby making it useful in indications where MRI would prove too expensive.

BSGI should also be considered in patients who meet the currently approved indications for MRI but are unable to undergo the prescribed study for the following reasons:

a. implanted pacemakers or pumps
b. ferromagnetic orthopedic surgical implants
c. obesity rendering them unable to be placed inside of the MRI bore
d. patients with breasts too large to be evaluated with in the breast coil
e. patients with acute claustrophobia
f. ferromagnetic vascular stents or clips
g. Other factors limiting compliance with a prescribed MRI study.

SCREENING INDICATIONS

1) **Detection of cancer in dense breast tissue of patients with normal or high risk-factors:**
   BSGI can be much more effective than mammography in patients with regionally or generally dense breast tissue. In such cases, the sensitivity of mammography is greatly reduced, about 44% (8). In contrast, BSGI is not impaired by breast density and has been found to be useful in this population. (9, 10).
2) **Detection of cancer in dense breast tissue of patients with normal or high risk-factors who can not undergo MRI evaluation.**
   In these patients, BSGI can prove to be extremely valuable as an alternative when MRI is indicated, but excluded by circumstance. It has been found to be equal to, if not better for several indications (2 – 7)
3) **Evaluation of a palpable mass not demonstrated in Mammogram and/or ultrasound.**
   In some cases, a palpable mass is occult in mammography and ultrasound. Although sensitivity of mammography and US combined is good, about 97.4%, it is reduced in cases with dense breasts (8). In such cases, BSGI can be effective in detection as it is not affected by breast tissue density.
4) **Evaluation of a palpable mass not demonstrated in Mammogram and/or ultrasound in patients who can not comply with an MRI.**
   BSGI can be used to replace MRI in patients with contraindications for MRI, see the list in the MRI section.
5) **Monitor for recurrent disease in patients who have post-treatment tissue changes compromising the sensitivity of mammography.**

Post-treatment cases can be challenging to monitor, particularly if there are significant fibrous dense changes associated with scarring. These patients are both at high risk for breast cancer and suffer from factors making mammography less sensitive. BSGI can provide a high-sensitivity modality with very good specificity.

6) **Monitor for recurrent disease in patients who have post-treatment tissue changes compromising mammography and who can not undergo MRI.**
   BSGI can be used to replace MRI in patients with contraindications for MRI, see the list in the MRI section.
7) **Detection of breast cancer in patients with axillary nodal adenocarcinoma and a suspected primary breast cancer occult in mammography and clinical examination.**
   Although no study has explicitly examined this subpopulation, there have been reported cases of this use in the current user base and the accuracy may be inferred by the overall sensitivity and specificity of this technique in other populations.
8) **Evaluation of densities of low to intermediate concern with disconcordance between mammography and ultrasound.**
   There is a high degree of clinical confusion and frustration with masses present in screening mammography but not confirmed in additional studies such as spot compression magnification views or ultrasound. Since BSGI can provide a measure of physiological activity not available with these other techniques, it can increase diagnostic confidence in these cases. In combined studies containing 164 patients, BSGI has demonstrated a NPV of 99% and in an additional study, it proved to be an effective addition to the triple assessment protocol (11,12).

DIAGNOSTIC INDICATIONS

1) **Detection of the extent of disease as well as multicentric and/or multifocal disease in patients with a biopsy confirmed carcinoma.**
   BSGI can visualize sub-centimeter and occult lesions with a high sensitivity and specificity providing an additional layer of diagnostic confidence and multi-lesion detection (2, 9, 10,13). This is true for both the primary and contralateral breast. In many cases, BSGI has also correctly identified larger extent of the primary lesion than indicated in mammography or ultrasound. This is important as some studies have found an increased occurrence of metastatic disease when positive margins are found in the primary lumpectomy specimen (14).
2) **Detection of the extent of disease as well as multicentric and/or multifocal disease in patients with a biopsy confirmed carcinoma that can not undergo MRI evaluation.**
   In these patients, BSGI can prove to be extremely valuable as an alternative when MRI is indicated, but excluded by circumstance.
3) **Patients with multiple masses, clusters of microcalcifications or other areas of low to intermediate suspicion identified in mammography.**
   In such cases, depending on the location of these masses, it is often impractical, expensive or dangerous to obtain a biopsy from all areas. Since BSGI can provide images of physiologic activity, it can be useful in this patient group to aid in the determination of the optimal biopsy site.
4) **Patient with breast implants who present clinically with a mass, calcifications or other suspicious area of low to intermediate concern near the implant.**
   The risk of rupturing the implant may be unacceptable in situations of lesser concern for malignancy. MRI is an alternative examination, but with a significantly high false positive

rate. Since BSGI has equivalent sensitivity and in some studies, considerably better specificity, it provides a lower cost examination with equivalent or greater accuracy.

5) **Assessment of axillary nodes to aid in pre-operative treatment planning and patient consultation after a primary breast diagnosis is made via tissue biopsy.**

   Localized surgery and therapy is preferred and appropriate in many patients with limited breast carcinoma without indications of metastatic disease. Axillary node status is the primary indicator of metastatic risk and prognosis. Sentinel node biopsy is an effective tool for the localization and excision of the primary drainage pathway, but is often performed in conjunction with lesion lumpectomy. This practice has resulted in an underutilization of neoadjuvant therapies in patients who could benefit from them. Earlier detection of these metastases could make neoadjuvant therapy possible, increase the confidence in therapy planning and improve the quality of patient consultation. In studies, scintimammography has provided a preoperative means of nodal evaluation with a high sensitivity and PPV (15,16). It should not be used to obviate sentinel node biopsy, but can establish the increased risk of metastatic disease thereby altering treatment planning.

6) **Determination of chemotherapeutic resistance prior to neoadjuvant or adjuvant therapy.**

   Studies have been conducted demonstrating that the washout of sestamibi is closely associated with the p-glycoprotein receptor and therefore may give an indication of resistance to certain chemotherapeutic protocols prior to patient enrollment (17,18, 19 and 20). Avoiding ineffective regimen and altering patient planning to more effective treatments is of profound benefit.

7) **Monitor chemotherapeutic response in patients undergoing neoadjuvant or adjuvant therapy.**

   BSGI may also be used to monitor tumor response to chemotherapy (21, 22 and 23). The ability to monitor response can allow the therapy to be modified dynamically in order to maximize effectiveness. In addition early chemotherapeutic response has been correlated with better prognosis, it is an important parameter in patient work up and monitoring response with mammography and ultrasound has proven to be ineffective.

8) **Monitor chemotherapeutic response in patients undergoing neoadjuvant or adjuvant therapy in patients who can not comply with MRI.**

   BSGI can be used to replace MRI in patients with contraindications for MRI, see the list in the MRI section.

References:

[1] Schillaci O, Buscombe JR. Breast scintigraphy today: indications and limitations. Eur J Nucl Med Mol Imaging. 2004 Jun;31 Suppl 1:S35-45. Epub 2004 Apr 23.

[2] Rhodes DJ, O'Connor MK, Phillips SW, Smith RL, Collins DA. Molecular Breast Imaging: A New Technique Using Technetium Tc99m scintimammography to detect small Tumors of the Breast.

[3] Petrovitch I, Brem R, Rapelyea J, Young H, Raub J. High resolution Molecular Breast Imaging with 99m-MIBI and Magnetic Resonance Imaging in the Assessment of Breast Cancer. Oral presentation, 2005 RSNA annual meeting, Chicago Il, Nov 29th, 2005.

[4] Imbriaco M, Del Vecchio S, Riccardi A, Pace L, Di Salle F, Di Gennaro F, Salvatore M, Sodano A. Scintimammography with 99mTc-MIBI versus dynamic MRI for non-invasive characterization of breast masses. Eur J Nucl Med 2001 Jan;28(1):56-63.

[5] Fenlon HM, Phelan NC, O'Sullivan P, Tierney S, Gorey T, Ennis JT. Benign versus malignant breast disease: comparison of contrast-enhanced MR imaging and Tc-99m tetrofosmin scintimammography. Radiology 1997 Oct;205(1):214-20.

[6] Palmedo H, Grunwald F, Bender H, Schomburg A, Mallmann P, Krebs D, Biersack HJ. Scintimammography with technetium-99m methoxyisobutylisonitrile: comparison with mammography and magnetic resonance imaging. Eur J Nucl Med 1996 Aug;23(8):940-6.

[7] Tiling R, Khalkhali I, Sommer H, Moser R, Meyer G, Willemsen F, Pfluger T, Tatsch K, Hahn K. Role of technetium-99m sestamibi scintimammography and contrast-enhanced magnetic resonance imaging for the evaluation of indeterminate mammograms. Eur J Nucl Med 1997 Oct;24(10):1221-9.

[8] Kolb TM,Lichy J,Newhouse JH. Comparison of the performance of screening mammography, physical examination and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology. 2002;225:165-175.

[9] Coover LR, Caravaglia G, Kuhn P. Scintimammography with dedicated breast camera detects and localizes occult carcinoma. J Nucl Med. 2004 Apr;45(4):553-8.

[10] Brem R, Rapelyea J, Zisman G, et al. Occult breast cancer: scintimammograpy with high-resolution breast-specific gamma camera in Women at High Risk for Breast Cancer. Radiology. 2005;237:274-280

[11] Kieper D. Brem R. Keppel C. Majewski S. Weisenberger A. Welch B. An Introduction to Breast Specific Gamma Imaging. NCBC Annual Conference, Las Vegas Nevada, Feb 28 – Mar 3, 2003.

[12] Wilczek B, Asplen P, Bone B, Pegerfalk A, Frisell J, Danielsson. Complimentary use of Scintimammography with Tc99-MIBI to triple diagnostic procedure in palpable and non-palpable breast lesions. Acta Radiologica 44 (2003) 288–293

[13] Kieper D, Green TD, Hoefer R, Keppel C, Wymer DC, Weisenberger AG, Welch B. Data analysis methods for a small field-of-view combined scintimammography/digital X-ray system in breast lesion management. Nucl Instr and Meth A. 2003; 497: 135-140.

[14] Simpson-Herren L, Sanford AH, Holmquist JP, Effects of surgery on the cell kinetics of residual tumor. Cancer Treat Rep 1976; 60:1749-60

[15]Taillefer R, Robidoux A, Turpin S, Lambert R, Cantin J, Leveille J. Metastatic axillary lymph node technetium-99m-MIBI imaging in primary breast cancer. Nucl Med. 1998 Mar;39(3):459-64.

[16] Chen J, Wu H, Zhou J, Hu J.Using Tc-99m MIBI scintimammography to differentiate nodular lesions in breast and detect axillary lymph node metastases from breast cancer. Chin Med J (Engl). 2003 Apr;116(4):620-4.

[17] Van de Wiele C, Rottey S, Goethals I, et al. 99mTc sestamibi and 99mTc tetrofosmin scintigraphy for predicting resistance to chemotherapy: a critical review of clinical data. Nucl Med Commun 2003; 24:945–950.

[18] Pwnica-Worms D, Chiu ML, Budding M, et al. Functional imaging of multidrug-resistant P-glycoprotein with an organotechnetium complex. Cancer Res 1993; 53:977–984.

[19] Mezi S, Primi F, Capoccetti F, Scopinaro F, Modesti M, Schillaci O. In vivo detection of resistance to anthracycline based neoadjuvant chemotherapy in locally advanced and inflammatory breast cancer with technetium-99m sestamibi scintimammography. Int J Oncol. 2003 Jun;22(6):1233-40.

[20] Salvatore M, Del Vecchio S. Dynamic imaging: scintimammography. Eur J Radiol. 1998 May;27 Suppl 2:S259-64.

[21] Claudio JA, Emerman JT. The effects of cyclosporin A, tamoxifen, and medroxyprogesterone acetate on the enhancement of adriamycin cytotoxicity in primary cultures of human breast epithelial cells. Breast Cancer Res Treat. 1996;41(2):111-22.

[22] Alonso O, Delgado L, Nunez M, Vargas C, Lopera J, Andruskevicius P, Sabini G, Gaudiano J, Muse IM, Roca R.. Predictive value of (99m)Tc sestamibi scintigraphy in the evaluation of doxorubicin based chemotherapy response in patients with advanced breast cancer. Nucl Med Commun. 2002 Aug;23(8):765-71.

[23] Dunnwald LK, Gralow JR, Ellis GK, Livingston RB, Linden HM, Lawton TJ, Barlow WE, Schubert EK, Mankoff DA. Residual tumor uptake of [(99m)Tc]-sestamibi after neoadjuvant chemotherapy for locally advanced breast carcinoma predicts survival. Cancer. 2005 Jan 6