Review

Current Approaches and Challenges in Early Detection of Breast Cancer Recurrence

Erika J. Schneble[1]✉, Lindsey J. Graham[1], Matthew P. Shupe[1], Frederick L. Flynt[1], Kevin P. Banks[1], Aaron D. Kirkpatrick[1], Aviram Nissan[2], Leonard Henry[3], Alexander Stojadinovic[4], Nathan M. Shumway[1], Itzhak Avital[4], George E. Peoples[1], and Robert F. Setlik[1]

1. San Antonio Military Medical Center (SAMMC), 3551 Roger Brooke Dr., Ft. Sam Houston, TX 78234, USA
2. Hadassah Medical Center, Kiryat Hadassah, POB 12000, Jerusalem, 91120, Israel
3. IU Health Goshen, 200 High Park Ave., Goshen, IN 46526, USA
4. Bon Secours Cancer Institute, 5855 Bremo Road, Richmond, VA 23226, USA

✉ Corresponding author: Erika J. Schneble. Brooke Army Medical Center, Department of General Surgery, 3551 Roger Brooke Dr. Ft. Sam Houston, TX 78234. Office: 210-916-0439. Fax: 210-916-0439. Email: erika.j.schneble.mil@mail.mil

Abstract

Early detection of breast cancer recurrence is a key element of follow-up care and surveillance after completion of primary treatment. The goal is to improve survival by detecting and treating recurrent disease while potentially still curable assuming a more effective salvage surgery and treatment. In this review, we present the current guidelines for early detection of recurrent breast cancer in the adjuvant setting. Emphasis is placed on the multidisciplinary approach from surgery, medical oncology, and radiology with a discussion of the challenges faced within each setting.

Key words: Breast cancer; Recurrence; Adjuvant; Surveillance; Follow-up

Introduction

The current rise in breast cancer prevalence intensifies the global need for long-term surveillance programs [1]. This is a consequence of increased diagnosis from breast cancer screening programs and decreased disease-related mortality secondary to improved treatment modalities. This review discusses the current approaches and challenges of early detection of recurrent breast cancer after primary treatment.

After curative primary therapy, follow up of breast cancer patients focuses on early detection of recurrent disease when potentially still curable. Studies show detection of asymptomatic breast cancer recurrences by clinical screening carries a more favorable prognosis than patients presenting with symptomatic disease [2]. A recent meta-analysis of 2,263 breast cancer survivors from thirteen studies supports this hypothesis where the early detection

group (asymptomatic recurrence found by mammography) exhibited superior survival in both the loco-regional and contra-lateral breast cancer recurrence groups compared to women who presented with symptoms due to recurrent cancer [3]. The authors were able to show the studies calculating follow up time from the date of recurrence had similar hazard ratios to those studies that calculated follow up time from the date of primary treatment of recurrence, suggesting the lead-time bias did not explain the effect on early detection.

The current standard of care for breast cancer follow-up requires a multi-disciplinary approach from radiologists, surgeons, and primary care physicians. At this time, surveillance for distant recurrence is not considered amenable to curative treatment or associated with a survival benefit [4, 5] and is thus not discussed in this review. The focus is the early detec-

tion of loco-regional or contralateral recurrence with intent to improve long-term survival. The challenges faced while sustaining efficient and effective surveillance practices are evaluated after a review of the current guidelines.

Surveillance Guidelines

Current recommendations for breast cancer screening involve radiographic and clinical evaluations. Radiographic studies provide a non-invasive means to detect recurrent or new disease. Mammography is the mainstay of surveillance imaging following curative treatment of breast cancer with 8%-50% of ipsilateral recurrences and 18%-80% of contralateral metachronous cancers detected by mammography alone [6]. Most treatment guidelines, including the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Center Network (NCCN), suggest annual mammography following breast-conserving therapy [7, 8]. This recommendation is based upon expert opinion as there are no adequate randomized controlled trials demonstrating mammography's benefit in the setting of surveillance.

Regular follow-up with a medical oncologist aims to identify new symptoms or changes on physical examination. Current NCCN guidelines recommend routine history and physical examination every 4 to 6 months for the first five years after primary therapy and annually thereafter [9]. ASCO, however, recommends routine history and physical examination every 3 to 6 months for first 3 years, every 6 to 12 months for years 4 and 5, then annually thereafter [8]. Both the NCCN and ASCO do not recommend the use of routine complete blood counts, chemistry panels, tumor markers, bone scans, computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, positron-emission computed tomography (PET) scans, or ultrasound examinations in asymptomatic patients without specific clinical examination findings [8, 9]. Dedicated breast MRI may be considered for post-therapy surveillance in women at high risk for bilateral disease, such as carriers of the BRCA 1/2 mutations [9].

Identifying the optimal imaging modality for surveillance imaging remains a significant challenge. There are no randomized clinical trials evaluating the effectiveness of breast MRI, ultrasound, or positron-emission computed tomography (PET/CT) in the setting of breast cancer surveillance. As discussed below, supplemental imaging may be considered in symptomatic patients and patients at high risk for recurrent disease. The majority of literature regarding each modality is retrospective in nature. Thus, there is no definitive evidence to support any of these methods as a primary imaging modality for surveillance [10].

Part of the challenge in early detection of recurrent disease after primary treatment is implementing effective strategies that safeguard optimal patient follow-up tracking and compliance while ensuring cost-effectiveness. Addressing these surveillance challenges is beyond the scope of this paper and will be discussed in a future review.

Clinical Assessment

The three tests usually considered for early detection in breast cancer screening include mammography, the clinical breast examination (CBE), and the self breast examination (SBE). Although data suggests recurrent disease detected by mammography correlates with increased survival [3], the utility of the SBE and CBE is debated despite continued recommendations by ASCO [11, 12] and NCCN [9]. These guidelines recommend periodic physical examination and CBE in addition to patient education of disease recurrence symptoms and SBE techniques to facilitate breast self-awareness [13].

Historically, most breast cancer recurrences are detected by the patient or clinician [14-16] with studies prior to 2000 reporting CBE detection rates of potentially treatable relapses as high as 46% [17]. However, the percentage of CBE-detected relapses has waned to approximately 15% in modern literature as experience with mammography grows [18-20]. The favor of CBE is largely as a safeguard against false negatives [21-24] with general screening mammography cited to miss 10-15% of palpable lesions [25, 26].

Although a benign and noninvasive intervention, the precision of the clinical assessment is limited by the multi-factorial nature of the breast examination. Estimates of breast examination sensitivity are dependent on a number of factors including the size of the lesion, individual breast characteristics, patient age, extent of follow-up to elucidate false negatives, and the skill of the examiner. For example, on a simulation-based assessment female examiners tend to display greater examination time and have a higher sensitivity compared to that of male counterparts [27]. Breast tissue heterogeneity also influences sensitivity where estimates of CBE detection on women aged 40-49 are approximately 10% lower at initial screen compared to women aged 50-59 [28]. Conversely, SBE accuracy decreases with advanced age from approximately 41% in women aged 35-39 to 21% in women aged 60-74 [29] with overall detection rates from 12% to 40% [20, 30]. The greatest challenge of both the CBE [24] and SBE [22, 31], regardless of age, is the detection of benign breast lesions leading to unnecessary invasive procedures.

The overall impact of clinical examinations on survival remains questionable. Although early detection of asymptomatic relapse is known to increase survival [32, 33], it is uncertain whether clinical examinations contribute to this benefit. SBE-detected cancer recurrences, in addition to mammographically detected lesions, are correlated with increased survival [3, 20, 34]. However, modern systematic literature reviews suggest no mortality benefit of CBE-detected relapses. Instead, patients may in fact have poorer outcomes than those whose relapse is diagnosed by SBE or mammography [17, 18, 20].

Overall, the precision of CBE and SBE is challenged by patient heterogeneity and lack of consistent and standardized examination techniques [24]. Efforts to increase early disease detection by increased frequency of clinical exams can result in increased false-positive tests with unnecessary, and likely more invasive diagnostic tests, increased healthcare costs, and heightened patient anxiety [35] without an associated mortality benefit. Clinical screening, particularly the CBE, requires the development of new techniques and protocols for greater standardization and precision for the detection of breast cancer relapses to be discussed in a subsequent review.

Laboratory Assessment

In addition to imaging and clinical examination, many oncologists employ the use of circulating serum tumor markers to predict relapse. Current ASCO guidelines state that there is insufficient evidence to support using circulating tumor markers such as CA 15-3 and CA 27-29, or carcinoembryonic antigen (CEA) to monitor for disease recurrence after primary therapy [11, 36]. It is important to note that this recommendation does not apply to monitoring disease in the metastatic setting, where the use of serum tumor markers is not discouraged. Although these markers may predict disease recurrence months in advance, there is no evidence showing subsequent improvements in survival or quality of life in the adjuvant (non-metastatic) setting. Multiple studies have assessed the use of tumor markers for monitoring for recurrence of disease. Some of these are listed in Table 1.

Table 1: Summaries from Recent Studies Using Serum Tumor Markers to Monitor for Recurrence in the Adjuvant Setting

Reference	Patients	Intervention	Outcome
Zervoudis (2007)[40]	358 patients with stage I breast cancer who were disease free after primary treatment.	Clinical exam, mammography, bone scintigraphy, annual CT of the chest and abdomen and multiple serum tumor markers including CEA, CA 15-3, CA 27-29 every 4 months	18 patients (5%) had increased tumor markers by cutoff values. All of them had negative workup for disease. After 5 years of follow up, 15 of those 18 patients remained free of local recurrence or metastatic disease and the other 3 were lost to follow up.
Nicolini (2006)[41]	268 breast cancer patients that were disease free at the start of the study. All stages seem to have been represented and were treated according to guidelines.	Serial serum CEA, CA 15-3, TPA, MCA were measured every 4-6 months. Bone scan, liver ultrasound, and chest x ray were performed every 24-36 months to detect any false negatives.	There were 19 relapses. Mean lead times between tumor marker elevation and the appearance of disease were between about 3-7 months depending on the tumor marker Sensitivities ranged from 10-68%. 222 patients were found to have tumor marker elevations for non-malignant reasons leading to specificities around 40-70%
Valenzuela (2002)[42]	318 patients who were disease-free after primary therapy	CA 15.3 and CEA were measured in serum at each routine follow up visit	59 patients relapsed, 28 of whom had elevated CA 15-3 levels and 31 of whom did not. 30 patients had false positive elevations of CA 15-3. 17 patients had elevated tumor markers (16 CA 15-3 and 1 CEA) before clinical appearance of metastases.
Pedersen (2013)[43]	9 patients with local recurrence and 83 patients who developed distant metastases after primary treatment. Patients who originally presented with distant metastases were excluded.	CA 15-3, CEA, and HER2 were measured. A result was considered positive if above a certain threshold.	None of the patients with local recurrence had elevated serum tumor markers. The most sensitive marker to detect recurrence was CA 15-3 (49.4%). The most sensitive combination was CA 15-3 and CEA (60.2%) In patients with HER2+ tumors, the sensitivity of serum HER2 was 55.6% and 21.2% in patients with HER2 negative tumors

CEA = carcinoembryonic antigen, MCA = mucin-like carcinoma associated antigen, TPA = tissue polypeptide. Of note, each study used different cutoff values for identifying a patient as positive, though all followed trends in this marker.

CA 15-3 and CA 27-29 are two separate assays that test for the same secreted mucin glycoprotein coded by the MUC1 gene. These assays are regarded as equivalent in their ability to detect the protein in serum [37]. MUC1 derived glycoprotein is aberrantly over-expressed in human breast cancer and can even antagonize the inhibitory effects of tamoxifen [38].

The human epidermal growth factor receptor 2 (HER2) has an extracellular domain, a transmembrane domain, and an intracellular domain. The extracellular domain (ECD) may be cleaved from the receptor and sent into circulation where it can be measured by the use of an immunoassay. Though more commonly used in the metastatic setting, it has been studied in the adjuvant setting as well to monitor recurrence [39]. Table 1 shows some of the recent studies exploring the use of serum tumor markers in the adjuvant setting to detect recurrence.

One of the challenges with the use of serum tumor markers is what to do with a positive marker in the setting of no radiographic evidence of disease. Early rises in markers may increase patient anxiety and lead to unnecessary testing and increased cost of care [4]. One potential way to enhance the effectiveness of tumor markers is to limit their use to those women at highest risk of relapse. In addition, molecular identification of breast cancer subtypes may also help determine the usefulness of different markers of disease recurrence. This shift towards personalized disease monitoring may improve the utility of serum tumor markers.

The current challenge of post-treatment follow up is to best predict which patients are at increased risk of recurrence and then explore the best surveillance strategy in those patients. At present, guidelines recommend estrogen receptor (ER), progesterone receptor (PgR), and HER2 expression testing to guide treatment decisions – namely the use of hormonal therapy and traztuzumab, respectively [36]. However, newer assays employing microarray technology may help provide both predictive and prognostic information. Current technology employs gene expression profiling such as the 21 gene expression test (Oncotype DX™) and 70 gene microarray test (MammaPrint®) and to better understand the molecular biology of individual breast cancer. In the accompanying article, we will discuss how this newer technology can be used to enhance the monitoring of occult disease.

Radiologic assessment

Over the past 20 to 30 years, improved screening and treatment strategies for breast cancer have contributed to significant decreases in breast cancer-related mortality. Breast-conserving surgery followed by radiation therapy results in similar survival outcomes as mastectomy, with local recurrence in the ipsilateral breast occurring 6-9% at 5 years and 14-20 % at 20 years [44]. Per the American Cancer Society (ACS) and the American College of Radiology (ACR) guidelines, this risk stratifies a woman with a personal history of breast cancer (excluding other risk factors) is considered intermediate risk (15-20% lifetime risk). The majority of literature supports the premise that early detection of asymptomatic local recurrence via appropriate surveillance techniques, to include breast imaging, improves long-term survival when compared to late symptomatic detection [3, 44, 45]. Therefore, sensitive, non-invasive, and cost-effective surveillance strategies to detect early local recurrence are necessary.

Mammography

Mammography is the mainstay of surveillance imaging following curative treatment of breast cancer with 8%-50% of ipsilateral recurrence and 18%-80% of contralateral metachronous cancer detected by mammography alone [6]. Most clinical guidelines suggest patients obtain their first post-treatment mammogram "1 year after the initial mammogram leading to diagnosis, but no earlier than 6 months after definitive radiation therapy" [11]. However, as stated above, recommendations for surveillance mammography are based upon expert opinion as there are no adequate randomized controlled trials demonstrating mammography's benefit in this setting. Most researchers agree that regular surveillance mammography in women diagnosed with early stage breast cancer improves long-term outcomes; however, the optimal interval for mammographic follow-up is currently debated. Some studies suggest benefit from biannual mammography in the initial 2-5 years following treatment, while other studies and most major treatment guidelines (including ASCO and NCCN) support annual mammography following breast conservation therapy [6, 46, 47]. One retrospective study and a meta-analysis of surveillance mammography found no benefit to semi-annual (6-month interval) screening mammography, while a recent retrospective single-institution review suggests a benefit from 5 years of semiannual mammographic surveillance [6, 48-50].

Supplemental Screening Modalities

Identifying the optimal imaging modality for surveillance imaging remains a significant challenge as there are no randomized clinical trials evaluating the effectiveness of breast MRI, ultrasound, or PET/CT in the setting of breast cancer surveillance. The majority of literature regarding each modality is

retrospective in nature. Thus, there is no definitive evidence to support any of these methods as a primary imaging modality for surveillance. Currently there is no ideal single modality for imaging surveillance that is non-invasive, cost effective, and has the appropriate balance of sensitivity and specificity. Although mammography is able to detect 25-45% of recurrences, the post-operative and post-radiation changes of breast conservation therapy decrease mammography's sensitivity and specificity compared with a standard screening population [44, 51]. Thus, the role of other breast imaging modalities as an adjunct screening tool to mammography and clinical examination is an active area of investigation.

Ultrasound

Neither the NCCN, nor the ASCO guidelines directly recommend supplementary screening with ultrasound [11, 52]. The ACR suggests considering supplemental ultrasography as an option in women with intermediate risk (to include those with a personal history of breast cancer) and dense breasts.[10] Furthermore, ultrasound is a useful option for high risk women who are not candidates for breast MRI [3, 44, 45, 53]. Berg et al recently demonstrated that an annual supplemental screening ultrasound in intermediate and high-risk women with mammographically dense breasts detects an additional 3.7 cancers per 1000 women screened [6, 54]. The majority of ultrasound-detected mammographically-occult breast cancers are small and node-negative [11, 55].

Although supplemental screening with ultrasound may detect mammographically-occult cancers, its role in the early detection of breast cancer is not well defined. Multiple independent studies evaluation intermediate to high-risk populations demonstrate that the combination screening mammography with supplemental ultrasound resulted in a higher false-positive rate and a lower positive predictive value when compared to screening mammography alone [6, 46, 47, 56]. Furthermore, in-situ cancers are often missed by sonography, and screening ultrasound is time intensive - often requiring direct physician supervision. There is no prospective outcome study demonstrating improved mortality rates through supplemental screening ultrasonography; which would require a large multicenter prospective trial. If supplemental screening ultrasonography is to become standard of care, then future studies will need to demonstrate a reduction in false positive results and appropriate utilization of resources. Currently, the primary role of ultrasound is in the evaluation of symptomatic patients [10, 52].

Breast MRI

The post-procedural and post-therapy changes of breast conservation therapy limit the sensitivity of mammography and ultrasound for detection of recurrence [6, 48-50, 57]. Multiple studies demonstrate high sensitivity and specificity for breast MRI in the detection of local recurrences [54, 58-61]. It also has high sensitivity, specificity, and accuracy in differentiating post-operative scar from recurrent tumor [62]. While breast MRI is superior to other modalities as a single option, it is expensive, resource intensive and frequently less tolerable for patients than mammography or ultrasound [54, 56].

The ACR practice guidelines for breast MR state that MRI is useful in women with a history of breast cancer and suspicion for disease recurrence when clinical, mammographic, or sonographic findings are inconclusive [49]. Similarly, an ACS panel concluded that the increased risk of local recurrence of contralateral metachronous disease in a woman with a personal history of breast cancer alone does not justify a recommendation for screening MRI after breast conservation therapy [63]. Recently, Brennan and colleagues identified 17 carcinomas in 144 women (12%) with personal history of breast cancer, but no family history - 10 of these cancers were mammographically occult and the positive predictive value of biopsy was 39% [64]. A separate study by Berg, et al demonstrated that supplemental MRI was less likely to prompt unnecessary recall or biopsy in women with a personal history of breast cancer than in those without a personal history of breast cancer [54]. Thus, the choice of adjunct surveillance with Breast MRI in women with a personal history of breast cancer is still under investigation and further studies for optimal patient selection are needed.

Annual screening MRI as an adjunct to mammography and clinical breast exam is recommended for certain high risk populations. This includes women 25 years or older with a genetic predisposition, such as known BRCA 1/BRCA 2 positivity, a greater than 20% lifetime risk for developing breast cancer as defined by various risk stratification models, and for women with a family history suggesting a genetic predisposition for breast cancer [10, 52]. A significant family history includes having 2 or more first-degree relatives with breast cancer, a first-degree relative with premenopausal breast cancer, a family history of breast and ovarian cancer, a first-degree relative with more than one independent cancer, and having a male relative with breast cancer. The NCCN guidelines also recommend consideration of annual MRI in women diagnosed with lobular carcinoma *in situ* (LCIS) and in women 25 years or older with a

history of chest irradiation beginning at age 40 or 8 to 10 years after radiation exposure.

Post-Mastectomy Imaging

Another significant challenge is identifying the appropriate algorithm and modality for surveillance in the post-mastectomy population. There are no definitive guidelines for surveillance in patients treated by mastectomy with or without reconstruction. Chest wall recurrence in mastectomy patients is between 5% and 30% [59, 61]. Case reports and retrospective reviews demonstrate that local recurrence can be detected by surveillance mammography in women with breast reconstruction following mastectomy, but no clear evidence exists to support or discourage routine imaging surveillance in this particular patient population [59, 61, 65]. Currently, surveillance imaging algorithms are institutional dependent.

Other Imaging Modalities

As previously discussed, mammography is the only imaging modality universally recommended for surveillance of women with a history of breast cancer [11]. Molecular imaging studies such as bone scans or FDG (fluorodeoxyglucose) PET-CT are currently not indicated in an otherwise asymptomatic patient without specific clinical complaints or findings on physical examination. Unlike MRI or US, this holds true even for women with a personal history of breast cancer or high risk for breast cancer. This position is based primarily upon two large randomized prospective trials performed in the early 1990's as well as a more recent systematic review of studies comparing the outcome of patients followed with mammography and clinical examinations, with those followed using an intense regimen of imaging and laboratory testing. Each study found no survival benefit or improvement in quality of life associated with the more comprehensive follow-up [5, 66, 67]. Critics of this approach argue these studies were based upon older and less sensitive imaging tests (i.e. did not include FDG PET or PET-CT) and did not have the advantage of newer therapies such as aromatase inhibitors [68].

Once recurrent disease is suspected, FDG PET is very effective in confirming the presence or absence of disease and accurately assessing its extent. Two retrospective studies showed a sensitivity of 92-97%, an accuracy of 87-90%, and a specificity ranging from 75-82% for FDG PET predicting recurrent disease[69, 70]. PET-CT has shown even more effective in assessing recurrent breast cancer as well as many other malignancies [71]. In an evaluation of thirty-four patients with suspected breast cancer, PET-CT demonstrated a significant increase in sensitivity and specificity (96% versus 88% and 89% versus 78% respectively) compared with PET alone. In one of the largest studies to date, a review of 228 symptomatic patients with rising serum CA 15-3 and/or CEA levels, FDG PET-CT demonstrated a sensitivity of 94% and specificity of 85% with an accuracy of 92% [72]. This same study compared FDG PET-CT to conventional imaging techniques (contrast-enhanced CT, abdominal ultrasound, chest x-ray and/or bone scan) in a subset of 67 women and reaffirmed the superior sensitivity (95% versus 33%) and accuracy (94% and 48%) of PET-CT. Many smaller studies confirm these results (Table 2).

Table 2: Review of PET-CT in Assessment of Women with a History of Breast Cancer and Suspected Recurrence

Lead Author	Year	# Pt	Sens	Spec	Accuracy	% Change Mgmt	Comparison
Champion[72]	2011	228	94%	85%	92%	54%	Conventional WU
Evangelista[68]	2011	111	81%	52%	60%	56%	Conventional WU
Grassetto [73]	2010	89	NR	NR	NR	45%	Conventional WU
Fueger [74]	2005	58	94%	84%	90%	NR	PET
Aukema [75]	2010	56	97%	92%	95%	48%	Conventional WU
Dirisamer [76]	2009	52	93%	100%	NR	NR	CECT
Filippi [77]	2011	46	87%	88%	87%	50%	
Radan [78]	2006	46	90%	71%	80%	51%	CECT
Haug [79]	2007	34	96%	89%	NR	NR	CECT
Schmidt [80]	2008	33	91%	90%	NR	NR	WB MRI

WU = work up, CECT = contrast enhanced CT, WB = whole body

In addition to FDG PET-CT, two other molecular imaging modalities are available for the assessment of breast cancer recurrence. Both are helpful in the setting of skeletal relapse. Tc99m-disphosphonate bone scanning (BS) and 18F-Sodium Fluoride (NaF) PET/PET-CT are useful for imaging osseous metastases based upon the lesions' increased blood flow and pathologic osteoblastic activity. Bone scintigraphy has been shown to be particularly useful given its ability to evaluate the entire skeleton, with a good

diagnostic sensitivity of 87-88% in the assessment of patients with breast cancer bone metastases [81]. Though false-positive results can be seen due to degenerative disease, trauma, and other benign entities, its specificity can be appreciably improved through the use of SPECT (single-photon emission computed tomography) or SPECT-CT as well as correlative imaging [82]. It should be noted though that FDG PET-CT is as good as or better than bone scintigraphy in the detection and characterization of bone metastases. While early studies showed FDG PET to have a lower rate of detection than bone scintigraphy for osteoblastic lesions (but similar for mixed and osteolytic lesions) [83], a meta-analysis of 4 prospective and 2 retrospective studies found similar patient-based sensitivity (81% and 78% for PET-CT and BS respectively) and better patient and lesion-based specificity with FDG PET-CT when compared to bone scintigraphy (98% vs. 87%) [81]. These authors suggested that bone scintigraphy's improved lesion-based sensitivity may simply be due to the modality's increased field of view (all of the extremities and skull which are often not included in a standard 'whole-body' PET-CT). Given these findings, only one or the other modality is generally suitable as the sole means for assessing the presence and extent of bone metastases.

In contrast to BS and FDG PET-CT, 18F-NaF PET-CT has clearly shown superior sensitivity for the detection of bone metastases in patients with breast cancer and other malignancies. In a very recent study of 151 patients with various cancers, 72 of which had a history of invasive ductal carcinoma, Fluoride PET-CT was much more sensitive and had a greater negative predictive value regarding the presence of skeletal disease (100% sensitivity and negative predictive value vs. 73% and 80% for FDG PET-CT and similar outperformance versus bone scintigraphy) [84]. Other investigators have shown the same superiority of NaF PET-CT [85]. Thus, if there is a high index of suspicion for isolated skeletal metastases, NaF PET-CT may be the optimal choice.

There is insufficient evidence for the use of other modalities such as thermography, breast-specific gamma imaging, positron emission mammography, and optical imaging for breast cancer screening. Although patients and healthcare providers often prefer intensive screening and follow-up after a diagnosis of breast cancer, aside from annual mammography, the routine use of advanced imaging to evaluate for recurrence and/or metastatic disease does not result in increased survival or improved quality of life. There is little evidence to justify routine imaging with CT, MRI, radiography, or nuclear medicine studies for the detection of metastasis in asymptomatic women.

Future Directions and Challenges

Digital breast tomosynthesis (DBT) is an emerging modality with early clinical studies showing promising results. The potential use of DBT, contrast enhanced mammography, and molecular imaging as future modalities in breast cancer screening will be discussed in a separate manuscript.

Conclusion

Breast cancer relapses are rarely curable with estimates of only 1–1.5% of women who present each year with recurrent breast cancer having potentially curable disease [17, 20]. However, current data shows a survival benefit from early detection of asymptomatic loco-regional or contra-lateral breast cancer recurrences [3]. With as many as 40% of isolated loco-regional recurrences asymptomatic at the time of detection [86], the question remains how to solve surveillance challenges to increase this percentage. A multi-disciplinary approach requiring close collaboration between radiologists, medical oncologists, and surgeons is necessary. Surveillance techniques within each setting should strive for improved patient survival with attention to quality of life. Non-essential interventions cause increased patient anxiety, unnecessary testing, and increased cost of care and utilization of resources. Future strategies that optimize disease detection while maximizing patient well-being, resource utilization, and efficiency are to be discussed in a subsequent review.

Abbreviations

ASCO: American Society of Clinical Oncology; NCCN: National Comprehensive Cancer Center Network; CT: computed tomography; MRI: magnetic resonance imaging; PET: positron-emission tomography; PET/CT: positron-emission computed tomography; CBE: clinical breast examination; SBE: self breast examination; CEA: carcinoembryonic antigen; HER2: human epidermal growth factor receptor 2; ECD: extracellular domain; ER: estrogen receptor; PgR: progesterone receptor; ACS: American Cancer Society; ACR: American College of Radiology; LCIS: lobular carcinoma *in situ*; BS: bone scanning; NaF: Sodium Fluoride; DBT: digital breast tomosynthesis; FDG: fluorodeoxyglucose; SPECT: single-photon emission computed tomography

Competing Interests

The authors have declared that no competing interest exists.

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Author Biographies

Dr. Erika J. Schneble is a General Surgery resident at San Antonio Uniformed Services Health Education Consortium (SAUSHEC). She is currently spending her research year with the Cancer Vaccine Development Program at San Antonio Military Medical Center.

Dr. Matthew P. Shupe, DO graduated from A.T. Still University-Kirksville College of Osteopathic Medicine and completed residency in Internal Medicine at SAUSHEC. He is currently a Hematology/Oncology fellow at SAUSHEC.

Dr. Frederick L. Flynt is an Assistant Professor of Medicine at the Uniformed Services University of Health Sciences, School of Medicine, and the Associate Program Director for the Hematology/Oncology

Fellowship program at the San Antonio Uniformed Services Health Education Consortium.

Dr Leonard Henry is an associate professor of surgery at Indiana University-South Bend and the director of surgical oncology at the Indiana University Health Goshen Center for Cancer Care.

Dr Alexander Stojadinovic is a Professor of Surgery and Professor of Medicine at the Uniformed Services University of the Health Sciences, Medical Director of the Bon Secours Cancer Institute and the Society of Surgical Oncology Designee to the AJCC

Dr. Nathan M. Shumway is an Assistant Professor of Medicine at the Uniformed University of Health Sciences Medical School and the Program Director for the Hematology/Oncology Fellowship program at the San Antonio Uniformed Services Health Education Consortium. He has active research interests in the area of breast cancer vaccines and immunology, communication skills training, and medical education.