Potential Cost Savings of Contrast-Enhanced Digital Mammography

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OBJECTIVE. The purpose of this article is to discuss whether the sensitivity and specificity of contrast-enhanced digital mammography (CEDM) render it a viable diagnostic alternative to breast MRI.

CONCLUSION. That CEDM couples low-energy images (comparable to the diagnostic quality of standard mammography) and subtracted contrast-enhanced mammograms make it a cost-effective modality and a realistic substitute for the more costly breast MRI.

Keywords: breast MRI, CEDM, CESM, contrast-enhanced digital mammography, contrast-enhanced spectral mammography, costs, sensitivity, specificity

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In 2013, health care spending was approximately 17% of the U.S. gross domestic product, nearly twice that of other developed countries [1]. The Affordable Care Act created incentives for health care providers to focus on cost-effective, preventive, and outcome-focused strategies [2, 3]. Although the high cost of extraordinary services generally receives the most attention, routine care accounts for a considerable portion of the $2.7 trillion in annual U.S. health care spending [1]. In 2010, the estimated cost of screening mammography was $7.8 billion [4], with false-positive results generating additional diagnostic costs [5]. Nearly one-half of women more than 40 years old undergo annual screening mammography; therefore, a decrease in related diagnostic expenditures may lead to substantial cost savings. Advancements in technology and novel modalities, such as rapid-processing digital imaging techniques, are potential sources of both cost savings and improved cancer detection.

Screening mammography has reduced breast cancer mortality in a cost-effective manner [6] but has limitations [7, 8]. Mammography has an overall sensitivity of 75–85%, but in patients at high risk who have *BRCA* mutations or dense breasts, sensitivity decreases to 30–50% [9–13]. The reduced sensitivity of mammography in women with dense breasts most likely results from the masking effect of increased fibroglandular tissue [14]. Improved imaging techniques to detect breast cancer in patients at high risk include dedicated breast CT, breast MRI, and, more recently, contrast-enhanced digital mammography (CEDM), all of which entail the use of contrast medium to highlight the neovascularity of breast cancer induced by angiogenesis.

Dedicated breast CT and mammography yield comparable breast lesion visualization. Breast CT better depicts masses ($p = 0.002$), whereas mammography better depicts microcalcifications ($p = 0.006$) [15]. Breast MRI has sensitivity of 77–100% in the detection of breast cancer [16, 17], but calcifications cannot be identified with breast MRI, which results in variable sensitivity for in situ cancers [18–21]. Given its higher sensitivity, breast MRI is frequently used as a clinical tool for screening patients at high risk (women with > 20% lifetime risk of breast cancer), detecting and characterizing breast disease, screening the contralateral breast in patients with a new breast cancer, assessing the local extent of disease, evaluating neoadjuvant treatment response, localizing biopsy, and surveilling for recurrence. Use of breast MRI has increased more than 20-fold, from 6.5 examinations per 10,000 women in 2000 to 130.7 examinations per 10,000 women in 2009 [22].

CEDM is the newest contrast-enhanced technology for breast imaging and holds great promise for addressing clinical indications similar to those of breast MRI while also addressing its potential limitations. CEDM generates a high-resolution, low-energy, full-field digital mammography (FFDM) image and, as does MRI, a contrast-enhanced image that provides information on lesion vascularity

TABLE 1: Sensitivity and Specificity of Imaging Modalities in the Detection of Breast Cancer

			CEDM vs FFDM				CEDM vs MRI[a] or FFDM + Ultrasound[b]			
			CEDM		FFDM		CEDM		MRI or FFDM + Ultrasound	
Author	Year	No. of Lesions	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Fallenberg et al. [30]	2014	107	95	—	78	—	—	—	—	—
Badr et al. [31]	2014	37	95	85	—	—	—	—	—	—
Łuczyńska et al. [25]	2015	173	100	41	91	15	—	—	—	—
Jochelson et al. [22]	2013	52	96	—	81	—	96	—	96	—
Dromain et al. [29]	2011	142	93	63	78	58	93	63	90	47

Note—Adapted with permission from [32]. Dash (—) indicates not applicable. CEDM = contrast-enhanced digital mammography, FFDM = full-field digital mammography.
[a]Jochelson et al. [22], CEDM vs MRI.
[b]Dromain et al. [29], CEDM vs FFDM + ultrasound.

[17, 22–24]. The resulting contrast-enhanced subtraction images maximize depiction of iodinated contrast agent in the breast and decrease the structured noise of nonenhancing fibroglandular tissue, thus revealing lesions with higher neovascularity and extracellular leakage of contrast agent (two common characteristics of early neoplasm) (Fig. 1). The digital detector depicts lesion detail with 10-fold greater resolution than does breast MRI [25]. Because use of CEDM improves lesion detection and increases the overall specificity of screening mammography, it has potential as a substitute for breast MRI. Several blinded interobserver studies have shown that the sensitivity of CEDM (93–100%) is superior to that of conventional FFDM (78–91%) [26–29] (Table 1).

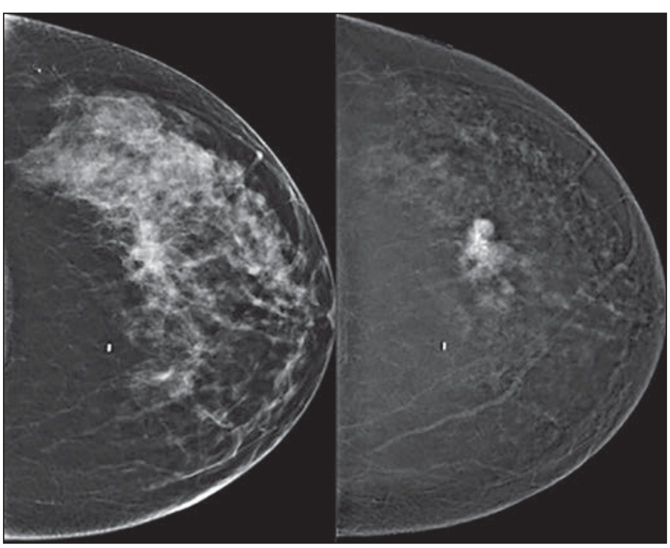
Contrast-Enhanced Digital Mammographic Technique

Installation of CEDM is straightforward and requires a power injector, a review of risk mitigation policies regarding contrast administration, a standard software upgrade, and the insertion of a copper filter into an existing mammography unit. The CEDM technique has been previously described [32].

Relative Efficacy of Contrast-Enhanced Digital Mammography Versus Breast MRI

Although some studies have shown that CEDM and MRI result in comparable sensitivity (96–100% of index tumors) [18], more recent studies have shown that CEDM may have lower false-positive rates (Table 1). At our institution, we successfully identified 97 of 99 pathologically proven cancers using CEDM (98%) [33]. Of the two false-negative cases, one tumor in a 35-year-old woman with a triple-negative cancer had marked background enhancement (Fig. 2). The other was a malignant recurrence along the medial chest wall and was therefore excluded from the FOV.

CEDM also has comparable effectiveness to that of MRI with regard to the preoperative assessment of disease extent [23]. One study showed statistically significant improvement in microcalcification visualization on low-energy CEDM images compared with FFDM images [34]. This suggests that CEDM could increase diagnostic accuracy for ductal carcinoma in situ because the low-



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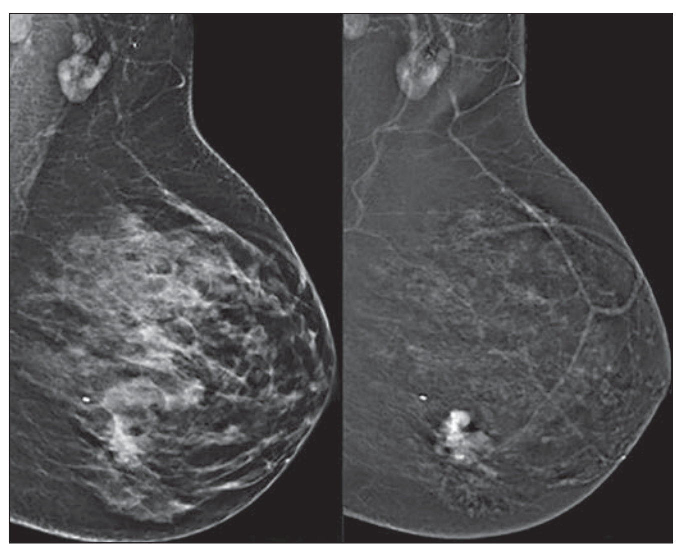

B

Fig. 1—54-year-old woman with biopsy-proven invasive ductal carcinoma.
A and **B**, Craniocaudal (**A**) and mediolateral oblique (**B**) low-energy (*left*) and subtracted contrast-enhanced (*right*) digital mammogram show heterogeneously dense left breast. Focal asymmetry is evident in left central and inferior breast, mid depth, corresponding to area of avid enhancement of irregular mass on digitally subtracted enhanced image.

TABLE 2: Summary of Cost Comparison of Mammography, MRI, and Contrast-Enhanced Digital Mammography (CEDM)

Charge	Screening			Diagnostic		
	FFDM	FFDM + MRI	CEDM	FFDM	MRI	CEDM
Screening FFDM	179.10	179.10				
Diagnostic FFDM			179.01	179.01		179.01
Breast MRI		586.10			586.10	
Breast MRI computer-assisted detection		150.00			150.00	
Gadolinium contrast agent		39.00			39.00	
Iodinated contrast agent			17.00			17.00
Total	179.10	954.20	196.01	179.01	775.10	196.01

Note—Values are U.S. dollars. FFDM = full-field digital mammography.

energy images may capture the extent of disease more effectively than does MRI.

Although additional studies and larger clinical trials of CEDM are needed, the rest of this discussion follows from the assumptions that CEDM is comparable to MRI in sensitivity and specificity and that the images are not of lesser quality than MR images. We discuss reasons for implementing CEDM from perspectives of quality, overall cost of care, health care access, and patient comfort. We also discuss efficiencies that may be realized through accessibility, allocation of resources, and ease of image reading. Our survey of the literature indicated that this is the first report to discuss the potential cost savings associated with implementing CEDM at an institution.

Patient Cost Savings

For comparative purposes, we assume standard 2015 Medicare costs for diagnostic imaging. A screening MRI study with contrast administration costs $586, plus approximately $39 for 10 mL of contrast medium and $150 for computer-assisted detection (Table 2). Screening MRI generally requires that a patient also undergo FFDM at a cost of $179, which brings the total patient cost of screening MRI to $954. Currently, our institution bills CEDM as diagnostic mammography, plus the cost of contrast material. We expect that as use increases, CEDM will receive a separate billing code, which may increase because of the cost of IV line placement and extra technologist resources. Because the low-energy CEDM image is equivalent to a standard FFDM image [35], a separate screening mammogram is not required. The current patient fee for CEDM is $196 ($179 for FFDM plus $17 for 100 mL of contrast material). Based on current Medi-

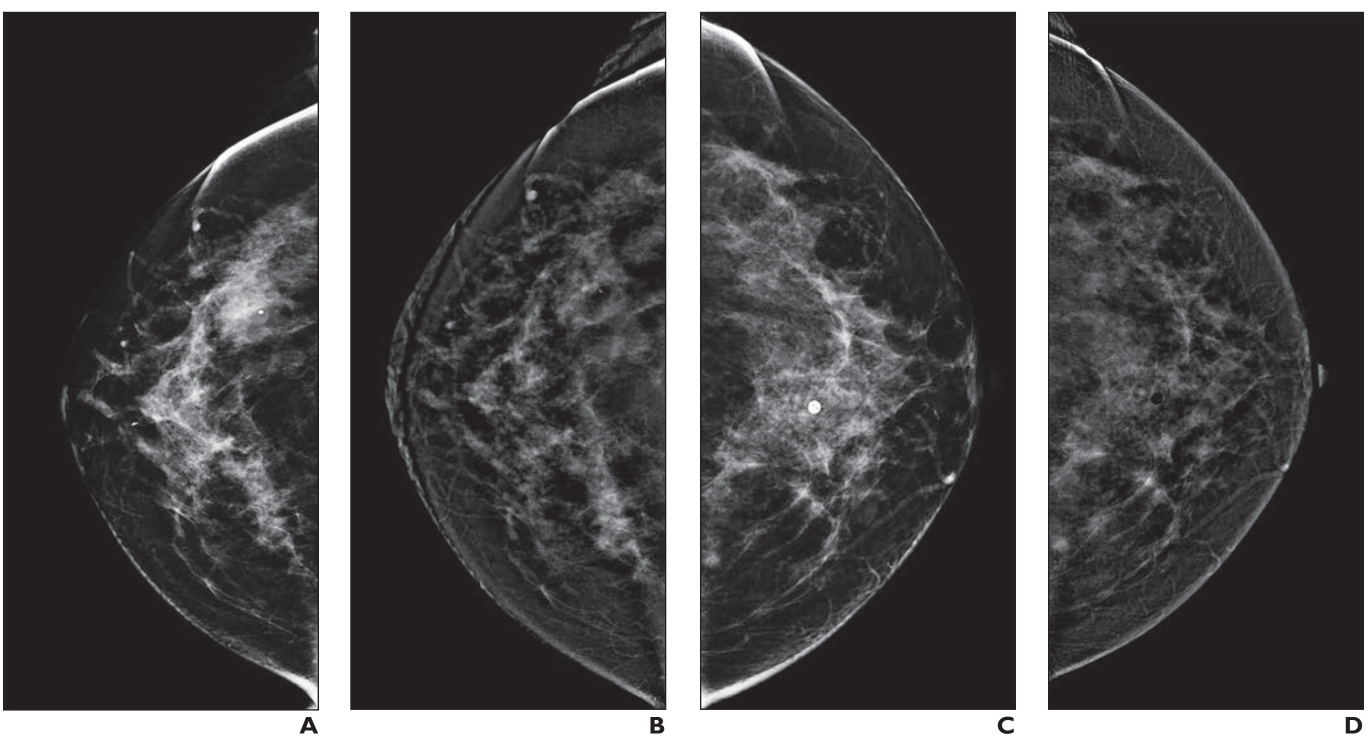

Fig. 2—37-year-old woman with two palpable abnormalities in right breast biopsied at outside institution; both were found to be invasive ductal carcinoma.
A and **B,** Craniocaudal low-energy (**A**) and subtracted contrast-enhanced (**B**) digital mammograms show heterogeneously dense right breast with postbiopsy clips in area of biopsy-proven cancers.
C and **D,** Craniocaudal low-energy (**C**) and subtracted contrast-enhanced (**D**) digital mammograms show contralateral heterogeneously dense left breast. Marked background enhancement limits ability to detect two right-sided breast cancers.

TABLE 3: Comparison of Equipment Costs for Contrast-Enhanced Digital Mammography (CEDM) and MRI

Equipment Cost	CEDM	Breast MRI
System cost	275,000	600,000
CEDM upgrade	95,000	
MRI breast coil		85,000
MRI CAD software		50,000
Power injector	25,000	32,000
Maintenance		
Year 2	40,000	98,000
Year 3	40,000	98,000
Year 4	40,000	98,000
Year 5	40,000	98,000
Year 6	40,000	98,000
Year 7	40,000	98,000
Total	635,000	1,355,000

Note—Values are U.S. dollars. CAD = computer-assisted detection.

care rates, the cost of screening MRI is approximately four times that of CEDM.

Studies have shown that patients have a higher overall preference for CEDM relative to MRI because of reduced procedure time, less noise, and reduced feelings of claustrophobia [36]. The examination time savings is substantial: MRI acquisition in most institutions lasts approximately 30–60 minutes [36], whereas CEDM requires 7–10 minutes. As in MRI, an additional 10–15 minutes is required for contrast injection and to ensure that laboratory values are within normal limits, so we schedule 30 minutes for each CEDM examination. There are also potential savings for the 1–15% of patients who need sedation during MRI because of associated claustrophobia [24]. Patient anxiety and satisfaction are a complex measure, but studies have shown improvements with CEDM [24].

Institutional Savings

Assessing the costs associated with MRI versus CEDM at an institutional level is complex because of the many infrastructure, process, and staffing-related costs. Use of CEDM instead of MRI may alleviate the high direct and indirect costs associated with screening MRI examinations.

Equipment

The median price of a 1.5-T MRI machine including coils is approximately $685,000, with an annual maintenance cost of $98,000. An MRI-safe injector costs $32,000 (Table 3). The cost of a 2D mammography unit with CEDM is approximately $370,000 with annual maintenance costs of $40,000; a single-head injector costs $25,000. Existing mammography units can be upgraded to include CEDM capabilities at a cost of approximately $95,000. CEDM can be implemented with relative ease without the additional cost and space requirements of an MRI magnet.

Staffing Needs

Breast MRI protocols typically require up to 40 minutes and generate several hundred images [37]. In contrast, CEDM acquisition time is a maximum of 10 minutes. Both modalities require 10–15 minutes for placing an IV line and reviewing laboratory values. A CEDM examination requires 25 minutes of a technologist's or nurse's time versus 60 minutes for an MRI examination. Thus, CEDM requires approximately 59% lower unit staffing expense. At our institution, a breast imaging nurse or technologist assists with IV line placement, contrast administration, and breast biopsy procedures (Fig. 3), which accounts for approximately 10% of his or her day. We recognize that not all institutions use similar staffing models, but the reduced staffing requirements of CEDM remain compelling.

MRI also requires more radiologist interpretation time. In our experience, breast MRI requires 3–10 minutes for interpretation, whereas mammographic screening is simpler and more highly standardized [37]. Specialized screening radiologists can batch-read as many as 100 mammograms per hour [37]. At our institution, a full CEDM study can be interpreted in approximately 1–2 minutes.

Potential approaches to decreasing MRI protocol and image interpretation time have been proposed. Kuhl et al. [37] developed an abbreviated breast MRI protocol that consists of acquiring one unenhanced and one contrast-enhanced image. This abbreviated protocol reduces image acquisition time from a reported 17 minutes to 3 minutes; the abbreviated examination can be read in 28 seconds. Although abbreviated breast MRI is becoming more common, CEDM provides similar information at a lower cost.

Advocates of breast MRI may claim that the lack of dynamic imaging in dual-energy CEDM limits the interpretation of images; however, enhancement of both invasive breast cancers and ductal carcinoma is best visualized in the early arterial phase after contrast injection. Other phases and additional pulse sequences traditionally used in MRI protocols have been used to characterize, rather than detect, enhancing structures [37].

Accessibility

Patient access to breast MRI is limited [38–40]. One study [41] showed that 30% of women in the United States live more than 20 minutes from the nearest breast MRI site, whereas 85% of women live within 20 minutes of mammographic services. As a result, the relative ease with which CEDM can be implemented at sites that already have mammography units may result in increased access to contrast-enhanced imaging.

Dose

The ionizing radiation dose from CEDM continues to be studied, and the current literature varies. Low-energy mammography is the main contributor to total glandular breast dose [42]. One study [30] showed that CEDM resulted in a dose comparable to that of mammography (1.72 vs 1.75 mGy). Dromain et al. [26] reported that CEDM radiation dose was comparable to that of standard mammography and was 20% higher than the FFDM dose. Other studies [31, 43, 44] showed CEDM radiation doses 1.54–1.81 times those of FFDM. The authors speculated that variability in dose may be related to the use of a prototype CEDM unit that requires manually setting exposure on the basis of breast thickness and glandularity. Commercially available products determine settings with automatic exposure control [43]. Overall, studies have shown that

CEDM radiation is well below the maximum mammographic dose. Prospective phantom studies are being performed to more accurately determine the mean glandular dose of CEDM. MRI requires no ionizing radiation, but FFDM is still frequently prescribed in conjunction with MRI because MRI is not effective for imaging of calcifications, which may indicate cancer.

Contrast Reactions

The risk of a severe adverse reaction to iodinated contrast medium in CEDM is 0.2–0.4% (similar to that for CT contrast reaction) [45], whereas the rate of adverse gadolinium reactions in MRI examinations is quoted at 0.001–0.01% [46–49]. Recent research, however, has shown that IV gadolinium exposure may be associated with neuronal tissue deposition, even with normal renal function. Although additional studies are needed to investigate the clinical significance of these findings, it is an important consideration in women undergoing annual high-risk screening MRI [50]. Mild allergic reactions, such as hives, nausea, vomiting, headaches, and vasovagal episodes, occur in approximately 1% of patients receiving iodinated contrast material. No publications on CEDM have reported severe reactions or death. To address these potential reactions, however, all staff should undertake routine training to handle these rare but potentially dangerous situations. At our institution, a dedicated breast imaging radiologist or nurse is always present who is capable of managing contrast reactions. For institutions where this may not be the case, the cost of training personnel to manage contrast reactions should be accounted for.

Future Advanced Contrast-Enhanced Breast Imaging Techniques

Contrast-enhanced tomosynthesis (CET) has been proposed as an alternative to address limitations of CEDM due to tissue superimposition. In a study of 13 patients, Chen et al. [51] found that dual-energy contrast-enhanced breast tomosynthesis had results similar to those of MRI in lesion localization, assessment of breast cancer margins and morphologic features, and kinetic assessment. A more recent study [52] showed that MRI, CET, and CEDM had greater sensitivity than conventional FFDM and unenhanced tomosynthesis. That study is the largest (n = 185) to date to our knowledge, and the results suggest that MRI, CEDM, and CET have comparable accuracy in the diagnosis of primary breast cancer in patients with abnormal mammographic findings.

Dedicated breast CT is another emerging mammographic technique that exploits neovascular angiogenesis in breast cancers. In a study that included 46 women, Prionas et al. [53] found that malignant lesions were visualized statistically significantly better with contrast-enhanced breast CT than with unenhanced breast CT or mammography. A more recent study of 42 women [54] showed that contrast-enhanced breast CT may have an advantage over mammography by reducing the rate of false-positive examinations when calcifications are analyzed, in particular facilitating differentiation of ductal carcinoma in situ from benign calcifications. Further studies are needed to directly compare these contrast-enhanced modalities and the amount of radiation exposure.

Conclusion

CEDM is a viable alternative to breast MRI, having comparable sensitivity and specificity. Compared with breast MRI, CEDM is an affordable alternative for patients and is less costly for practices to implement and operate than is breast MRI. Existing mammographic equipment can be modified with relative ease to enable CEDM, possibly increasing patient access to contrast-enhanced breast imaging at minimal incremental cost while improving clinical resource efficiency.

When the American Cancer Society issued screening MRI guidelines in 2007, it

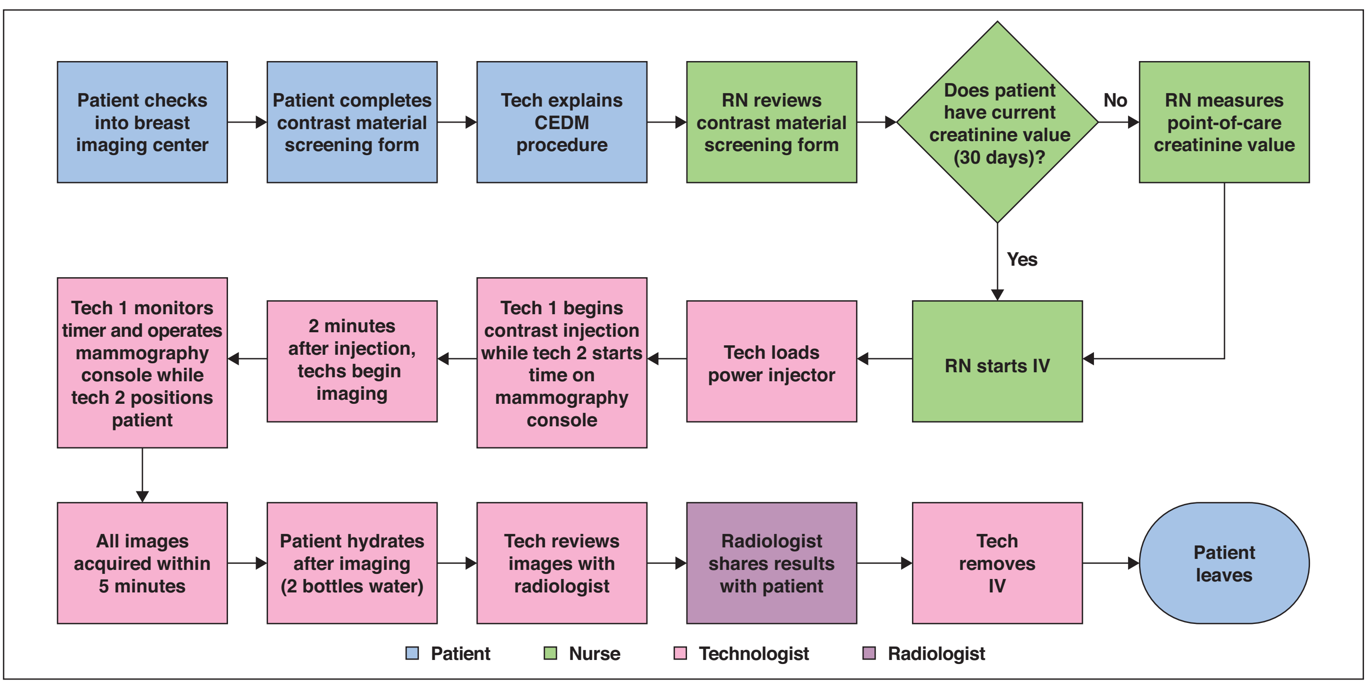

Fig. 3—Chart shows work flow for contrast-enhanced digital mammography (CEDM) at breast imaging center. RN = registered nurse, IV = IV line, Tech = technologist. (Adapted from Palmieri J, DeYoung D, McDonough M, Patel B, Eversman W. How to implement a successful contrast-enhanced digital mammography program. Presented at the 2016 ARRS Annual Meeting, Los Angeles, CA. Used with permission.)

was estimated that as many as 1.4 million women would qualify for breast MRI screening [18]. If CEDM were deemed a viable substitute for breast MRI, at current Current Procedural Terminology codes and Medicare reimbursement rates, the savings would be approximately $750 per examination and as much as $1.1 billion annually ($750 per study × 1.4 million studies). If only a portion of the women in the breast MRI screening population were to qualify for CEDM, there would still be the potential for substantial efficiencies. Nearly 250,000 cases of invasive breast cancer were expected to be diagnosed in 2016 [55], and many of the women with these cancers would benefit from a preoperative contrast-enhanced study to better assess the extent of disease. The use of CEDM in lieu of MRI in these patients may also result in substantial efficiencies.

CEDM couples low-energy FFDM-quality images with contrast-enhanced subtracted images in a manner that achieves sensitivity and specificity superior to those of FFDM and comparable to those of breast MRI. The use of CEDM continues to be validated, but the resulting efficiencies and acceptable levels of radiation suggest that it may be a promising modality for routine screening and a potential substitute for costlier breast MRI.

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References

1. Hartman M, Martin AB, Lassman D, Catlin A; National Health Expenditure Accounts Team. National health spending in 2013: growth slows, remains in step with the overall economy. *Health Aff (Millwood)* 2015; 34:150–160
2. Owens DK, Qaseem A, Chou R, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. High-value, cost-conscious health care: concepts for clinicians to evaluate the benefits, harms, and costs of medical interventions. *Ann Intern Med* 2011; 154:174–180
3. Qaseem A, Alguire P, Dallas P, et al. Appropriate use of screening and diagnostic tests to foster high-value, cost-conscious care. *Ann Intern Med* 2012; 156:147–149
4. O'Donoghue C, Eklund M, Ozanne EM, Esserman LJ. Aggregate cost of mammography screening in the United States: comparison of current practice and advocated guidelines. *Ann Intern Med* 2014; 160:145
5. Chubak J, Boudreau DM, Fishman PA, Elmore JG. Cost of breast-related care in the year following false positive screening mammograms. *Med Care* 2010; 48:815–820
6. Rosenquist CJ, Lindfors KK. Screening mammography beginning at age 40 years: a reappraisal of cost-effectiveness. *Cancer* 1998; 82:2235–2240
7. Howlader N, Noone AM, Krapcho M, et al., eds. SEER cancer statistics review, 1975–2009 (vintage 2009 populations). Bethesda, MD: National Cancer Institute. seer.cancer.gov/csr/1975_2009_pops09. November 2011. Accessed June 8, 2016
8. Elmore JG, Armstrong K, Lehman CD, Fletcher SW. Screening for breast cancer. *JAMA* 2005; 293:1245–1256
9. Kerlikowske K, Carney PA, Geller B, et al. Performance of screening mammography among women with and without a first-degree relative with breast cancer. *Ann Intern Med* 2000; 133:855–863
10. Kuhl CK, Schmutzler RK, Leutner CC, et al. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. *Radiology* 2000; 215:267–279
11. Warner E, Plewes DB, Hill KA, et al. Surveillance of *BRCA1* and *BRCA2* mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. *JAMA* 2004; 292:1317–1325
12. Leach MO, Boggis CR, Dixon AK, et al.; MARIBS Study Group. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet* 2005; 365:1769–1778
13. Kriege M, Brekelmans CT, Boetes C, et al.; Magnetic Resonance Imaging Screening Study Group. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N Engl J Med* 2004; 351:427–437
14. Boyd NF, Guo H, Martin LJ, et al. Mammographic density and the risk and detection of breast cancer. *N Engl J Med* 2007; 356:227–236
15. Lindfors KK, Boone JM, Nelson TR, Yang K, Kwan AL, Miller DF. Dedicated breast CT: initial clinical experience. *Radiology* 2008; 246:725–733
16. Warner E. The role of magnetic resonance imaging in screening women at high risk of breast cancer. *Top Magn Reson Imaging* 2008; 19:163–169
17. Gillman J, Toth HK, Moy L. The role of dynamic contrast-enhanced screening breast MRI in populations at increased risk for breast cancer. *Womens Health (Lond Engl)* 2014; 10:609–622
18. Saslow D, Boetes C, Burke W, et al.; American Cancer Society Breast Cancer Advisory Group. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin* 2007; 57:75–89
19. Lehman CD. Role of MRI in screening women at high risk for breast cancer. *J Magn Reson Imaging* 2006; 24:964–970
20. Brennan M, Spillane A, Houssami N. The role of breast MRI in clinical practice. *Aust Fam Physician* 2009; 38:513–519
21. Misra S, Solomon NL, Moffat FL, Koniaris LG. Screening criteria for breast cancer. *Adv Surg* 2010; 44:87–100
22. Jochelson MS, Dershaw DD, Sung JS, et al. Bilateral contrast-enhanced dual-energy digital mammography: feasibility and comparison with conventional digital mammography and MR imaging in women with known breast carcinoma. *Radiology* 2013; 266:743–751
23. Fallenberg EM, Dromain C, Diekmann F, et al. Contrast-enhanced spectral mammography versus MRI: initial results in the detection of breast cancer and assessment of tumour size. *Eur Radiol* 2014; 24:256–264
24. Hobbs MM, Taylor DB, Buzynski S, Peake RE. Contrast-enhanced spectral mammography (CESM) and contrast enhanced MRI (CEMRI): patient preferences and tolerance. *J Med Imaging Radiat Oncol* 2015; 59:300–305
25. Łuczyńska E, Heinze-Paluchowska S, Hendrick E, et al. Comparison between breast MRI and contrast-enhanced spectral mammography. *Med Sci Monit* 2015; 21:1358–1367
26. Dromain C, Thibault F, Diekmann F, et al. Dual-energy contrast-enhanced digital mammography: initial clinical results of a multireader, multicase study. *Breast Cancer Res* 2012; 14:R94
27. Cheung YC, Lin YC, Wan YL, et al. Diagnostic performance of dual-energy contrast-enhanced subtracted mammography in dense breasts compared to mammography alone: interobserver blind-reading analysis. *Eur Radiol* 2014; 24:2394–2403
28. Diekmann F, Freyer M, Diekmann S, et al. Evaluation of contrast-enhanced digital mammography. *Eur J Radiol* 2011; 78:112–121
29. Dromain C, Thibault F, Muller S, et al. Dual-energy contrast-enhanced digital mammography: initial clinical results. *Eur Radiol* 2011; 21:565–574
30. Fallenberg EM, Dromain C, Diekmann F, et al. Contrast-enhanced spectral mammography: does mammography provide additional clinical benefits or can some radiation exposure be avoided? *Breast Cancer Res Treat* 2014; 146:371–381
31. Badr S, Laurent N, Regis C, Boulanger L, Lemaille S, Poncelet E. Dual-energy contrast-enhanced digital mammography in routine clinical practice in 2013. *Diagn Interv Imaging* 2014; 95:245–258
32. Lewis TC, Pizzitola VJ, Giurescu ME, et al. Contrast-enhanced digital mammography: a single-institution experience of the first 208 cases. *Breast J* 2016; 23:67–76
33. Ali-Mucheru M, Patel B, Pockaj B, et al. Contrast-enhanced digital mammography in the surgical management of breast cancer. *Ann Surg Oncol* 2016; 23 (suppl 5):649–655

34. Lalji UC, Jeukens CR, Houben I, et al. Evaluation of low-energy contrast-enhanced spectral mammography images by comparing them to full-field digital mammography using EUREF image quality criteria. *Eur Radiol* 2015; 25:2813–2820
35. Francescone MA, Jochelson MS, Dershaw DD, et al. Low energy mammogram obtained in contrast-enhanced digital mammography (CEDM) is comparable to routine full-field digital mammography (FFDM). *Eur J Radiol* 2014; 83:1350–1355
36. Carpenter AP, Leemis LM, Papir AS, Phillips DJ, Phillips GS. Managing magnetic resonance imaging machines: support tools for scheduling and planning. *Health Care Manag Sci* 2011; 14:158–173
37. Kuhl CK, Schrading S, Strobel K, Schild HH, Hilgers RD, Bieling HB. Abbreviated breast magnetic resonance imaging (MRI): first postcontrast subtracted images and maximum-intensity projection: a novel approach to breast cancer screening with MRI. *J Clin Oncol* 2014; 32:2304–2310
38. Cott Chubiz JE, Lee JM, Gilmore ME, et al. Cost-effectiveness of alternating magnetic resonance imaging and digital mammography screening in *BRCA1* and *BRCA2* gene mutation carriers. *Cancer* 2013; 119:1266–1276
39. Lowry KP, Lee JM, Kong CY, et al. Annual screening strategies in *BRCA1* and *BRCA2* gene mutation carriers: a comparative effectiveness analysis. *Cancer* 2012; 118:2021–2030
40. Wernli KJ, DeMartini WB, Ichikawa L, et al.; Breast Cancer Surveillance Consortium. Patterns of breast magnetic resonance imaging use in community practice. *JAMA Intern Med* 2014; 174:125–132
41. Onega T, Hubbard R, Hill D, et al. Geographic access to breast imaging for US women. *J Am Coll Radiol* 2014; 11:874–882
42. Yakoumakis E, Tzamicha E, Dimitriadis A, Georgiou E, Tsapaki V, Chalazonitis A. Dual-energy contrast-enhanced digital mammography: patient radiation dose estimation using a Monte Carlo code. *Radiat Prot Dosimetry* 2015; 165:369–372
43. Jeukens CR, Lalji UC, Meijer E, et al. Radiation exposure of contrast-enhanced spectral mammography compared with full-field digital mammography. *Invest Radiol* 2014; 49:659–665
44. James JR, Pavlicek W, Hanson JA, Boltz TF II, Patel B. Breast radiation dose with CESM compared with 2D FFDM and 3D tomosynthesis mammography. *AJR* 2017; 208:362–372
45. American College of Radiology Committee on Drugs and Contrast Media. ACR manual on contrast media: version 10.2. American College of Radiology website. https://www.acr.org/~/media/37D84428BF1D4E1B9A3A2918DA9E27A3.pdf. 2016. Accessed June 22, 2016
46. Hunt CH, Hartman RP, Hesley GK. Frequency and severity of adverse effects of iodinated and gadolinium contrast materials: retrospective review of 456,930 doses. *AJR* 2009; 193:1124–1127
47. Murphy KJ, Brunberg JA, Cohan RH. Adverse reactions to gadolinium contrast media: a review of 36 cases. *AJR* 1996; 167:847–849
48. Runge VM. Safety of approved MR contrast media for intravenous injection. *J Magn Reson Imaging* 2000; 12:205–213
49. Runge VM. Safety of magnetic resonance contrast media. *Top Magn Reson Imaging* 2001; 12:309–314
50. McDonald RJ, McDonald JS, Kallmes DF, et al. Intracranial gadolinium deposition after contrast-enhanced MR imaging. *Radiology* 2015; 275:772–782
51. Chen SC, Carton AK, Albert M, Conant EF, Schnall MD, Maidment AD. Initial clinical experience with contrast-enhanced digital breast tomosynthesis. *Acad Radiol* 2007; 14:229–238
52. Chou CP, Lewin JM, Chiang CL, et al. Clinical evaluation of contrast-enhanced digital mammography and contrast enhanced tomosynthesis: comparison to contrast-enhanced breast MRI. *Eur J Radiol* 2015; 84:2501–2508
53. Prionas ND, Lindfors KK, Ray S, et al. Contrast-enhanced dedicated breast CT: initial clinical experience. *Radiology* 2010; 256:714–723
54. Aminololama-Shakeri S, Abbey CK, Gazi P, et al. Differentiation of ductal carcinoma in-situ from benign micro-calcifications by dedicated breast computed tomography. *Eur J Radiol* 2016; 85:297–303
55. American Cancer Society website. About breast cancer. www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-key-statistics. Last revised May 4, 2016. Accessed August 2, 2016