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REVIEW

Rate of radial scars by core biopsy and upgrading to malignancy or high-risk lesions before and after introduction of digital breast tomosynthesis

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Abstract

Purpose Radial scars (RS) commonly present mammographically as architectural distortions, but these lesions may be associated with non-invasive and invasive breast cancer. Digital breast tomosynthesis (DBT) has resulted in higher detection rates of architectural distortion particularly in patients with dense breast tissue. We hypothesized that rates of clinically relevant lesions confirmed surgically would be lower in patients who received DBT imaging compared with those who received standard digital breast imaging.

Methods We performed a retrospective review of 223 patients diagnosed with pure RS by core biopsy and surgical excision before and after DBT was introduced. The rate of upgrading to malignancy or high-risk lesion was evaluated. Demographics, biopsy type, and histologic data were analyzed. Univariable logistic regression analysis was used to identify variables that may be associated with upgrading.

Results The rate of identifying RS increased from 0.04–.13% ($P < 0.0001$) with DBT imaging. The upgrade rate on surgical specimen to invasive or non-invasive cancer was similar before and after DBT; 6% versus 3%, as were findings of a high-risk lesion; 12% versus 22%. No predictive factors were identified for patients upgraded to malignant neoplasms or high-risk lesions.

Conclusions The likelihood of identifying RS has increased with DBT imaging, but rates of upgrading to a malignant neoplasm or high-risk lesion were similar to those before DBT. Although the rate of upgrading to malignancy after DBT was low, an excisional biopsy should be considered as 22% of patients were upgraded to high-risk lesions. These patients are candidates for chemoprevention and/or high-risk surveillance.

Keywords Radial scar · Breast cancer · Core biopsy · Excisional biopsy · Upgrade · Digital breast tomosynthesis

Introduction

Radial scars (RS) are benign proliferative breast lesions. Histologically, they are defined as sclerosing lesions with a central, sclerotic nidus (often associated with fibroelastotic

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change), from which ducts and lobules radiate circumferentially [1]. On mammographic imaging, radial scars have a spiculated outline with translucent center and can appear as architectural distortion, which can be associated with microcalcifications [2–4]. These lesions are often difficult to distinguish from a malignant neoplasm on mammography, therefore they are commonly recommended for a core biopsy.

Radial scars diagnosed by core biopsy may be associated with findings of invasive cancer and/or an atypical hyperplastic lesion and lobular neoplasm at subsequent surgical excision. Reported rates of radial scar upgraded to a malignancy on final pathology range from 0 to 40% [5–15]. Conlon et al [10] performed a meta-analysis of 20 studies with RS excision and found an upgrade rate of 7.5% for RS without atypia. Although more recent studies have shown low rates of upgrading to malignancy, the rate of identifying a high-risk lesion (atypical hyperplasia or lobular neoplasia) at surgical excision ranges from 20 to 26% [13, 16, 17].

Digital breast tomosynthesis (DBT) allows for three-dimensional reconstruction of the breast that offers advantages over two-dimensional mammographic imaging. This technology allows opportunities to better distinguish and characterize masses, asymmetries, and architectural distortion [18, 19]. Patient recall rates for architectural distortion and rates of identifying a malignant neoplasm have increased with the use of DBT imaging [20–24]. If DBT imaging detects higher rates of architectural distortion, which can represent a radial scar, malignant neoplasm, or non-malignant lesion, we questioned whether these higher detection rates were associated with a decrease in rates of finding clinically relevant lesions at surgical excision. The technological advantages of DBT infer that patients may benefit from having to undergo fewer unnecessary surgical excisions; that is, fewer surgical excisions with a pathologic result of pure RS.

The aim of this study was to review our experience with patients diagnosed with pure RS by core biopsy and the rates of upgrading to a malignant neoplasm or high-risk lesion with standard digital mammographic imaging compared to DBT imaging. We hypothesized that the rate of radial scars by core biopsy would be higher with DBT imaging compared with standard digital mammographic imaging, but rates of clinically relevant lesions confirmed surgically would be lower.

Methods

Following approval by the local Institutional Review Board, a single institution review was performed to identify patients diagnosed with RS by core needle biopsy with or without atypia who underwent subsequent surgical excision at Carolinas Medical Center from January, 2007 through December, 2017. Patients were included if they were diagnosed with pure RS by core biopsy. In this study, pure radial scar was defined as radial scar diagnosed by core biopsy with or without proliferative breast changes. Exclusion criteria included patients who were followed at an outside facility, personal history of breast cancer, and additional findings by core biopsy such as malignancy, atypical ductal hyperplasia, atypical lobular carcinoma in situ, papilloma with or without atypia, or flat epithelial atypia.

The upgrade rates to malignancy and high-risk lesions were evaluated. An upgrade to malignant neoplasm included the presence of non-invasive or invasive carcinoma at surgical excision. An upgrade to high-risk lesions included the presence of atypical hyperplasia or lobular carcinoma in situ at surgical excision. Variables of interest included age, family history of breast cancer, race, biopsy type, and histological findings.

Digital breast tomosynthesis was introduced at our institution on August, 20, 2013. All study patients from January 1, 2007 through August 19, 2013 received standard digital mammography. All study patients from August 20, 2013 through December 31, 2017 received DBT.

Statistical analysis

Patient characteristics were summarized by using the frequency and percent for categorical variables, and descriptive statistics, including mean and standard deviation. The Chi square test (χ^2), Fisher's exact test, and Student's t test for categorical variables were performed to identify characteristics associated with upgrading to cancer and high-risk lesions. Univariable logistic regression models were used to evaluate individual associations between factors related to RS diagnosed by core biopsy and cancer or high-risk lesions identified at surgical excision. Statistical analyses were performed by using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Of the 431 patients diagnosed with radial scar by core biopsy, 223 met inclusion criteria. Of these 223 patients, 65 patients were diagnosed by standard digital mammographic imaging, and 158 patients were diagnosed with DBT imaging (Fig. 1). A total of 208 patients did not meet inclusion criteria. Seventy-eight of these patients were excluded because of a concurrent diagnosis as follows: atypical ductal hyperplasia (31), atypical lobular hyperplasia (18), lobular carcinoma in situ (4), flat epithelial atypia (3), papilloma with atypia (1), and papilloma without atypia (21). The remaining 130 patients were excluded due to the

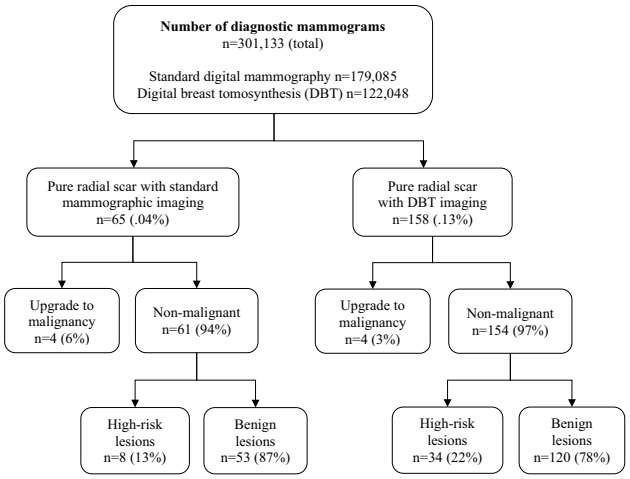

Fig. 1 CONSORT flow diagram of patients diagnosed with radial scar by core biopsy and underwent surgical excision

following: 6 with a personal history of breast cancer, 14 who elected observation, and 110 who were followed at an outside facility.

Of the patients included in the study, the mean age was 53 years (range, 26 years–81 years). The majority were diagnosed by stereotactic core vacuum-assisted biopsy with 9-gauge needles (57%) followed by ultrasound guided core biopsy with 14-gauge or 18-gauge needles (43%). Patient demographics, type of biopsy, and excisional biopsy results are summarized in Tables 1 and 2. There were 179,085 diagnostic mammograms performed with standard digital mammographic imaging and 122,048 diagnostic mammograms performed with DBT imaging. After the introduction of DBT imaging, there was a 0.09% increase in the rate of RS diagnosed by core biopsy; 0.04% (65 of 179,085 patients) were diagnosed with radial scars before DBT compared with 0.13% (158 of 122,048 patients) after DBT ($P < 0.0001$).

Of the patients diagnosed with RS by core biopsy who underwent surgical excision, 6% (4 of 65) were upgraded to malignancy with standard digital mammographic imaging and 3% (4 of 158) were upgraded to malignancy with DBT imaging. In contrast, 12% (8 of 65) were upgraded to high-risk lesions with standard digital mammographic imaging and 22% (34 of 158) were upgraded with DBT imaging. Although there was a decrease in the rate of upgrading to cancer and an increase in the rate of upgrading to high-risk lesions with DBT imaging, these findings were not statistically significant ($P = 0.24$, $P = 0.10$, respectively) (Tables 1, 3). There was a statistically significant difference in the type of biopsy used (ultrasound or stereotactic) before DBT compared with after DBT ($P = 0.001$) (Table 1). No predictive factors were identified

Table 1 Demographics, type of biopsy, and excisional biopsy results

	Standard digital mammographic imaging $n = 65$ (%)	Digital breast tomosynthesis imaging $n = 158$ (%)	P value[b]
Mean age in years (range)[a]	50.4 (30–79)	54.5 (26–81)	.02[d]
Race[c]			0.74
White	51 (78)	120 (76)	
African American	7 (11)	23 (15)	
Other	7 (11)	15 (9)	
Family history of breast cancer	22 (34)	48 (30)	0.4
Microcalcification on biopsy[c]	29 (45)	81 (51)	0.37
Biopsy type[c]			0.001
Stereotactic	26 (40)	101 (64)	
Ultrasound	39 (60)	57 (36)	
Upgrade to malignancy[c]	4 (6)	4 (3)	.24[e]
High-risk lesion[c]	8 (12)	34 (22)	0.10
Atypical ductal hyperplasia	6	20	
Atypical lobular hyperplasia	2	11	
Lobular carcinoma in situ	0	3	
Either upgrade to cancer or high-risk lesion[c]	12 (18)	38 (24)	0.36

[a]Value expressed as mean age and range in parentheses

[b]Value expressed represents statistical result with Chi square test (χ^2) unless otherwise noted

[c]Value expressed as number and percentage in parentheses

[d]Value expressed represents statistical result with Student's t test

[e]Value expressed represents statistical result with Fisher's exact test

Table 2 Demographics, type of biopsy, and excisional biopsy results for upgrade

	No upgrade, $n=173$ (%)	Upgrade to malignancy or high-risk lesion $n=50$ (%)	P value[b]
Mean age in years (range)[a]	52.8 (26–81)	55.2 (38–79)	0.2
Race[c]			0.2
White	129 (75)	42 (84)	
African American	24 (14)	6 (12)	
Other	20 (11)	2 (4)	
Family history of breast cancer (yes)	54 (31)	16 (32)	0.9
Microcalcification on biopsy (yes)	85 (49)	25 (50)	0.9
Biopsy type[c]			0.6
Stereotactic	100 (58)	27 (54)	
Ultrasound	73 (42)	23 (46)	

[a]Value expressed as mean age and range in parentheses

[b]Value expressed represents statistical result with Chi square test

[c]Value expressed as number and percentage in parentheses

Table 3 Clinical finding and characteristics of malignant tumor found at surgical excision

Year	Non-invasive or Invasive cancer	Hormone status	Grade
2007	T1mi	ER+, PR+, HER2−	Intermediate[a]
2008	T1b	ER+, PR+, HER2−	Low[a]
2009	DCIS	Not available	Low[b]
2011	T2	ER + PR−, HER2−	Intermediate[a]
2015	DCIS	ER+	High[b]
2017	T1a	ER+, PR+, HER2−	Low[a]
2017	T2	ER+, PR+, HER2−	Low[a]
2017	T1mi	ER+, PR+, HER2−	Not available

DCIS ductal carcinoma in situ

[a]Denotes histologic grade

[b]Denotes nuclear grade

for patients who were upgraded to malignant neoplasms or high-risk lesions on univariable logistic regression analyses (Tables 4, 5).

Some patients who had high-risk lesions on subsequent surgical excision were placed on chemoprevention and/or underwent additional high-risk screening. Of the 41 patients who qualified for chemoprevention, 16 (39%) began treatment and 25 (61%) declined treatment. Of the 31 patients who met National Comprehensive Cancer Network guidelines for high-risk screening including annual mammograms and breast magnetic resonance imaging (MRI) based on the Gail risk assessment model or Tyrer-Cuzick model, 12 (39%) underwent high-risk screening, 5 (16%) declined, and 14 (45%) did not have MRI largely due to fat replaced breast.

Table 4 Univariable logistic regression analyses of predictors of upstaging to cancer and high-risk lesions

Variables	Upgrade to malignancy Univariable associations			Upgrade to high-risk lesions Univariable associations		
	$P <$	Odds ratio	Confidence interval	$P <$	Odds ratio	Confidence interval
Race						
Caucasian	Ref	Ref	Ref	Ref	Ref	Ref
African American	0.975	< 0.001	(0.000–> 999)	0.481	0.98	(0.37–2.58)
Other	0.978	< 0.001	(0.000–> 999)	0.263	0.41	(0.09–1.85)
Age at diagnosis	0.747	1.01	(0.95–1.07)	0.429	1.01	(0.98–1.04)
Type of core biopsy						
Stereotactic	0.667	0.73	(0.17–3.01)	0.865	0.94	(0.47–1.87)
Ultrasound	Ref	Ref	Ref	Ref	Ref	Ref
Calcification on biopsy (yes)	0.957	1.04	(0.25–4.26)	0.733	1.13	(0.57–2.23)
DBT (yes)	0.168	0.37	(0.09–1.52)	0.174	1.79	(0.77–4.13)
Family history (yes)	0.754	1.26	(0.29–5.44)	0.917	0.96	(0.46–2.00)

DBT digital breast tomosynthesis

Table 5 Combined univariable logistic regression analyses of predictors of upstaging to cancer or high-risk lesions

Variables	Upgrade to malignancy or high-risk lesions Univariable associations		
	P <	Odds ratio	Confidence interval
Race			
Caucasian	Ref	Ref	Ref
African American	0.623	0.76	(0.28–1.97)
Other	0.199	0.32	(0.07–1.42)
Age at diagnosis	0.404	1.01	(0.98–1.04)
Type of core biopsy			
Stereotactic	0.711	0.89	(0.46–1.68)
Ultrasound	Ref	Ref	Ref
Calcification on biopsy (yes)	0.757	1.12	(0.58–2.09)
DBT (yes)	0.559	1.24	(0.59–2.58)
Family history of breast cancer (yes)	0.967	1.02	(0.51–2.00)

DBT digital breast tomosynthesis

Discussion

This study illustrates that despite a significant increase in the rate of radial scars by core biopsy identified with DBT imaging compared to standard digital mammographic imaging, the rates of upgrade to a malignant neoplasm on surgical excision were similar. In this series, the rate of upgrading to malignancy at surgical excision with DBT imaging was 3% (4 of 158 patients), whereas the rate of upgrading to a high-risk lesion was 22% (34 of 158 patients).

This study was one of the larger series to evaluate the upgrade rates of malignant neoplasms and high-risk lesions in patients with pure RS identified by core needle biopsy particularly after the introduction of DBT. Although previous studies reported variable rates of upgrading to malignant neoplasms ranging from 0 to 40% [5–15], more recent studies report lower rates of upgrading to malignancy ranging from 1 to 8% [10, 12–14, 16, 17, 25]. This may be attributed to the finding of careful radiological-pathological correlation and the exclusion of history of breast cancer and atypical proliferative lesions [10, 13, 14, 16]. Studies that support the excision of RS by core biopsy reported higher rates of upgrade to malignancy or high-risk lesions in their results [7, 15].

The wide range of upstage rates and variable imaging techniques reported in the literature has led to different practice patterns. The reported low rate of upgrade to a malignancy with non-suspicious findings on mammography has led to the consideration of conservative management with radiographic follow-up [10, 11, 26]. Other groups support observation if they meet criteria of size < 1–2 cm, radiology-pathology concordance, no associated high-risk lesions, and not clinically palpable [12, 27]. In addition to meeting these criteria, others favor observation if able to obtain at least 6–12 core specimens using at least an 11-gauge needle [8, 12, 27, 28]. Most malignant neoplasms found on surgical excision that are associated with RS diagnosed by core biopsy are low nuclear grade or histologic grade 1 or 2 [7, 14, 25]. Our series was consistent with this finding with the exception of one patient who had high grade ductal carcinoma in situ (DCIS).

Study limitations included a single institution cohort and inherent bias due to retrospective study design. A number of patients were excluded for various reasons, which may have biased our results. Other potential predictive factors, such as radiologic characteristics and number of specimens obtained per core biopsy were not evaluated.

The rate of identifying RS by core biopsy increased with DBT imaging compared to the rate with standard digital mammographic imaging, but the rates of identifying malignant neoplasm and high-risk lesions were not statistically different. Because our results showed that nearly one in five patients with radial scars by core biopsy with DBT imaging had a high-risk lesion confirmed surgically, we advocate that follow-up care should be commensurate with current guidelines and include discussion of chemoprevention. In our practice, we support excisional biopsy in the setting of RS identified by core biopsy.

Conclusion

Although the likelihood of identifying radial scars diagnosed by core biopsy has increased since the introduction of DBT imaging, the rates of identifying malignant neoplasms or high-risk lesions have remained stable. Given an upgrade rate to high-risk lesions of 22%, excisional biopsy of RS should be considered as these patients may benefit from chemoprevention and additional surveillance.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study has received ethical approval by the Carolinas HealthCare System Institutional Review Board as it satisfies requirements of 45 CFR 46 110, category #5.

Informed consent This was a retrospective study. For this type of study, formal consent was not required by the IRB.

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