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Locoregional Treatment of Breast Cancer in Women With and Without Preoperative MRI

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Abstract

Background—Preoperative magnetic resonance imaging (MRI) use has increased among older women diagnosed with breast cancer. MRI detects additional malignancy, but its impact on locoregional surgery and radiation treatment remains unclear.

Methods—We examined the associations of preoperative MRI with initial locoregional treatment type (mastectomy, breast conserving surgery (BCS) with radiation therapy (RT), BCS without RT) and BCS reoperation rates for SEER-Medicare women diagnosed with stage 0–III breast cancer from 2005–2009 (N=55,997).

Results—We found no association of initial locoregional treatment of mastectomy (OR 1.04, 95% CI (0.98–1.11)) or reoperation after initial BCS (OR 0.96, 95% CI (0.89–1.03)) between women with preoperative MRI (16.2%) compared to women without MRI. However, women with MRI who had initial BCS were more likely to undergo RT (OR 1.09 (1.02–1.16)).

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Conclusion—Preoperative breast MRI in Medicare-enrolled women with stage 0–III breast cancer was not associated with increased mastectomy. However, in older women with MRI undergoing BCS, there was a greater use of RT.

Keywords

preoperative MRI; breast cancer; breast conserving surgery; mastectomy

Introduction

Preoperative breast magnetic resonance imaging (MRI) use has increased in breast cancer treatment planning for women with invasive cancer and ductal carcinoma in situ (DCIS). (1) Previous SEER-Medicare studies report a dramatic increase in preoperative MRI use in older women diagnosed in 2005 (10%) to 25% – 50% in 2008/2009 (1–5), and a recent Canadian study reported close to 15% of women diagnosed with breast cancer in Ontario, Canada received a preoperative MRI. The same study noted that preoperative MRI was associated with aggressive surgical interventions. (6) Despite the increasing trend in MRI utilization, the value of preoperative MRI is widely debated. (7) While MRI is more sensitive than mammography and finds additional otherwise-occult malignancy in approximately 16% of women in the ipsilateral breast, the evidence has yet to show clinical benefit of preoperative MRI and the downstream associated treatments. (8, 9) This uncertainty is seen in conflicting guidelines around appropriate use of preoperative MRI. The current guidelines from the National Comprehensive Cancer Network (NCCN) recommend preoperative MRI as optional for DCIS and invasive cancer. (10) The European Society of Breast Cancer Specialists (EUSOMA) recommendations state that acceptable indications for preoperative MRI include a diagnosis of invasive lobular carcinoma, a discrepancy greater than 1 cm between mammography and ultrasound size with expected impact on treatment, and consideration for partial breast irradiation. (11) The ACR Practice Guidelines for MRI of the Breast, state that preoperative MRI may be useful to determine extent of disease. (12)

The impact of preoperative MRI on the surgical management of women newly diagnosed with breast cancer continues to be poorly understood. Multiple single-institution studies have shown that preoperative MRI is associated with increased mastectomy rates. (13–15) Sommer et al. found higher mastectomy rates for Medicare-enrolled women (N=46,824) from 2003–2005 who received preoperative MRI (40.8%) as compared to those who did not (38.8%) (p=.04).(4) Prior studies have shown conflicting results on the ability of MRI to decrease reoperation rates, diminish ipsilateral breast tumor recurrence, or improve survival. (9)

Because the relationship of MRI use to types of treatment remain unclear, our objective was to evaluate the association between preoperative MRI use and locoregional surgical and radiation treatment of breast cancer among women diagnosed with Stage 0–III breast cancer enrolled in Medicare fee for service. Additionally, in women with initial BCS, we investigated the impact of preoperative MRI on reoperation.

Methods

Data

We used the Surveillance, Epidemiology and End Results (SEER)-Medicare database (2004–2010), which combines clinical and sociodemographic information from population-based cancer registries with claims information from records of Medicare beneficiaries with cancer.(16) The SEER-Medicare database is a collaboration of the National Cancer Institute (NCI), the SEER registries and the Centers for Medicare and Medicaid Services (CMS), (17) and includes records from 1.8 million people with cancer (233,000 with breast cancer).

Study Population

We included women in the SEER Medicare database diagnosed with non-metastatic breast cancer (DCIS (Stage 0) or Stage I–III invasive breast cancer) between 2005 and 2009 who received a mastectomy or BCS (with or without radiation therapy) within six months after their breast cancer diagnosis. Women were included if they were 66 years or older at the time of their breast cancer diagnosis, and had a pathologically confirmed diagnosis as defined by SEER. (10) To ensure complete claims data capture, we included women enrolled in Medicare Part A (Hospital Insurance) and Medicare Part B (Medical Insurance) Fee-For-Service plans from one year prior to six months following breast cancer diagnosis. We excluded women with a prior personal history of breast cancer and those whose source of diagnosis was a nursing home.

Definitions

Current Procedural Terminology (CPT)/Healthcare Common Procedure Coding System (HCPCS) and International Classification of Diseases (ICD-9) diagnosis and procedure codes (Supplemental Table 1) from the Outpatient and Carrier Medicare claims files were used to identify the biopsy closest to the time of diagnosis, the initial surgical treatment, reoperation following an initial BCS, and preoperative MRI use. As described in a previous publication (1), because SEER does not capture exact diagnosis date, the breast cancer diagnosis date was defined as the breast biopsy date closest to the SEER diagnosis date or the first day of the month of the SEER diagnosis date if a biopsy claim was not found (approximately 3% of women). The preoperative window was limited to a maximum of six months from the date of breast cancer diagnosis to the date of the first breast surgery found in claims. We defined the initial locoregional treatments as mastectomy or BCS with or without RT. Reoperation after initial BCS was a secondary outcome, defined as a second surgery (BCS or mastectomy) within 6 months after the initial BCS. Receipt of preoperative MRI within the preoperative window was our primary exposure of interest. (1)

Analysis

We compared the distribution of surgical treatment types, including reoperation, by diagnosis year among those with and without MRI. Differences in MRI utilization across the study period were assessed using a chi-square test.

Separate unadjusted and multivariable logistic regression models estimated odds ratios for initial treatment type (mastectomy vs. BCS; among those treated with BCS: RT vs. no RT,

and reoperation within 6 months following initial BCS vs. no reoperation), in relation to receipt of MRI. Model results are reported as crude and adjusted odds ratios (OR) with 95% confidence intervals (95% CI). Models were adjusted for patient, tumor, and hospital characteristics. Comorbidities were defined using the Klabunde adaptation of the Charlson Index (18). We calculated the median and interquartile range of the number of days to reoperation by type of reoperation surgery (mastectomy or BCS) to compare MRI groups. For all analyses, we used SAS 9.4 SAS (SAS Institute Inc. 2015. SAS® 9.4 System Options: Reference, Fourth Edition. Cary, NC: SAS Institute Inc.).

Results

Among the 55,997 women in the SEER Medicare database with stage 0–III breast cancer diagnosed from 2005 to 2009, preoperative MRI was performed on 9,055 women (16.2%). For initial locoregional treatment, 20,793 women (37.1%) received a mastectomy and 35,204 (62.9%) received BCS. Of the women receiving initial BCS, 61.2% (N = 21,545) had BCS with RT and 38.8% (N = 13,659) had BCS without RT. Table 1 and Table 2 show the distribution of patient, tumor and hospital characteristics for the sample overall, by initial treatment type, and by reoperation following initial BCS. Additional patient and tumor characteristics are provided in Supplemental Table 2.

Preoperative MRI increased from 7% in 2005 to 24% in 2009 ($p<0.0001$). Calendar year trends in initial locoregional treatment types for women with and without MRI are displayed in Figure 1a (mastectomy vs BCS) and Figure 1b (among women with initial BCS: RT v no RT and reoperation). The proportions of women receiving mastectomy compared to BCS ranged from 39% in 2005 to 38% in 2009 in the no MRI group and from 38% in 2005 to 32% in 2009 for the MRI group (Figure 1a). Of women who had initial BCS, the proportions with RT compared to no RT were higher in the MRI group. There were no differences in reoperation following initial BCS between the MRI groups and no MRI groups over the study period (Figure 1b).

Preoperative MRI and surgical treatment type of mastectomy vs. BCS showed lower odds of receiving a mastectomy among women receiving MRI (OR 0.84 (95% CI (0.80–0.88)). However, in the adjusted model, we found no association (OR 1.04 (95% CI (0.98–1.11)) (Table 3). Mastectomy was most strongly associated with older age, rural residence, lower income, Medicaid enrollment, comorbidities, high grade, stage II or III, nodal and ER status, large tumors, invasive lobular histology (compared to invasive ductal), non-teaching hospitals, and cancer or other hospitals (compared to general hospital), as shown in Figure 2.

For women treated with initial BCS (N=35,204), women who received preoperative MRI were significantly more likely to receive RT than those who did not receive MRI (OR 1.45 95% CI (1.37–1.54)). This association remained after adjustment (OR 1.09 95% CI (1.02–1.16); Table 3). Young age, urban residence, high income, few comorbidities, small tumors, and surgery occurring in a general or cancer hospital (compared to ‘other’ hospital types) were factors associated with BCS with RT (Figure 2). Additionally, a reoperation was performed in 7,268 women (20.6%) among those whose initial treatment was BCS. The unadjusted and adjusted models found no association between MRI and odds of reoperation

(Table 3). Factors associated with a reoperation included young age, DCIS and invasive lobular (compared to invasive ductal), large tumors and non-cancer and other hospitals (Figure 2). A median of 28 days (IQR 19–42 days) for a reoperation of a mastectomy for women undergoing preoperative MRI vs. 28 days (IQR 15–44 days) without MRI was calculated. Similarly, time to reoperation of a BCS was 14 days (IQR 9–25 days) for women with preoperative MRI vs. 16 days (IQR 9–28 days) without MRI.

Discussion

In Medicare-enrolled women with stage 0–III breast cancer diagnosed from 2005 to 2009, preoperative MRI increased in frequency. However, the increase was not associated with an increase in mastectomy rates over the time. Of note, we found significantly higher rates of post-BCS RT among women who had preoperative MRI. This is the first study of preoperative breast MRI in older women in the U.S. to identify no associated increase in mastectomies and the first to evaluate frequencies of RT after BCS related to MRI use. These patterns do not necessarily imply causality, but are important findings, as we better understand treatment patterns around preoperative MRI.

There have been several recently published studies evaluating trends in preoperative MRI use and associations between preoperative MRI and surgical treatment of breast cancer. Most recently, Arnaout et al. (6) published a Canadian population-based study of women with stage 1–III breast cancers from 2003 to 2012, and reported increasing MRI use and greater frequency of mastectomy with MRI (OR, 1.73; 95% CI, 1.62–1.85). Their study included women at younger ages and within a closed health system, which may explain their mastectomy results. Killelea, et al. used SEER-Medicare data from 2000 to 2009, and reported a significant increase in preoperative breast MRI use and a greater rate of bilateral mastectomies in the preoperative MRI group.(3) However, they looked at women with stage I–III breast cancers. In this group of women, they reported that in their adjusted model, MRI was associated with a significantly higher rate of mastectomy in women with MRI (compared to BCS (adjusted OR =1.21 (95% CI (1.14–1.28)), but did not look at association between MRI and receipt of RT in women with BCS.

We found no difference in the frequencies of reoperation in women undergoing initial BCS who had MRI compared to those who did not have MRI. We found that factors associated with a reoperation included young age, DCIS and invasive lobular and large tumors. Prior observational studies and randomized controlled trials (RCTs) have evaluated the association between preoperative MRI use and reoperation rates among women who received BCS as their initial surgery. Using Medicare data from 2002–2007, Wang, et al. (19) evaluated the associations between preoperative breast MRI and multiple breast surgeries for 45,453 women aged 66 and older with stage 0–II cancer. 20.8% of these patients received multiple breast surgeries. While the researchers uncovered substantial variation in the rates of multiple surgeries in these women and large variation between individual surgeons, they found no significant differences in the rate of multiple surgeries between the two groups with or without preoperative breast MRI, suggesting preoperative breast MRI does not reduce the risk of receiving multiple surgeries.

Grouping women by histologic type, Fortune-Greeley, A.K., et al. examined whether there were differential benefits from preoperative breast MRI according to histology. (20) They examined the surgical outcomes—initial mastectomy, reoperation, and final mastectomy rates—among 20,333 women diagnosed with early-stage breast cancer from 2004–2007 in SEER-Medicare, 12.2% of whom had a preoperative breast MRI. They classified women as having invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), mixed ductal/lobular carcinoma (IDLC) or other histologic type. Their study provided evidence in support of the targeted use of preoperative breast MRI among patients with ILC to improve surgical planning; however, it did not find breast MRI to be significantly associated with a likelihood of a reoperation overall or among patients with IDC and IDLC, but was associated with greater odds of a final mastectomy.

Our study adds to the above studies in a number of ways. In contrast to prior studies, we found no increase in initial mastectomy frequency with preoperative breast MRI. There are several reasons why our results may differ from those of other investigations. We included a wider range of breast cancer stages at diagnosis, from 0–III, and examined these trends in older women only, with data from 2005 through 2009. Most previous studies have not included stage 0 cancers, and included older data starting prior to 2005. We also explored whether women with initial BCS received RT and report a positive association between MRI and RT. This is an important consideration when trying to understand the downstream effects of preoperative MRI. RT is generally considered the standard-of-care following BCS because it decreases local recurrence rates for both DCIS and invasive cancer. However, the NCCN guidelines state that it may be omitted in patients >= 70 years of age with T1, node negative and ER positive breast cancer who receive adjuvant endocrine therapy. Our results showing an increase of use of RT could be a marker of more appropriate care in women who are choosing BCS. However, it is also possible that patients and providers electing MRI prefer a more intensive treatment strategy. For example, physicians who routinely use preoperative MRI may be more likely to recommend RT following BCS. Alternatively, it is possible that women who receive MRI are motivated to seek more treatment for their breast cancer. This raises the question of whether MRI is changing the ultimate surgical procedure or if MRI is an indicator of more intensive interventions in general.

Limitations

Although we were able to account for a number of potential confounders, we were unable to control for all characteristics that may be associated with breast MRI and our outcomes, such as physician specific factors or patient preferences. We had no information on planned treatment course before or after preoperative MRI, so are unable to evaluate the influence of the MRI on ultimate treatment received, but are aware of no population-based data that can do this. Additionally, selection bias may exist for MRI and intensive treatment that is not related to what is observed on MRI, such as our finding that MRI is associated with RT women undergoing BCS. The SEER-Medicare dataset contains a large amount of data at the population level, which allows us to uncover national trends in the relationship of MRI and BCS, but it has several limitations. Notably, it does not include several clinical variables that may have informed the indications for ordering preoperative MRIs, such as breast density, multicentric disease, family history, BRCA mutations, or women’s preferences. These

variables will be important to include in future analyses. Our population of women was 66 years or older at the time of their diagnosis and our findings may not be generalizable to younger women, who are more likely to receive preoperative breast MRI. (19) In spite of these limitations, we believe that the study's considerable strengths outweigh the weaknesses.

Implications

To inform decision making regarding preoperative MRI use for breast cancer treatment, the potential impact on locoregional surgical and radiation therapy approaches need to be understood. MRI is supported by some as a useful tool in preoperative assessment, particularly in subsets of women such as those with denser breasts or those with invasive lobular carcinoma. (10) (11) (21) However, evidence to support its broad use is lacking. If MRI is finding additional disease, and if modifying treatment patterns accordingly will improve patient outcomes, then neglecting to use MRI is a missed opportunity. However, using MRI in lower-risk women is likely to increase the number of biopsies and may increase overtreatment. One major concern is whether using MRI is leading to unnecessary mastectomies. Our results mitigate concerns about unnecessary MRI-associated mastectomies in the older population, and may indicate MRI has an impact on decisions regarding RT. Our findings also suggest that preoperative MRI may be used differently for different age groups.

Conclusion

Preoperative MRI use continues to increase in older women diagnosed with breast cancer, with almost a quarter of women receiving MRI in recent years. Medicare-enrolled women receiving preoperative MRI are most likely to receive BCS with RT as the rate of mastectomy has decreased in recent years. Given the increasing trend in utilization of preoperative MRI, further analyses are imperative to determine the impact on long-term patient outcomes such as recurrence and survival.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the SEER Program tumor registries in the creation of the SEER-Medicare database.

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Summary

Preoperative breast MRI in Medicare-enrolled women with stage 0–III breast cancer was not associated with increased mastectomy. However, we found among older women with MRI undergoing BCS there was a greater use of RT. The results mitigate concerns about unnecessary MRI-associated mastectomies in this population, and raise the question of whether MRI is changing the initial locoregional surgical or radiation treatment or if MRI is an indicator of more intensive interventions in general.

Figure 1a

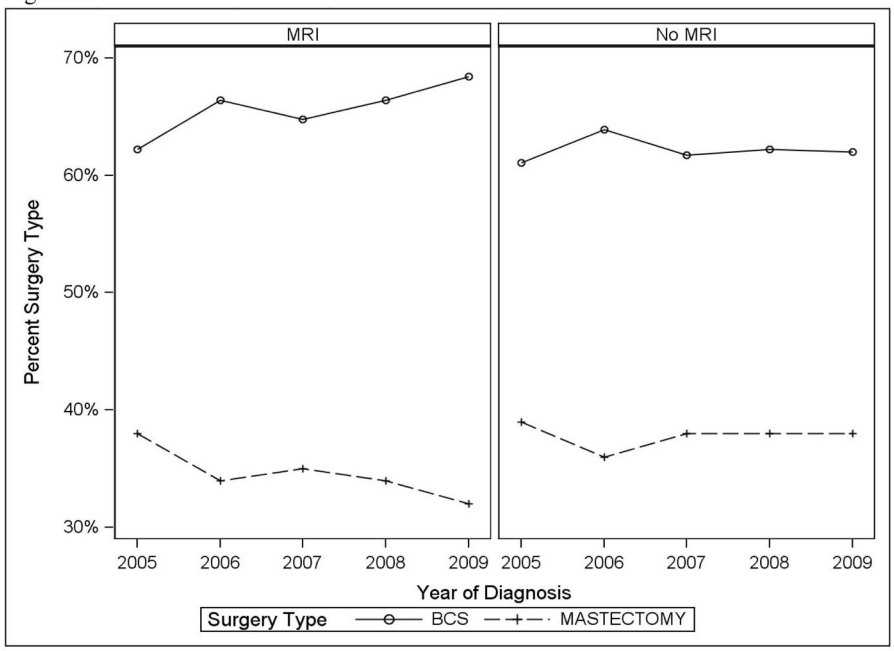

Figure 1b

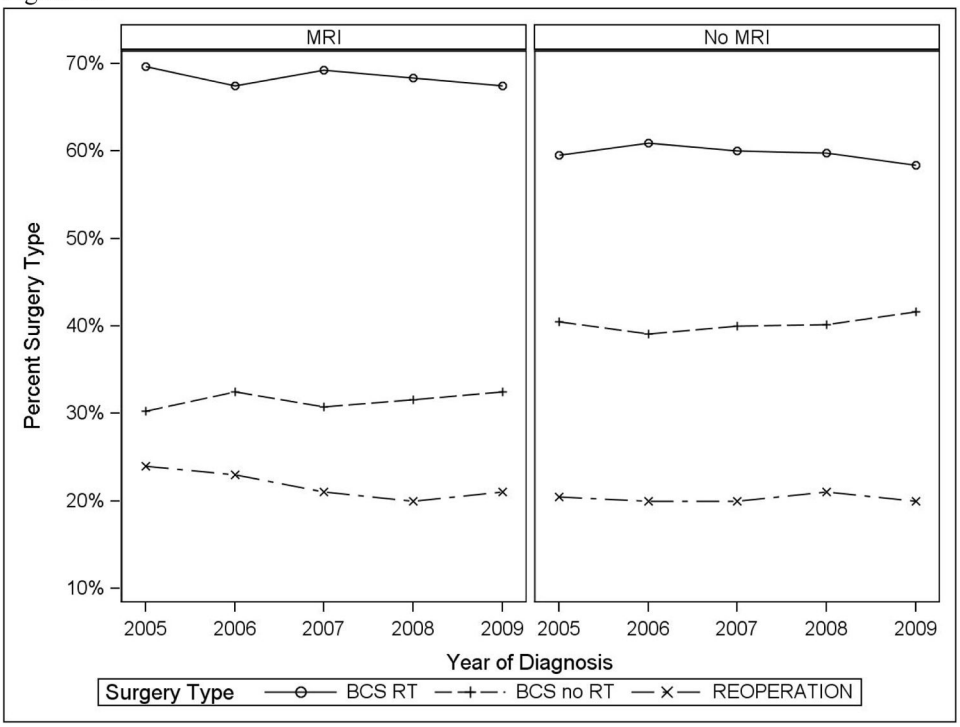

Figure 1.

Figure 1a Percent of surgery type (mastectomy v BCS) by diagnostic year among SEER Medicare women (N=55,997) diagnosed with non-metastatic breast cancer (2005–2009) with (N=9,055) and without (N=46,942) MRI

Abbreviations: MRI = Magnetic Resonance Imaging; BCS= Breast Conserving Surgery.

Figure 1b Among women with an initial BCS, percent of surgery type (RT vs. no RT) and reoperation by diagnostic year among SEER Medicare women (N=55,997) diagnosed with non-metastatic breast cancer (2005–2009) with (N=9,055) and without (N=46,942) MRI
Abbreviations: MRI = Magnetic Resonance Imaging; BCS= Breast Conserving Surgery; RT = Radiation Therapy.

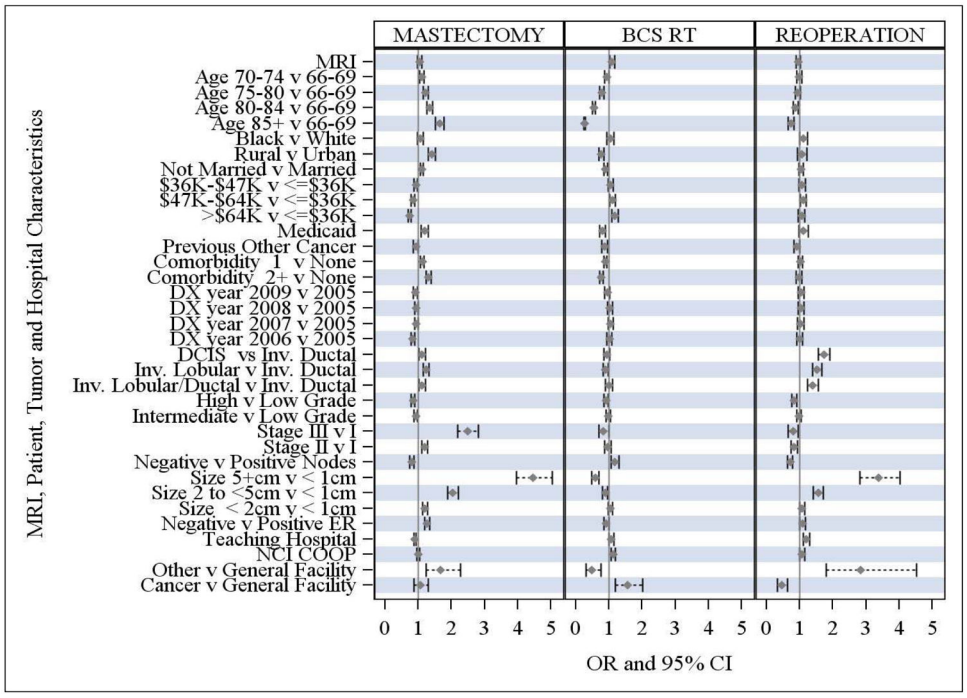

Figure 2.

Odds ratios (OR) and 95% confidence intervals (95% CI) for the initial surgery type (Mastectomy vs. BCS; BCS RT vs. BCS no RT) and reoperation after initial BCS vs. no reoperation by MRI use, patient, tumor and hospital characteristics among SEER Medicare women (N=55,997) diagnosed with non-metastatic breast cancer (2005–2009)

Abbreviations: MRI = Magnetic Resonance Imaging; BCS= Breast Conserving Surgery; RT = Radiation Therapy; DX=Diagnosis; Inv =Invasive; NCI COOP = National Cancer Institute Cooperative Oncology Group Member.

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Table 1

Distribution of patient and tumor characteristics overall, by initial surgery type, and reoperation (following an initial BCS) among SEER Medicare women (N=55,997) diagnosed with non-metastatic breast cancer (2005–2009)

			Initial Locoregional Treatment[1]			
	Total N= 55,997 (100.0%)		Mastectomy N=20,793 (37.1%)	BCS RT N=21,545 (38.5%)	BCS no RT N=13,659 (24.4%)	Reoperation[2] post BCS N=7,268/35,204 (20.6%)
Characteristics	**N**	**Col %**	**Col %**	**Col %**	**Col %**	**Col %**
No MRI	46,942	83.8	85.3	81.0	86.1	82.4
MRI	9,055	16.2	14.7	19.0	13.9	17.6
Patient						
Age						
66–69	11,474	20.5	18.4	24.8	16.7	23.4
70–74	14,277	25.5	23.8	29.6	21.6	27.9
75–79	13,154	23.5	23.8	24.3	21.9	23.7
80–84	10,122	18.1	19.4	15.3	20.4	16.3
85+	6,970	12.5	14.6	6.0	19.4	8.6
Tumor						
Histology						
DCIS	9,070	16.2	11.5	15.8	24.1	22.0
Invasive Ductal	34,545	61.7	63.0	64.4	55.3	55.1
Invasive Lobular	5,155	9.2	11.5	7.8	8.1	10.0
Invasive Ductal and Lobular	3,256	5.8	6.2	5.8	5.2	7.0
Other	3,971	7.1	7.8	6.2	7.4	6.0
Grade						
High	12,499	22.3	18.3	25.2	23.9	20.5
Intermediate	23,576	42.1	40.9	43.9	41.2	43.4
Low	16,032	28.6	33.7	25.7	25.5	29.1
Unknown	3,890	7.0	7.1	5.2	9.4	7.0
AJCC Stage[3]						
0	9,070	16.2	11.5	15.8	24.1	22.0
I	26,381	47.1	35.6	57.9	47.6	46.5

	Total N= 55,997 (100.0%)		Initial Locoregional Treatment[1]			Reoperation[2] post BCS N=7,268/35,204 (20.6%)
			Mastectomy N=20,793 (37.1%)	BCS RT N=21,545 (38.5%)	BCS no RT N=13,659 (24.4%)	
Characteristics	**N**	**Col %**	**Col %**	**Col %**	**Col %**	**Col %**
II	15,823	28.3	36.2	23.1	24.3	26.5
III	4,723	8.4	16.7	3.2	4.0	5.0
Size						
<1cm	12,830	22.9	14.5	29.0	26.2	23.5
1 to <2 cm	19,899	35.5	29.5	41.5	35.4	35.7
2 to <5cm	16,491	29.5	39.3	22.3	25.8	28.0
5+ cm	3,071	5.5	11.0	1.6	3.2	4.6
Unknown	3,706	6.6	5.8	5.7	9.4	8.3

Abbreviations: MRI = Magnetic Resonance Imaging; BCS= Breast Conserving Surgery; RT = Radiation Therapy; DCIS = Ductal Carcinoma In Situ.

[1]Initial locoregional treatment is defined as mastectomy, breast conserving surgery without radiation therapy and breast conserving surgery with radiation therapy.

[2]Reoperation is a subset of the women whose initial locoregional treatment was breast conserving surgery.

[3]Derived AJCC Stage Group, 6th ed. (2004+); http://seer.cancer.gov/seerstat/variables/seer/ajcc-stage/, accessed February 2016.

Table 2

Distribution of hospital characteristics overall, by initial surgery type, and reoperation (following an initial BCS) among SEER Medicare women (N=55,997) diagnosed with non-metastatic breast cancer (2005–2009)

	Total N= 55,997 (100.0%)		Initial Locoregional Treatment[1]			Reoperation[2] post BCS N=7,268/35,204 (20.6%)
			Mastectomy N=20,793 (37.1%)	BCS RT N=21,545 (38.5%)	BCS no RT N=13,659 (24.4%)	
Characteristics	**N**	**Col %**	**Col %**	**Col %**	**Col %**	**Col %**
Hospital						
Teaching[3]						
No	21,162	37.8	49.4	30.0	32.4	27.7
Yes	22,288	39.8	45.4	37.8	34.4	40.2
Unknown	12,547	22.4	5.2	32.2	33.3	32.1
NCI Cooperative Oncology Group[4]						
No	20,211	36.1	47.2	28.0	32.0	27.8
Yes	23,475	41.9	48.3	40.1	35.0	40.3
Unknown	12,311	22.0	4.5	31.9	33.0	31.9
Hospital Type[5]						
General	42,706	76.3	93.2	66.6	65.7	66.8
Cancer	526	0.9	1.0	1.1	0.7	0.6
Other	218	0.4	0.7	0.2	0.4	0.4
Unknown	12,547	22.4	5.2	32.2	33.3	32.2

Abbreviations: MRI = Magnetic Resonance Imaging; BCS= Breast Conserving Surgery; RT = Radiation Therapy; DCIS = Ductal Carcinoma In Situ.

[1] Initial locoregional treatment is defined as mastectomy, breast conserving surgery without radiation therapy and breast conserving surgery with radiation therapy.

[2] Reoperation is a subset of the women whose initial locoregional treatment was breast conserving surgery.

[3] Teaching hospital is based on the hospital where the breast surgery was performed.

[4] Membership in an NCI Cooperative group trial indicates if the hospital where the surgery was performed participated in at least one NCI trial.

[5] Hospital type defined as type of facility; http://healthcaredelivery.cancer.gov/seermedicare/privacy/Hospital.filedescription.pdf, accessed February 2016.

Table 3

Unadjusted and adjusted[1] odds ratio (OR) and 95% confidence intervals (95% CI) for association between MRI and initial surgery type and reoperation after initial BCS among SEER Medicare women (N=55,997) diagnosed with non-metastatic breast cancer (2005–2009)

	Mastectomy vs. BCS			BCS RT vs. BCS w/o RT			Reoperation vs. No Reoperation		
MRI	**OR**	**95% CI**		**OR**	**95% CI**		**OR**	**95% CI**	
Unadjusted	0.84	0.80	0.88	1.45	1.37	1.54	1.05	0.98	1.12
Adjusted	1.04	0.98	1.11	1.09	1.02	1.16	0.95	0.88	1.02

Abbreviations: MRI = Magnetic Resonance Imaging; BCS= Breast Conserving Surgery; RT = Radiation Therapy.

[1]Adjusted for age at diagnosis, race, SEER registry, marital status, median income, urban/rural status, Medicaid, previous other cancer, comorbidity index, year of diagnosis, histology, grade, stage, ER and nodal status, tumor size, teaching hospital, NCI cooperative oncology group member and hospital type.