Determinants of surgeon referral and radiation therapy receipt following breast conservation among older women with early-stage breast cancer

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Abstract

Purpose

Guidelines for early-stage breast cancer allow for radiotherapy (RT) omission following breast conserving surgery (BCS) among older women, though high utilization of RT persists. This study explores surgeon referral and the effect of a productivity-based bonus metric for radiation oncologists in an academic institution with centralized quality assurance (QA) review.

Methods

We evaluated patients ≥ 70 years of age treated with BCS for ER+ pT1N0 breast cancer at a single institution between 2015–2018. The primary outcomes were radiation oncology referral and RT receipt. Covariables included patient and physician characteristics, and treatment decisions before versus after productivity metric implementation. Univariable generalized linear effects models explored associations between these outcomes and covariables.

Results

Of 703 patients included, 483 (69%) were referred to radiation oncology and 273 (39%) received RT (among those referred, 57% received RT). No difference in RT receipt pre- versus post- productivity metric implementation was observed (p = 0.57). RT receipt was associated with younger patient age (70–74 years, OR 2.66, 95% CI 1.54–4.57) and higher grade (grade 3, OR 7.75, 95% CI 3.33–18.07). Initial referral was associated with younger age (70–74, OR 5.64, 95% CI 3.37–10.83) and higher performance status (KPS ≥ 90, OR 5.34, 95% CI 2.63–10.83).

Conclusion

Non-referral to radiation oncology accounted for half of RT omission, but was based on age and KPS, in accordance with guidelines. Lack of radiation oncologist practice change in response to misaligned financial incentives is reassuring, potentially reflecting centralized QA review. Multi-institutional studies are needed to confirm these findings.

Introduction

While adjuvant radiation is a standard component of breast-conservation [1], multiple randomized clinical trials show that radiation does not improve overall survival, distant metastasis, or rates of subsequent mastectomy among elderly patients with early-stage invasive ER-positive breast cancer [2-4]. As a result, in 2004 the National Comprehensive Cancer Network (NCCN) Guidelines incorporated omission of adjuvant RT as a category I option for older women meeting eligibility criteria for CALGB 9343 [5]. But
Despite availability of randomized evidence and practice guidelines, management of early-stage invasive breast cancer has remained largely unchanged in the United States. Adjuvant RT use was reduced by only 4% (79% to 75%) between 2001 and 2007 [6], though more recent population-based estimates suggest approximately 60% of patients in this low-risk population receive radiation [7].

Evidence suggests high variability between centers, with the proportion of patients receiving RT ranging from 49% to 93% among NCCN member institutions in 2009 [8]. Since variability can reflect underlying inefficiency and bias, it is important to understand factors potentially driving both physician and patient decision-making. For example, up to 40% of surgeons and 20% of radiation oncologists in a nationally-representative sample incorrectly cite a survival benefit for RT in this cohort [9]; this is important because patients report that trust in their physician’s recommendation is one of the most important factors guiding their decision [10]. While data on overall receipt of radiation is known, evidence regarding the role of surgeon referral versus radiation oncologist recommendation are less understood due to limitations of population-based datasets.

Once patients see a radiation oncologist, financial misalignment in a fee-for-service healthcare system could contribute to overtreatment [11]. Evidence supports financial incentives leading to practice change in oncology, most commonly de-prescribing in response to decreased reimbursement for systemic therapy [12]. Additionally, more frequent unnecessary procedures, specifically cystoscopy for bladder cancer, occur in response to increased reimbursement [13]. Little is known about the potential influence of institutional productivity-based bonus metrics, including on the use of unnecessary procedures in radiation oncology, despite this being the predominant practice payment model [14].

The current study was conducted in a large tertiary care center with a lower than average proportion of patients undergoing radiation (54% as of 2012 [15]) to better understand referral patterns and treatment decision-making. Specifically, we hypothesized that the enactment of a productivity-based bonus metric for radiation oncologists could have the negative consequence of increasing the proportion of patients receiving RT (among those referred). We also investigate physician, patient, and tumor-related determinants of RT receipt, as well as factors that are associated with initial referral to radiation oncology.

Methods

Dataset and Primary Analysis

This retrospective analysis includes all patients ≥70 years of age who underwent breast conserving surgery for ER+ pT1N0 breast cancer between 2015 and 2018 at XXX. Electronic medical records were reviewed for RT receipt (including RT at outside institutions), the primary endpoint. To confirm accuracy in assignment of RT receipt, a second abstractor performed a 10% random sample chart audit [16]. Patients undergoing BCS at outside institutions were not included. Throughout the study period, the Department of Radiation Oncology conducted weekly centralized quality assurance processes (i.e. peer review or “chart rounds”), in which radiation treatment plans for all patients undergoing breast radiation were reviewed by
at least two radiation oncologists specializing in breast cancer. Institutional Board Review approval was obtained for this study.

**Covariates**

Explanatory variables were collected and incorporated into adjusted models. A productivity-based bonus metric was instated for radiation oncologists in January 2017 based on the number of treatment “new starts” (with each patient treatment counting equally, rather than based on relative value units). Previously, a salary-based model without clinical productivity measures was used. Referred patients were grouped into ‘pre-metric’ and ‘post-metric’ cohorts to evaluate its effect on practice patterns.

Electronic medical records were reviewed for biologic variables (tumor size, tumor grade, presence of lymphovascular invasion, HER2 status, laterality, focality), patient clinical characteristics (Karnofsky Performance Status score, smoking status, age), patient-reported sociodemographic characteristics (race/ethnicity, highest level of education, preferred language; pulled from intake surveys), treating physicians (surgeons, radiation oncologists), and radiation clinical practice site. Physician years of experience was estimated from publicly available medical school graduation year. Level of specialization was based on the number of patients treated per physician within this dataset and dichotomized (<10 versus 10 or more consults).

Socioeconomic status (SES) was calculated using the University of Wisconsin's Neighborhood Atlas, as previously reported [17,18]. We determined the national percentile for each patient according to their home address and associated ADI ranking, with 1 indicating the least disadvantaged and 100 indicating the most disadvantaged neighborhood. Distances from patients’ homes to the nearest clinic site were calculated using Google Maps [19,20] by selecting the shortest recommended route. Distances were analyzed on a continuous scale and in 5-mile increments, based on prior research [21].

**Statistical Analyses**

Descriptive statistics were calculated for all variables. Univariable (UVA) generalized linear mixed effects models were used to explore associations between the binary outcome, RT receipt, and explanatory variables of interest among patients referred to radiation oncology. This same approach was used to evaluate associations between initial referral and explanatory variables among all patients. A logit link function was specified for each UVA model, and each included a random intercept and a random slope to account for random variation due to physician. For each surgeon, we reported radiation referral frequency and the median odds ratio (MOR) computed from an intercept-only model with no other fixed effects or random slopes (i.e. only a fixed intercept and random intercept) to quantify the variation between surgeons. Variation in treatment rates among radiation oncologists was demonstrated via a simplified approach, by calculating the median and interquartile range (IQR) of RT rate among those who treated 10 or more patients during the study period. False discovery rate (FDR) adjustments were used to account for multiple comparisons. Results were adjusted within outcomes (RT receipt or radiation oncology referral); for example, RT receipt results were adjusted based on the number of associations with RT
receipt that were tested. P-values were deemed significant if they were less than the FDR-adjusted significance threshold. All statistical computations were performed and all output was generated using SAS Software Version 9.4 (The SAS Institute, Cary, NC).

Results

Patient Characteristics

Among 703 patients who met inclusion criteria, 39% (n=273) received RT. The overall median age was 74, and most were non-Hispanic white with a median national SES percentile of 10. Median tumor size was 1.0 cm and most patients presented with grade 2 (56%), HER2 negative disease (96%) without lymphovascular invasion (84%). Patient characteristics pre- and post-metric implementation were comparable, as outlined in Table 1.

Covariates Associated with Radiation Receipt

Among 483 patients referred to radiation oncology, 57% (n=273) received RT. The median unadjusted proportion of patients receiving RT from radiation oncologists treating at least 10 patients in the study period (n=14 of 28 total radiation oncologists) was 67% (IQR 54-73), as seen in Figure 1. No significant difference was observed in the proportion of patients receiving RT pre- versus post-metric implementation (OR 1.16, 95% CI 0.68-1.98, p=0.57). Differences in unadjusted proportion of patients treated over time are shown in Figure 2. The only variables significantly associated with RT receipt after adjusting for multiple comparisons were younger patient age (70-74 years, OR 2.66, 95% CI 1.54-4.57, p=0.001) and higher tumor grade (grade 3, OR 7.75, 95% CI 3.33-18.07; grade 2, OR 1.83, 95% CI 1.11-3.02; p<0.001) (Table 2).

Of the 255 patients with RT plans available, 20% (n=52) received partial breast irradiation (PBI), which is delivered in 40Gy in 10 fractions, per our institutional standard [22]. The remaining patients received hypofractionated whole breast radiation over 3-4 weeks. The use of PBI did not change with implementation of the productivity metric (p=0.943).

Covariates Associated with Referral to Radiation Oncology

The median proportion of patients referred to radiation oncology among surgeons treating at least 10 patients during the study period (n=16 out of 17 total breast surgeons) was 77% (IQR 53-82), as seen in Figure 1. The MOR that quantifies variation in referral between all surgeons was 2.31. A univariable generalized mixed effects regression model revealed that younger patient age (70-74 years, OR 5.64, 95% CI 3.37-0.45, p<0.001) and higher performance status (KPS ≥90, OR 5.34, 95% CI 2.63-10.83, p<0.001) were significantly associated with surgeon referral to radiation oncology after adjusting for multiple comparisons (Table 2). No other post-FDR significant associations were observed between surgeon referral to radiation oncology and the remaining characteristics.

Discussion
In a large academic center with a relatively low rate of adjuvant radiation among elderly patients with early-stage ER+ breast cancer, we did not observe increased use of radiation in response to a productivity-based financial incentive for radiation oncologists. Approximately half of radiation omission was due to non-referral by surgeons, though this appears appropriate as patient age and KPS was associated with referral. Limited variation between radiation oncologists and lack of additional variables associated with treatment suggests the likely influence of patient preference.

The absence of physician practice change in response to a new financial incentive departs from much, but not all, of the prior literature in oncology [23,24,12,25]. It is therefore important to understand the context in which this finding may apply. Once the decision to treat a patient with radiation for breast cancer has been made, use of intensity-modulated radiation (a complex modality with historically higher reimbursement) has increased despite lack of evidence of benefit [26]. In the current study, we tested whether financial misalignment could instigate overtreatment, and found that it did not. In the single institution setting, there is greater potential for the influence of local culture to supersede a financial incentive. We hypothesize that existence of centralized quality assurance of radiation plans helps prevent inappropriate treatment. Although the practice of QA peer review is common in radiation oncology, there is limited data on its efficacy, particularly in the setting of a multi-site network with a centralized process led by subspecialists [27,28]. Understanding the consequences of such a capitated productivity-based bonus model as well as strategies to maintain treatment quality is relevant with the imminent planned implementation of bundled payments through the Radiation Oncology Alternative Payment Model (RO-APM) [29]. This model introduces the potential for physicians to lower their threshold to treat patient populations that previously were not routinely receiving treatment, as centers using long-course radiation observe decreased revenues under the new model.

It is notable that approximately half of radiation omission occurred due to non-referral, confirming the critical role of surgeons in the radiation decision-making process. Referral rates were nonetheless considered appropriate given referred patients were younger and healthier (78% with KPS>90), consistent with eligibility criteria for CALGB 9343 and NCCN recommendations [30,31]. This is also consistent with institutional guidelines later formalized in 2019 at the multidisciplinary level to make omission the default for patients 75 years or older.

While no tumor characteristics were significantly associated with surgeon referral, patients with high grade tumors were more likely to receive radiation once seen by radiation oncology. The PRIME II trial did prohibit patients from enrolling if they had both LVI and high grade tumors [32], and evidence supports grade (an important factor differentiating luminal A and luminal B subtypes) as a predictor of recurrence [33]. Although trends existed, neither LVI nor HER2 expression (which was not collected on prospective trials) were significant in this cohort. Future studies are being considered to evaluate recurrence in HER2+ patients. In general, variation by radiation oncologist in which at least 10 patients were treated (and therefore a reliable fraction could be estimated) was fairly small (IQR 54-73%), and patient volume was not significantly associated with a radiation oncologist’s likelihood to recommend RT [34,35].
Several studies have documented variability in RT receipt based on socioeconomic status [32,36,37] and race/ethnicity [30,36,31,38]. In this patient population, more educated patients may be more likely to be referred for a discussion, but there was insufficient evidence that they were more likely to be treated. Longer distance from a patient's home was also not significant, in contrast to prior studies, which may be due to the urban/suburban nature of this population with a median distance from home to clinic of 13 miles.

Limitations of this study include its retrospective single-institution design. The ability to generalize the lack of effect of a capitated financial incentive to other clinical settings may therefore be limited. Additionally, this was conducted in a setting of relatively high omission of radiation; if radiation use is already high, it could still obstruct efforts to de-implement low value care. This study provides insights into potential mitigating factors to overtreatment, and highlights the need for additional work to assess physician- and organizational-level factors that prevent overuse in the setting of such capitated incentives. Lastly, this study lacks data on patient preference. In this highly selected patient population, we may have limited ability to detect disparities in radiation receipt by socioeconomic or geographic factors. Similarly, this study may have been underpowered to detect a difference based on HER2 status and LVI, which were present in relatively low frequencies among the cohort (3% and 12%, respectively).

In conclusion, referral and treatment patterns for older women with early-stage breast cancer at a single academic institution were largely consistent with CALGB 9343 and national guidelines, with the proportion of patients receiving radiation noted to be lower than population level estimates. The lack of effect of productivity-based financial incentives is reassuring, and possibly related to a centralized system for quality assurance. Additionally, the limited number of significantly associated patient or physician variables suggests that other unmeasured 'factors' such as patient preference plays an important role. Larger-scale studies with more diverse patient populations are warranted to further explore and better generalize these results.

Declarations

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**Conflicts of interest/competing interests**: The authors declare that they have no conflict of interest.

**Availability of data and material**: The authors declare that the data supporting the findings of this study are available within the article.

**Code availability**: Not applicable.

**Authors’ contributions**: Mira Patel - conceptualization, data curation, writing. Elaine Cha - data curation, writing. Stephanie Lobaugh - formal analysis, writing. Zhigang Zhang - formal analysis, writing. Beryl McCormick - conceptualization, revision. Lior Braunstein - conceptualization, revision. Oren Cahlon - conceptualization, revision. Simon Powell - conceptualization, revision. Monica Morrow -
conceptualization, revision. Atif Khan - conceptualization, revision. Erin Gillespie - conceptualization, data curation, funding acquisition, writing, revision.

**Ethics approval:** This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of Memorial Sloan Kettering Cancer Center approved this study.

**Consent to participate:** Not applicable.

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Tables
### Table 1. Patient characteristics, grouped by referral status and pre- vs. post-metric status

|                                | All patients n=703 | Referral status among all patients (n=703) | Pre- vs. post-metric status among referred patients (n=483) |
|--------------------------------|--------------------|-------------------------------------------|-------------------------------------------------------------|
|                                | Referral status    | Not referred to RO, n=220 (31.3%)          | Pre-metric, n = 182 (37.7%)                                  |
|                                |                    | Referred to RO, n = 483 (68.7%)           | Post-metric, n = 301 (62.3%)                                 |
|                                | n (%)              | n (%)                                     | n (%)                                                       |
|                                |                    | n (%)                                     | n (%)                                                       |
| **Age**                        | Median (Range)     | 74 (70-92)                                | 73 (70-90)                                                  |
|                                |                    | 77 (70-92)                                | 73 (70-90)                                                  |
|                                |                    | 59 (26.8)                                 | 303 (62.7)                                                  |
|                                |                    | 161 (73.2)                                | 180 (37.3)                                                  |
|                                | ≥ 75               | (51.5)                                    | (37.3)                                                      |
|                                |                    | 362                                        | 72 (39.6)                                                   |
|                                |                    | 341                                        | 108 (35.9)                                                  |
|                                |                    | (48.5)                                    |                                                             |
| **Education**                  |                    | 232 (33)                                  | 187 (38.7)                                                  |
|                                |                    | 45 (20.5)                                 | 78 (42.9)                                                   |
|                                |                    | 129 (58.6)                                | 50 (27.5)                                                   |
|                                | College or higher  | 202 (91.8)                                | 201 (41.6)                                                  |
|                                | Below college      | 177                                        | 131 (27.1)                                                  |
|                                | Missing            | 294                                        | 125 (26.7)                                                  |
|                                |                    | (41.8)                                    |                                                             |
|                                |                    | 177                                        | 131 (27.1)                                                  |
|                                |                    | 294                                        | 125 (26.7)                                                  |
|                                |                    | (41.8)                                    |                                                             |
| **Race**                       |                    | 609                                        | 407 (84.3)                                                  |
|                                |                    | 202 (91.8)                                | 160 (87.9)                                                  |
|                                | Non-white          | 177                                        | 131 (27.1)                                                  |
|                                | Missing            | 294                                        | 125 (26.7)                                                  |
|                                |                    | (41.8)                                    |                                                             |
| **Ethnicity**                  |                    | 618                                        | 420 (87)                                                    |
|                                | Non-hispanic       | 177                                        | 131 (27.1)                                                  |
|                                | Hispanic           | 202 (91.8)                                | 160 (87.9)                                                  |
|                                | Missing            | 294                                        | 125 (26.7)                                                  |
|                                |                    | (41.8)                                    |                                                             |
| **Preferred language**         |                    | 580                                        | 400 (82.8)                                                  |
|                                | English            | 202 (91.8)                                | 151 (83)                                                    |
|                                | Not English        | 177                                        | 131 (27.1)                                                  |
|                                | Missing            | 294                                        | 125 (26.7)                                                  |
|                                |                    | (41.8)                                    |                                                             |
| **Marital status**             |                    | 557                                        | 380 (78.7)                                                  |
|                                | Married            | 177                                        | 131 (27.1)                                                  |
|                                | Single/widowed     | 202 (91.8)                                | 160 (87.9)                                                  |
|                                | Divorced           | 177                                        | 131 (27.1)                                                  |
|                                | Missing            | 294                                        | 125 (26.7)                                                  |
|                                |                    | (41.8)                                    |                                                             |
| **Smoking status**             |                    | 319                                        | 214 (44.3)                                                  |
|                                | Yes/prior          | 105 (47.7)                                | 79 (43.4)                                                   |
|                                | No                 | 180 (81.8)                                | 151 (83)                                                    |
|                                | Missing            | 269                                        | 8 (4.4)                                                     |
|                                |                    | (59.8)                                    |                                                             |
| **Practice setting**           |                    | 12 (1.7)                                  | 8 (4.4)                                                     |
|                                | Main campus        | —                                          | 8 (4.4)                                                     |
|                                | Regional site      | —                                          | 8 (4.4)                                                     |
|                                | Missing            | —                                          | 8 (4.4)                                                     |
| **Tumor grade**                |                    | 377 (11)                                  | 375 (77.6)                                                  |
|                                | 3                  | 77 (11)                                   | 375 (77.6)                                                  |
|                                | 2                  | 112 (50.9)                                | 280 (58)                                                   |
|                                | 1                  | 71 (32.3)                                 | 102 (21.1)                                                  |
|                                | Missing            | 173                                        | 43 (23.6)                                                   |
|                                |                    | (55.8)                                    |                                                             |
|                                |                    | 21 (9.5)                                  | 40 (8.3)                                                    |
|                                |                    | (24.6)                                    |                                                             |
|                                |                    | 61 (8.7)                                  |                                                             |
| **KPS score**                  |                    | 427                                        | 375 (77.6)                                                  |
|                                | ≥ 90               | 52 (23.6)                                 | 141 (77.5)                                                  |
|                                | Missing            | 144 (65.5)                                | 375 (77.6)                                                  |
|                                |                    | 196                                        | 141 (77.5)                                                  |
|                                | < 90               | 24 (10.9)                                 | 20 (11)                                                     |
|                                | Missing            | 56 (11.6)                                 | 20 (11)                                                     |
|                                |                    | 36 (12)                                   |                                                             |
|                                |                    | 21 (11.5)                                 | 20 (11)                                                     |
|                                |                    | 31 (10.3)                                 |                                                             |
|                | Positive/suspicious | Negative | Missing | Positive/suspicious | Negative | Missing | Positive/suspicious | Negative | Missing | Positive/suspicious | Negative | Missing | Positive/suspicious | Negative | Missing |
|----------------|---------------------|----------|---------|---------------------|----------|---------|---------------------|----------|---------|---------------------|----------|---------|---------------------|----------|---------|
| LVI            | 86 (12.2)           | 22 (10)  | 64 (13.3)| 28 (15.4)           |          |         | 36 (12)            |          |         |
|                | 590                 | 187 (85) | 403 (83.4)| 147 (80.8)           |          |         | 256 (85)           |          |         |
|                | (83.9)              | 11 (5)   | 16 (3.3) | 7 (3.8)              |          |         | 9 (3)              |          |         |
| HER2 status    | 24 (3.4)            | 3 (1.4)  | 21 (4.3) | 8 (4.4)              |          |         | 13 (4.3)           |          |         |
|                | 677                 | 216 (98.2)| 461 (95.4)| 174 (95.6)           |          |         | 287 (95.3)         |          |         |
|                | (96.3)              | 1 (0.5)  | 1 (0.2)  | 0 (0)                |          |         | 1 (0.3)            |          |         |
| Multifocal     | Yes                 | 81 (11.5)| 18 (8.2) | 63 (13)              | 22 (12.1)|         | 41 (13.6)          |          |         |
|                | No                  | 622      | 202 (91.8)| 420 (87)             | 160 (87.9)|         | 260 (86.4)         |          |         |
| Tumor laterality| Left               | 362      | 112 (50.9)| 250 (51.8)           | 100 (54.9)|         | 150 (49.8)         |          |         |
|                | Right               | 341      | 108 (49.1)| 233 (48.2)           | 82 (45.1)|         | 151 (50.2)         |          |         |
| Tumor size, cm | Median (Range)      | 1.0 (0.1-2.0) | 0.9 (0.1-1.9)| 1.0 (0.1-2.0)       | 1.0 (0.1-2.0)| 1.1 (0.1-2.0) |
| Radiation receipt | Received       | —        | —        | 273 (56.5)           | 101 (55.5)|         | 172 (57.1)         |          |         |
|                | Did not receive    | —        | —        | 210 (43.5)           | 81 (44.5)|         | 129 (42.9)         |          |         |
| Radiation dose, cGy | Median (Range) | —        | —        | 4000 (0-6000)        | 4000 (0-6000)| 4000 (0-5740)|
|                | Missing             | —        | —        | 18 (3.7)             | 11 (6.0) |         | 7 (2.3)            |          |         |
| Distance to nearest clinic, mi | Median (Range) | 13 (1-1993) | 13 (1-1993) | 12 (1-1594)       | 13 (1-1165)| 12 (1-1594)|
|                | 1-5 mi              | 146      | 43 (19.5)| 85 (17.6)            | 30 (16.5)|         | 55 (18.3)          |          |         |
|                | 6-10 mi             | 11-15 mi | 128      | 17 (7.7)             | 56 (11.6)|         | 35 (11.6)          |          |         |
|                | >20 mi              | 162 (23) | 3 (1.4)  | 11 (2.3)             | 6 (3.3)  |         | 5 (1.7)            |          |         |
|                | Missing             | 73 (10.4)| 180      | 14 (2)               |          |         |                    |          |         |
| National percentile | Median (Range) | 10 (1-100) | 10 (1-100) | 8 (1-100)          | 8 (1-100) |         | 11 (1-100)         |          |         |
|                | Missing             | 18 (2.6) | 1 (0.5)  | 17 (3.5)             | 9 (4.9)  |         | 8 (2.7)            |          |         |

Abbreviations: RO, radiation oncology; KPS, Karnofsky performance status; LVI, lymphovascular invasion
| Variable                  | Referral to radiation oncology among all patients | Radiation receipt among referred patients |
|--------------------------|-----------------------------------------------|------------------------------------------|
|                          | n (no. of events) OR (95% CI) p-value       | n (no. of events) OR (95% CI) p-value    |
|                          | OR (95% CI) p-value                           |
| Tumor characteristics    |                                              |                                          |
| Size, cm                 | 1.43 (0.93-2.20) 0.09                       | 1.56 (0.99-2.44) 0.05                   |
| Grade                    |                                              |                                          |
| 1                        | 1.43 (0.93-2.20) 0.04                       | 1.56 (0.99-2.44) 0.05                   |
| 2                        | 1.86 (0.98-3.52) 0.05                       | 7.75 (3.33-18.07) 0.001*                |
| 3                        | 2.95 (1.22-7.11) 0.05                       |                                          |
| LVI                      |                                              |                                          |
| Negative                 | 1.33 (0.73-2.45) 0.32                       | 1.37 (0.74-2.52) 0.30                   |
| Positive/suspicious      | 1.86 (0.98-3.52) 0.04                       | 3.55 (0.82-15.45) 0.09                  |
| HER2 status              |                                              |                                          |
| Negative                 | 1.83 (1.11-3.02) 0.04                       | 0.88 (0.57-1.37) 0.55                   |
| Positive/suspicious      | 7.75 (3.33-18.07) 0.001*                    | 2.16 (1.06-4.40) 0.03                   |
| Multifocal               |                                              |                                          |
| No                       | 1.67 (0.80-3.47) 0.15                       | 0.88 (0.57-1.37) 0.03                   |
| Yes                      | 1.35 (0.90-2.03) 0.14                       |                                          |
| Laterality               |                                              |                                          |
| Left                     | 0.88 (0.57-1.37) 0.55                       | 1.35 (0.90-2.03) 0.03                   |
| Right                    |                                              |                                          |
| Laterality*              |                                              |                                          |
| Left                     | 0.88 (0.57-1.37) 0.55                       | 1.35 (0.90-2.03) 0.03                   |
| Right                    |                                              |                                          |
| Patient characteristics  |                                              |                                          |
| Age                      | 5.64 (3.37-9.45) 0.001*                     | 2.66 (1.54-4.57) 0.001*                 |
| < 75                     | 362 (303) ref                                | 303 (200) ref                           |
| ≥ 75                     | 341 (180) ref                                | 180 (73) ref                            |
| KPS score                | 5.34 (2.63-10.83) 0.04                      | 0.46 (0.23-0.95) 0.04                   |
| ≥ 90                     | 427 (375) ref                                | 375 (211) ref                           |
| < 90                     | 80 (56) ref                                  | 56 (23) ref                             |
| Race                     | 6.49 (3.07-14.66) 0.08                      | 4.86 (2.15-10.99) 0.08                  |
| White                    | 6.73 (3.54-12.82) 0.08                      | 5.19 (2.55-10.56) 0.08                  |
| Non-white                | 5.23 (2.31-11.79) 0.05                      | 3.83 (1.83-8.02) 0.05                   |
| Ethnicity                | 4.35 (0.82-23.13) 0.08                      |                                            |
| Non-hispanic             | 6.63 (3.04-14.56) 0.08                      | 4.26 (1.91-9.45) 0.08                   |
| Hispanic                 | 3.23 (0.67-15.39) 0.08                      | 3.83 (1.83-8.02) 0.05                   |
| Ethnicity*               | 5.23 (2.31-11.79) 0.05                      | 3.83 (1.83-8.02) 0.05                   |
| Preferred language       | 0.79 (0.33-1.89) 0.05                       | 0.42 (0.20-0.90) 0.03                   |
| English                  | 580 (400) ref                                | 400 (241) ref                           |
| Not English              | 69 (50) ref                                  | 50 (19) ref                             |
| Education                | 0.52 (0.31-0.86) 0.04                       | 0.98 (0.61-1.57) 0.06                   |
| College or higher        | 232 (187) ref                                | 187 (106) ref                           |
| Missing                  | 294 (165) ref                                | 165 (99) ref                            |
| Below college            | 177 (131) ref                                | 131 (68) ref                            |
| National percentile      | 1.00 (0.98-1.01) 0.75                       | 0.99 (0.98-1.00) 0.07                   |
| Distance to nearest clinic | > 20 mi | 1-5 mi | 6-10 mi | 11-15 mi | 16-20 mi |
|---------------------------|---------|--------|---------|----------|---------|
| 689 (472)                | 180 (117) | 146 (110) | 128 (85) | 162 (104) | 73 (56) |
| ref | 2.16 (1.25-3.73) | 1.41 (0.82-2.43) | 1.37 (0.83-2.26) | 2.07 (1.03-4.14) | 0.06 |

Treated pre- or post-metric implementation

| | Pre-metric | Post-metric |
|---|----------|------------|
| 472 (267) | ref | 0.19 |

| | ref |
|---|---|
| 1.6 (0.47-1.58) | 0.19 |
| 1.4 (0.82-2.43) | 1.37 (0.83-2.26) |
| 1.3 (0.82-2.43) | 2.07 (1.03-4.14) |

| | 73 (56) |
|---|---|
| 0.06 |
| 0.16 (0.47-1.58) | 0.19 |
| 0.86 (0.47-1.58) | 0.19 |
| 0.77 (0.41-1.43) | 0.77 (0.41-1.43) |
| 0.95 (0.52-1.72) | 0.95 (0.52-1.72) |
| 0.44 (0.21-0.89) | 0.44 (0.21-0.89) |

**Table 2 Continued.** Univariable generalized linear mixed effects regression results for predictors of referral and radiation receipt

### Physician characteristics

| | Main campus | Regional site |
|---|-------------|---------------|
| Practice setting | — | — |
| — | ref | — |
| — | ref | — |
| — | ref | — |
| — | ref | — |

| | ref |
|---|---|
| 1.75 (0.75-4.05) | 0.15 |
| 1.16 (0.68-1.98) | 0.57 |
| 0.86 (0.47-1.58) | 0.79 |
| 0.92 (0.47-1.80) | 0.79 |

| | 703 (483) |
|---|---|
| 700 (480) | Did not converge |
| 700 (480) | Did not converge |
| 3 (3) | Did not converge |
| 3 (3) | Did not converge |

| | ref |
|---|---|
| 468 (258) | 0.65 |
| 468 (258) | 0.65 |
| 403 (220) | 0.85 (0.41-1.75) |

**Abbreviations:** OR, odds ratio; CI, confidence interval; LVI, lymphovascular invasion; KPS, Karnofsky performance status

* Indicates significant p-value following false discovery rate adjustments

Estimates were obtained using a Residual Pseudo-Likelihood estimation technique with a random effects solutions expansion locus, and denominator degrees of freedom were computed using the containment method. Exceptions are denoted with superscripts as follows:

a Estimation technique: Maximum Likelihood (LAPLACE)
b Denominator degrees of freedom computation method: Kenward and Roger (1997)