

10 Wire Localization vs Radar Reflector Localization: A Comparison

Karisa Beebe,¹ Elissa Dalton,¹ Candice Ford,¹ Lianteng Zhi,¹ Karen Louie,¹ Dawn J. Leonard,¹ Dennis Witmer,¹ Christopher Verdone,¹ Jennifer Sims Mourtada,¹ Valerie L. Staradub¹

¹Christiana Care, Newark, DE.

Background

Image-guided localization is a standard component of breast-conserving surgery (BCS) for nonpalpable malignancies. Although wire localization (WL) is the most widely used approach, several nonwire methods are available. Some newer localization methods purport superiority in optimizing adequate margins. We compared traditional wire localization with radar reflector localization (RRL) over 1 year to evaluate differences in margin status and lumpectomy to tumor size ratio (LTTSR).

Methods

Retrospective review of patients treated with BCS using image-guided localization for stage 0-II breast cancer at

Christiana Care Health System (CCHS) in 2021. Patients identified from the CCHS tumor registry were stratified by localization method (WL vs RRL) Pearson χ^2 or Fisher exact statistical analysis was performed comparing combined positive margin (PM, tumor on ink) and, in cases of pure ductal carcinoma in-situ (DCIS), close margin (CM, tumor ≤ 2 mm from margin) rates between WL and RRL groups. LTTSR was defined as the largest dimension of the primary lumpectomy specimen divided by the largest tumor dimension. Median LTTSR for each group was compared using Mann-Whitney U test. A P value of ≤ 0.05 was significant.

Results

259 patients (180 WL and 79 RRL). PM/CM rate for the entire cohort: 21.2%. No statistical difference in PM/CM rates between WL and RRL for invasive cancer or DCIS. No significant difference in the LTTSR between the 2 localization techniques.

Conclusions

We conclude that RRL and WL are equivalent localization techniques for invasive breast cancer and DCIS, yielding similar rates of adequate excision and specimen sizes.

23 Trends in Screening and Diagnostic Mammogram Reimbursement From 2002 to 2022

Alexander L. Hsu,¹ Cheng-Han Lee,¹ Naveen Galla,¹ Julian Franko,¹ Karanveer Purewal²

¹Department of Radiology, Icahn School of Medicine at Mount Sinai (West), New York, NY.

²Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, MD.

Background

In the United States, the Centers for Medicare and Medicaid Services (CMS) effectively determines the amount reimbursed for examinations and procedures. Health care reimbursement plays an important role in the operations of diagnostic radiology. Understanding reimbursement mechanisms, particularly in breast imaging, and its trends in context with other radiological examinations can offer insight into the fundamental operations and future of breast imaging.

Materials and Methods

CMS reimbursement amounts for screening bilateral mammograms and diagnostic bilateral mammograms were acquired by inputting their associated CPT codes into the CMS physician fee schedule database. Technical component reimbursement, professional component reimbursement, and total reimbursement for each exam were recorded for every other year from 2002 to 2022. The same process was additionally applied for 3 other common radiological exam types outside of breast imaging: one-view chest radiograph, computed tomography (CT) of the head without contrast, and CT of the abdomen and pelvis without contrast. The data were recorded, and linear regression analysis was performed using Microsoft Excel.

Results

A total of 11 reimbursement data point sets were acquired from 2002 to 2022. Six data point sets could be acquired for the CT abdomen and pelvis without contrast exam from 2012 to 2022. The correlation coefficients for total reimbursements for screening bilateral mammograms was -1.5, diagnostic bilateral mammogram was 3.1, chest radiograph 1-view was -0.8,

CT head without contrast was -25.1, and CT abdomen and pelvis without contrast was -8.3.

Conclusions

In the 20-year study period, radiological examinations in general demonstrated decreasing reimbursement over time. However, mammograms appear to be less affected by this negative trend with screening and diagnostic bilateral mammogram reimbursement, exhibiting relative stability

compared with CT examinations of the head as well as abdomen and pelvis. In fact, diagnostic bilateral mammogram reimbursement was the only examination that demonstrated a positive correlation coefficient and an increase in reimbursement over the 20-year period. This stability in reimbursement portends a positive outlook for breast imaging and reinforces the role of this crucial imaging from a public health perspective.

38 Comparing Risk Stratification and Radiotherapy Benefit for Patients With DCIS Using a 7-Gene Biosignature as Compared to a Clinicopathologic Nomogram

Julie Margenthaler,¹ Karuna Mittal,² Frank Vicini,³ Chirag Shah,⁴ Rachel Rabinovitch,⁵ Pat Whitworth,⁶ Brian Czerniecki,⁷ David Dabbs,² G. Bruce Mann,⁸ Fredrik Wärnberg,⁹ Sheila Weinmann,¹⁰ Michael Leo,¹⁰ Steven C. Shivers,² Troy Bremer²

¹Washington University School of Medicine, St Louis, MO.

²PreludeDx, Laguna Hills, CA.

³GenesisCare, Farmington Hills, MI.

⁴Cleveland Clinic, Cleveland, OH.

⁵University of Colorado, Colorado Springs, CO.

⁶Nashville Breast Center, Nashville, TN.

⁷Moffitt Cancer Center, Tampa, FL.

⁸University of Melbourne, Melbourne, Australia.

⁹University of Gothenburg, Gothenburg, Sweden.

¹⁰Kaiser Permanente Center for Health Research, Portland, OR.

Background

Multiple prospective trials show over 70% of women with ductal carcinoma in situ (DCIS) do not recur after breast-conserving surgery (BCS) alone and radiotherapy (RT) had a clinically meaningful reduction in 10-year risk after BCS. Clinicopathologic (CP) factor-based criteria or nomograms have been used to select for whom to de-escalate treatment, assessing the 10-year ipsilateral breast recurrence (IBR) rate after BCS. In this study, we compared the classification of women by a CP model similar to the MSKCC DCIS nomogram with the 7-gene biosignature and their associated total 10-year IBR rates with and without RT.

Materials and Methods

DCIS patients (n = 926) from 4 international cohorts treated with BCS (negative margins) with (n = 641) and without RT

(n = 335) were evaluated for clinicopathological models and the 7-gene biosignature with residual risk subtype (RRt). Formalin-fixed, paraffin-embedded tissue samples for each patient were analyzed at a CLIA lab for the 7-gene biosignature, DCISionRT with RRt. The biosignature reported a decision score (DS) of 0-10 and the presence/absence of the RRt subtype. The CP model used MSKCC DCIS nomogram factors and weighting but omitted the number of excisions and close margin and was categorized using a score <220 as CP low risk. The MSKCC-like score was calculated using the equation score = 100*(RT = 0) + 76*(ET = 0) + FAMHX(pos)*30 + Detection(clinical)*34 + (Grade ≥2)*26 + Necrosis (Present)*12 + Year of Diagnosis (≤1998)*58 + (134-1.49*AGE); margin (no-ink on tumor) = 0, number of excisions ≥3 (incomplete) = 0, evaluate with RT = 0. 10-year total IBR rates were evaluated using Cox proportional hazards and Kaplan-Meier analysis by treatment and risk groups in patients treated with and without RT.

Results

The biosignature classified 37% of women treated with BCS as low risk (n = 338) and 63% (n = 588) were classified into the combined Elevated/Residual Risk group. The 10-year IBR rate for patients who did not receive RT in the low-risk group was 5.6% (95% CI, 2.5%-12.1%). RT did not reduce the IBR rate in the low-risk group (P = .71), where the 10-year IBR rate was 4.8% (95% CI, 2.5%-9.1%) after RT. The CP model classified 320 (34%) as CP low risk (score <220) with an 8.3% 10-year IBR rate for BCS without RT and a non-significant slightly lower rate with RT (4.7%; HR, 0.5; 95% CI, 0.2-1.2, P = .12). Eighty-seven percent (n = 277) of the MSKCC low-risk group patients were treated with endocrine therapy (ET), whereas 32% (n = 124) of the biosignature low-risk patients were treated with ET. Thirty-seven percent (n = 124) of the biosignature low-risk and 30% (n = 98) of the MSKCC low-risk patients were not treated with RT. The biosignature reclassified 63% of these CP low-risk patients as DS elevated risk, with 10-year IBR rates of 12.3% for BCS without RT and 4.8% with RT (HR, 0.2; 95% CI, 0.1-0.8, P <.01).

Conclusions

Using 10-year outcome data (n = 926) from multiple contemporary published validation studies, the biosignature reclassified nearly two-thirds of patients in the CP low-risk (MSKCC-like nomogram) group as elevated risk. The re-classified CP low-risk patients had elevated 10-year

IBR rates after BCS without RT and had an 80% relative benefit from RT, demonstrating they potentially could have been undertreated. This demonstrates the ability of the 7-gene biosignature to better risk-stratify patients with DCIS following BCS and identify patients with low-risk CP who may benefit from RT.

39 7-Gene Predictive Biosignature Improves Risk Stratification for Breast Ductal Carcinoma In Situ Patients Compared to Clinicopathologic Criteria, Identifying a Low-Risk Group Not Clinically Benefiting From Adjuvant Radiotherapy

Rachel Rabinovitch,¹ Frank A. Vicini,² Chirag Shah,³ Julie A. Margenthaler,⁴ Brian Czerniecki,⁵ Pat Whitworth,⁶ David Dabbs,⁷ G Bruce Mann,⁸ Fredrik Wärnberg,⁹ Sheila Weinmann,¹⁰ Michael Leo,¹⁰ Jess Savala,⁷ Steven C. Shivers,⁷ Karuna Mittal,⁷ Troy Bremer⁷

¹University of Colorado Cancer Center, Aurora, CO.

²GenesisCare, Farmington Hills, MI.

³Cleveland Clinic Taussig Cancer Institute, Cleveland, OH.

⁴Washington University School of Medicine, St Louis, MO.

⁵Moffitt Cancer Center, Tampa, FL.

⁶Nashville Breast Center, Nashville, TN.

⁷PreludeDx, Laguna Hills, CA.

⁸University of Melbourne, Royal Women's Hospital, Parkville, Australia.

⁹University of Gothenburg, Gothenburg, Sweden.

¹⁰Kaiser Permanente Center for Health Research, Portland, OR.

Background

Prognostic and predictive tools are needed to optimize treatment for women diagnosed with ductal carcinoma in situ (DCIS). While radiotherapy (RT) is the standard of care for DCIS after breast-conserving surgery (BCS), those at low risk ($\leq 10\%$) for ipsilateral breast recurrence (IBR) risk may be treated without RT. Historically, "low risk" has been defined as the absence of "high risk" clinicopathological factors, which include younger age (< 50 yrs), tumors ≥ 2 cm, palpable tumors, or high nuclear grade (G) tumors. All prospective trials demonstrate that RT reduces IBR by $\sim 50\%$, even in low-risk patients (RTOG 9804). In this study, we analyzed a cohort of women with DCIS treated with BCS +/- RT to determine if the

biosignature could identify a subset of women who do not benefit from RT and evaluate the biosignature in patients meeting "low risk" or "high risk" clinicopathological criteria.

Materials and Methods

DCIS patients (n = 926) from 4 international cohorts (median follow-up, 8.5 yrs; 1st-3rd quartile, 5.8-10.2 yrs) treated with BCS (negative margins) with RT (n = 641) and without RT (n = 335), were evaluated for favorable clinicopathological criteria (age > 50 or grade 1-2, and RTOG 9804-like disease [G1-2, screen detected, negative margins]) and clinical outcomes. Formalin-fixed, paraffin-embedded tissue samples for each patient were analyzed at a CLIA lab for the 7-gene biosignature and a residual risk subtype (RRt). The biosignature reported a decision score (DS) of 0-10 and the presence/absence of the RRt. A low-risk group ($DS \leq 2.8$ without RRt) was compared with the combined elevated risk ($DS > 2.8$ without RRt) and residual risk groups ($DS > 2.8$ with RRt), where 10-yr total IBR rates were evaluated using Cox proportional hazards and Kaplan-Meier analysis by treatment, biosignature risk group, and clinicopathological criteria.

Results

The biosignature classified 37% of women treated with BCS as low-risk (n = 338) and 63% (n = 588) into the combined elevated/residual risk group. Among patients who did not receive RT, those in the elevated/residual risk group had higher IBR rates ($P < .001$) than those in the low-risk group with corresponding 10-yr IBR rates of 25.7% (95% CI, 18.8%-34.4%) vs 5.6% (95% CI, 2.5%-12.1%), respectively. RT did not reduce IBR in the low-risk group (HR, 0.8; $P = .71$), where the 10-yr IBR rate was 4.8% (95% CI, 2.5%-9.1%) with RT and 5.6% without RT, corresponding to a number needed to treat (NNT) of ~ 100 . The elevated/residual risk group benefited from RT (HR, 0.2; $P < .001$), with an absolute reduction of 14.5% (10-yr IBR, 8%), for a NNT of 6. About 50% of patients defined as clinicopathological low-risk by 9804-like (51%) or favorable Age/G (58%) criteria were reclassified by the biosignature to elevated/residual risk. These pts had significant RT benefit: 9804-like group: HR 0.3; $P = .007$; absolute 10-yr IBR reduction of 12.7%; favorable Age/G group: HR, 0.34; $P = .012$, absolute

10-yr IBR reduction of 11.2%. The corresponding NNTs were ~8-9. For patients in clinicopathological high-risk groups, 23% of not-9804-like and 31% of age<50 or G3 pts were reclassified as biosignature low-risk. RT did not significantly reduce IBR in any low-risk biosignature group, including those in clinicopathological high-risk groups. IBR for not-9804-like group was 5.9% vs 3.0% without and with RT ($P = .52$), and for (age<50 or G3) pts was 4.4% vs 3% without and with RT ($P = .70$).

Conclusions

The biosignature identified a low-risk group with excellent

outcomes and no significant RT benefit even in those with G3 disease or aged <50 yrs. 10-yr IBR rates with or without RT remained independent of clinicopathological criteria, further supporting the identification of a true low-risk group who may forgo RT. In contrast, biosignature elevated/RRt patients had clinically meaningful IBR benefits with RT, even for those in favorable clinicopathologic groups (10-yr IBR reduction of 13%-26% with RT). These patients should not be offered RT omission, and these data highlight the lack of accuracy of clinicopathological factors in assessing RT benefit. The 7-gene biosignature provided a superior prediction of 10-yr risk and RT benefit than standard clinicopathological risk models.

40 Characterization of Recurrence Risk After Lumpectomy and Radiotherapy in HER2-Positive Ductal Carcinoma In Situ of the Breast Using a 7-Gene Predictive Biosignature: Implications for the NSABP-B43 Trial Results

Frank A. Vicini,¹ Chirag Shah,² Rachel Rabinovitch,³ Pat Whitworth,⁴ Julie A. Margenthaler,⁵ Brian Czerniecki,⁶ David J. Dabbs,⁷ Sheila Weinmann,⁸ Michael Leo,⁸ G. Bruce Mann,⁹ Fredrik Wärnberg,¹⁰ Jess Savala,⁷ Steven C. Shivers,⁷ Karuna Mittal,⁷ Troy Bremer⁷

¹GenesisCare, Farmington Hills, MI.

²Cleveland Clinic Taussig Cancer Institute, Cleveland, OH.

³University of Colorado Cancer Center, Aurora, CO.

⁴Nashville Breast Center, Nashville, TN.

⁵Washington University School of Medicine, St Louis, MO.

⁶Moffitt Cancer Center, Tampa, FL.

⁷PreludeDx, Laguna Hills, CA.

⁸Kaiser Permanente Center for Health Research, Portland, OR.

⁹University of Melbourne, Royal Women's Hospital, Parkville, Australia.

¹⁰University of Gothenburg, Gothenburg, Sweden.

Background

HER2-positive versus HER2-negative ductal carcinoma in situ (DCIS) of the breast has been associated with an increased risk of local recurrence after breast-conserving surgery (BCS) and radiotherapy (RT). NSABP-B43 was designed to determine if 2 doses of trastuzumab would improve local control after BCS plus RT in women with HER2 (3+) DCIS. The trial demonstrated a statistically insignificant advantage to the drug in reducing ipsilateral breast recurrence (IBR). The predictive 7-gene DCIS

biosignature, DCISionRT with Residual Risk Subtype (RRt) by PreludeDxTM, has been shown to classify DCIS patients into 2 distinct groups of patients with substantially different rates of IBR following BCS plus RT. Based upon these differences in outcome, we assessed the IBR rate in patients with HER2 (+) DCIS treated with BCS and RT who were or were not in the residual risk subtype group defined using DCISionRT, while accounting for the varying clinicopathologic profiles of the patients.

Materials and Methods

DCISionRT with the integrated residual risk biosignature (DCISionRT with RRt) was evaluated on a subset of 178 women with HER2(3+) DCIS who were treated with BCS and RT in a multinational cohort of 926 patients from the United States of America, Sweden, and Australia who were used in the validation studies for DCISionRT. Central pathology review and biosignature testing were performed at a CLIA-certified lab. HER2(+) DCIS was defined as patients with a HER2 (3+) immunohistochemistry $\geq 10\%$ (ASCO/CAP). The biosignature identified patients either classified into the residual risk group or not. The IBR rate was calculated for the overall group of HER2(3+) patients and those in the residual risk group. Individual patient outcome and biosignature results were analyzed using Kaplan-Meier and Cox proportional hazard analyses.

Results

The biosignature classified 113 of 178 HER2 (3+) women (63%) into the residual risk group ($DS > 2.8$ with RRt). Grade 3 was more common in the residual risk group than the not residual risk group (87% vs. 63%, respectively). Patients in the residual risk group had a significantly higher 10-year total IBR rate of 16.2% (95% CI, 9.7%-26.5%) versus 1.6% (95% CI, 0.2%-10.9%; $P = .012$) for all other HER2 (3+) patients. In univariate analysis, younger patients tended to have higher IBR rates after BCS plus RT, but

only residual risk was significantly associated with IBR rates after BCS plus RT. Multivariable analysis demonstrated that the residual risk group was 8 times more likely to recur after BCS and RT, while clinicopathologic factors (age, grade, tumor size) were not associated with a higher IBR rate.

Conclusions

The new, integrated biosignature was predictive for 10-year

IBR risk after BCS plus RT in women with HER2 (3+) DCIS. Approximately 40% of patients with HER2 (3+) DCIS would be expected to achieve low rates of recurrence with BCS and RT, while about 60% of these women (classified as residual risk) would have higher recurrence rates. Collectively, this suggests that there is a subpopulation of HER2 (3+) DCIS that may benefit from further therapy, such as HER2-directed therapies.

41 Changes in Treatment Recommendation for Patients With Ductal Carcinoma In Situ Using a 7-Gene Predictive Biosignature: Analysis of the PREDICT Study

Pat W. Whitworth,¹ Steven C. Shivers,² Chirag Shah,³ Rakesh Patel,⁴ Karuna Mittal,² Troy Bremer,² Charles E. Cox⁵

¹University of Tennessee, Knoxville, TN.

²PreludeDx, Laguna Hills, CA.

³Cleveland Clinic, Cleveland, OH.

⁴Good Samaritan Hospital, Los Gatos, CA.

⁵University of South Florida Morsani College of Medicine, Tampa, FL.

Background

The role of adjuvant radiotherapy (RT) following breast-conserving surgery (BCS) for women with ductal carcinoma in situ (DCIS) remains controversial. Although definitive trials provide level 1 evidence supporting the use of RT in reducing the risk of local recurrence, the same randomized trials demonstrate that approximately 70%-80% of DCIS patients do not have a local recurrence at 10 years after BCS alone. The DCISionRT test is a 7-gene predictive biosignature that uses tumor biology in conjunction with clinicopathologic factors. The test provides a validated score (DS) for women receiving BCS that assesses the 10-year risk of DCIS recurrence and development of invasive breast cancer with and without adjuvant RT. We established a registry to evaluate the decision impact of the 7-gene predictive biosignature on DCIS treatment recommendations.

Materials and Methods

The PREDICT study is a prospective, multi-institutional registry for patients who received DCISionRT testing as part of their routine care. The registry includes females 26 and older who are diagnosed with DCIS and are candidates for BCS and eligible for RT or systemic therapy. Treating

physicians completed treatment recommendation forms before and after receiving test reports to capture surgical, radiation, and hormonal treatment (HT) recommendations and patient preferences. The primary end point is to identify the proportion of patients where testing led to a change in RT recommendation. Additional analyses include changes in recommendations in patient subgroups based on clinicopathologic factors or clinician specialty.

Results

Analysis was performed in 2304 patients treated at 63 clinical sites. The median age of patients was 62 years old (18% < 50 years old), the nuclear grade was high in 33%, and tumor size was 2.5 cm or greater in 11%. Test results were DS low risk (DS ≤ 3) for 63% of women and 37% were DS elevated risk (DS > 3). Overall, the RT recommendation (yes/no) was changed for 38% of women after the 7-gene biosignature testing and the HT recommendation was changed for 11%. There was a net decrease in RT recommendation from 71% pre-assay to 53% post-assay ($P < .001$), where RT recommendations decreased by 53% in DS low-risk patients but increased by 25% in DS elevated risk patients.

Surgeons were more likely to change their RT recommendation (47%) than radiation oncologists (35%). When test results indicated DS elevated risk, both surgeons (79%) and radiation oncologists (88%) were likely to recommend RT, but when the results were DS low risk, surgeons were more likely than radiation oncologists to recommend omitting RT (82% vs. 60%, respectively). Compared to traditional clinicopathologic features, the factor most strongly associated with RT recommendation was the biosignature result with other factors of importance being patient preference, tumor size, and grade.

Conclusions

This analysis demonstrates significant changes in recommendations to add or omit RT based on the 7-gene predictive biosignature in 2304 patients. The integration of DCISionRT into clinical decision processes has a substantial impact on recommendations aimed at optimal management to prevent over- or under-treatment.