DCISionRT® Clinical Evidence Summary in 3,500+ Patients

	Purpose	Study	Summary
ANNALS OF SURGICAL ONCOLOGY	**Validation** *Decision Impact Study: Evaluate impact of DCISionRT on clinicians' recommendations for adjuvant radiation therapy (RT).*	Within cohort of 539 women diagnosed with DCIS, physicians' treatment recommendations were captured pre- and post- DCISionRT testing.	• Post-testing, a change in radiation therapy recommendations were made in 42% of the patients • When compared with traditional clinicopathologic features used to determine RT recommendations, the DCISionRT result was the factor most strongly associated with radiation therapy recommendations.
	Shah, C. et al. Ann Surg Oncol 2021; Abstract: The Clinical Utility of DCISionRT® on Radiation Therapy Decision Making in Patients with Ductal Carcinoma In Situ Following Breast-Conserving Surgery		
SSO SOCIETY OF SURGICAL ONCOLOGY LEADING. TOGETHER.	**Validation** *Determine the utility of DCISionRT Decision Scores to predict ipsilateral breast event risk after breast conserving surgery and the benefit of radiation therapy.*	183 women had Decision Scores (DS) and outcomes available with a median follow-up of 73 months. 72 of these women received RT (39%) and 66 received endocrine therapy (ET, 36%).	• After breast conserving surgery, those with a Low DS had a non-significant 2% difference in outcome with and without RT, while those with Elevated DS had a significant 27% benefit from RT. • Consistent with prior validation studies, DCISionRT upstaged 43% of patients to elevated risk who were previously identified as "low risk" by individual clinical pathology factors (Grade 1/2, size ≤25mm)
	Mann, GB et al. SSO 2021; Abstract: DCIS Biologic Risk Signature Predicts Risk of Recurrence and RT Benefit After BCS		
Miami Breast Cancer CONFERENCE®	**Validation** *Investigated the association of DCISionRT® test results with breast cancer mortality (BCM)*	Case control study identified 96 women who died of breast cancer and 318 controls from a population of 6,964 in Sweden diagnosed with DCIS without microinvasion	• The DCISionRT score, DS, was significantly associated with breast cancer mortality, while clinicopathologic factors were not. • High Decision Scores (DS>6) were strongly associated with increased risk for breast cancer mortality (BCM). • DCISionRT may help to identify women with more aggressive disease that warrants more aggressive upfront treatment
	Wadsten, C et al. MBCC 2021; Poster: A Biomarker Assay Predicts Women Diagnosed with DCIS without Microinvasion at Increased Risk for Breast Cancer Specific Death		
SAN ANTONIO BREAST CANCER SYMPOSIUM®	**Validation** *Determine the utility of DCISionRT in reclassifying patients who met RTOG 9804 or ECOG-ACRIN E5194 'low-risk' clinicopathologic criteria but remained at elevated invasive risk after BCS and benefited from RT.*	Complete biomarker and clinical data for 535 women meeting 'good risk' clinicopathologic criteria (negative margins vs wide margins) and 660 women meeting ECOG E5194 grade 1 or 2 criteria	Outcomes in clinicopathological low-risk DCIS women after breast cancer surgery (BCS): • DCISionRT Elevated Risk patients had substantial risk of 10-year invasive occurrence • DS Elevated Risk patients (>3) had significant RT benefit (8-15% absolute difference) • DS Low RIsk patients (≤3) had minimal RT benefit (1-2% absolute difference)
	Vicini, F et al. SABCS 2020; Poster: DCIS biosignature reclassified patients who met RTOG 9804 or ECOG-ACRIN E5194 low-risk clinicopathologic criteria into an elevated invasive risk group who benefited significantly from radiation therapy		
SAN ANTONIO BREAST CANCER SYMPOSIUM®	**Validation** *Investigate the change in adjuvant RT recommendation by physicians based on DCISionRT.*	513 patients from 32 sites in U.S. with DCISionRT testing completed after treatment with breast conserving surgery, but prior to radiation therapy decision.	• DCISionRT demonstrates high clinical utility by impacting radiation therapy recommendations in 45% of women overall • Recommendations for RT increased 37% in patients initially recommended to omit RT in clinicopathologic low risk groups • DCISionRT may help precent over- and under- treatment of DCIS
	Shah, C et al. SABCS 2020; Poster: Clinical utility of a biologic signature to assess DCIS recurrence risk in patients meeting good-risk criteria (RTOG 9804, ECOG E5194): interim analysis of the DCISionRT PREDICT study		

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	Vicini, F et al. SABCS 2020; Abstract: DCIS biosignature reclassified patients who met RTOG 9804 or ECOG-ACRIN E5194 low-risk clinicopathologic criteria into an elevated invasive risk group who benefited significantly from radiation therapy		
ASTRO TARGETING CANCER CARE	**Development** *Assessment of a poor response-type (RSt) signature with breast conserving surgery to potentially identify women at elevated risk after surgery and radiation.*	284 eligible patients with biomarker data and 102 received hormone therapy and 233 received radiation therapy. The RSt biosignature was calculated using specific biomarkers scored by board certified pathologists in a CLIA certified laboratory.	• A new biosignature identified a Poor Response Type in women with early stage invasive breast cancer • Women with a Poor Response Type had high risk for ispilateral breast events after BCS + RT • Women with a Good Response Type had an excellent outcome after BCS + RT
	Bremer, TM et al. ASTRO 2020; Poster: A Novel Biosignature to Assess Residual Risk in Early Stage Invasive Breast Cancer after Standard Breast Conserving Surgery		
ASTRO TARGETING CANCER CARE	**Validation** *Assessed discordance of Decision Score (DS) with a variety of clinical factors used to make treatment decisions*	De-identified datasets totaling 1,797 women grouped by age, tumor size, nuclear grade and RTOG 9804-like criteria	• Clinicopathologic factors have limited utility to true low risk group • 48% of women under the age of 50 are Low Risk by DCISionRT • 48% of women with low to intermediate grade are Elevated Risk by DCISionRT
	Bremer, TM et al. ASTRO 2020; Poster: Age and Grade as a Function of Decision Score in Women Diagnosed with DCIS		
CLINICAL CANCER RESEARCH	**Validation** *Independent clinical validation of DCISionRT after breast conserving surgery in a Kaiser Permanente NW population*	455 health plan members of Kaiser Permanente Northwest diagnosed with DCIS and treated with BCS or BCS+RT from 1990-2007	• The continuous and categorical DS was prognostic for both TotBE and InvBE risk after adjusting for RT • Further reinforces DCISionRT's ability to correctly reclassify patients into Low (42%) and Elevated risk (58%) groups • Clinically relevant Low Risk Group -10-yr invasive risk: BCS: 5% I BCS+RT:3% -Minimal 2% RT benefit • DCISionRT decisively outperforms and correctly reclassifies 49% of RTOG 9804 "good risk" criteria as Elevated risk patients • >70% risk reduction from RT in Elevated Group for invasive breast events
	Weinmann et al. Validation of a ductal carcinoma in situ biomarker profile for risk of recurrence after breast-conserving surgery with and without radiation therapy, Clinical Cancer Research 2020, Published Online 4/27/2020		

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JNCI	**Validation** *External analysis of the cost-effectiveness of the DCISionRT test to guide treatment of DCIS.*	Used a Markov model simulating 10-year outcomes for 60-year old women with DCIS based on non-randomised data.	• When compared to giving RT to all women with DCIS, the use of DCISionRT to guide the decision for RT was cost-effective and minimized the number of women undergoing RT per future ipsilateral breast event.
	Raldow, AC et al. JNCI Cancer Spectrum; Abstract: Cost Effectiveness of DCISionRT for Guiding Treatment of Ductal Carcinoma in Situ		
Miami Breast Cancer Conference®	**Development** *A radiation-response type (RRT) biosignature for elevated risk lesions was developed with a first cohort and validated in a second cohort for differential response to RT.*	Two observational cohorts of patients treated with and without whole breast RT after Breast Conserving Surgery (BCS) were consecutively collected in Sweden (1986-2004) and the USA (1999-2008).	• A new biosignature identified a subset of women with DCIS at high risk for ipsilateral breast events after BCS + RT. • A subset of women with grade 3 tumors and HER2+ had a poor response type. • Women with a good response type had a substantial apparent benefit from RT.
	Bremer, TM et al. MBCC 2020; Poster: A Novel Biosignature Identifies DCIS Patients with Elevated Residual Risk After Breast Conserving Surgery and Radiation Therapy		
Miami Breast Cancer Conference®	**Validation** *A post-market decision impact registry study is being conducted to assess the impact of DCISionRT score (DS) in changing treatment recommendations for women diagnosed with pure DCIS.*	This is a planned interim analysis of the study with the first 532 patients with complete data from 32 sites.	• This second PREDICT interim analysis demonstrates a significant net change in RT recommendation based on DCISionRT. • Treatment recommendations were changed post-assay in 45% of women for RT and 15% of women for HT. • The integration of DCISionRT into clinical-decision processes will enable clinicians and patients to identify optimal treatments while preventing over- or under-treatment.
	Shivers, SC et al. MBCC 2020; Poster: Interim Analysis of the PREDICT Registry: Clinical Utility of a Biologic Signature Predictive of Radiation Therapy (RT) Benefit in Patients with DCIS		
Miami Breast Cancer Conference®	**Validation** *The PREDICT Registry is a prospective cohort study for patients diagnosed with ductal carcinoma in situ (DCIS) of the breast.*	The primary objective of the study is to create a deidentified database of patients, test results, treatment decisions and outcomes that can be queried to determine the utility of the DCISionRT test in the diagnosis and treatment of ductal carcinoma in situ of the breast.	• The PREDICT Study has consented 747 women with 458 consented in 2019. There are 42 sites enrolled and an additional 25 sites pending activation. • The aim of PREDICT is to activate up to 100 sites and consent 2,500 patients diagnosed with DCIS.
	Shivers, SC et al. MBCC 2020; Poster: The PREDICT Registry: A prospective registry study to evaluate the effect of a Biologic Signature Predictive of Radiation Therapy (RT) Benefit on treatment decisions in patients with DCIS following breast conserving therapy		
San Antonio Breast Cancer Symposium®	**Validation** *The PREDICT Registry is a prospective cohort study for patients diagnosed with ductal carcinoma in situ (DCIS) of the breast.*	The primary objective of the study is to create a deidentified database of patients, test results, treatment decisions and outcomes that can be queried to determine the utility of the DCISionRT test in the diagnosis and treatment of ductal carcinoma in situ of the breast.	• The PREDICT Study has consented 747 women with 458 consented in 2019. There are 42 sites enrolled and an additional 25 sites pending activation. • The aim of PREDICT is to activate up to 100 sites and consent 2,500 patients diagnosed with DCIS.
	Shivers, SC et al. SABCS; Poster: The PREDICT Registry: A prospective registry study to evaluate the effect of the DCISionRT test on treatment decisions in patients with DCIS following breast conserving therapy		

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ASCO®	**Development** *To develop a biologic signature for 10-year ipsilateral invasive breast events in luminal stage 1 breast cancer patients treated with BCS with or without adjuvant RT.*	Studied a cohort of 423 patients from Sweden diagnosed with Stage 1 breast cancer between 1987 and 2004. Treatment was neither randomized nor strictly rules based.	• The biologic risk signature identified subgroups of patients with early-stage breast cancer who will benefit from RT. • For patients with luminal breast cancer, the biologic signature provided both prognostic and predictive value for benefit from adjuvant RT.
Wadsten, C et al. ASCO; Abstract: Risk stratification in early stage luminal breast cancer patients treated with and without RT			
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Wadsten, C et al. ASCO; Poster: Risk stratification in early stage luminal breast cancer patients treated with and without RT			
THE AMERICAN SOCIETY OF Breast Surgeons	**Validation** *A planned early interim analysis of the DCISionRT PREDICT Study, a registry designed to assess the impact of the DCISionRT score (DS) in changing treatment recommendations for women diagnosed with pure DCIS.*	Analyzed the first 197 patients with complete data from 18 sites across the US.	• Demonstrated a significant absolute overall change in RT recommendation based on DCISionRT. • Treatment recommendations were changed post-assay for 51% of women for RT and 13% of women for HT. • Integration of DCISionRT impacts the clinical decision process as clinicians and patients consider strategies aimed at reducing overtreatment and minimizing undertreatment.
Whitworth, PW et al. ASBS; Abstract: Interim Analysis of the DCISionRT PREDICT Study: Clinical Utility of a Biologic Signature Predictive of Radiation Therapy Benefit in Patients with DCIS			
THE AMERICAN SOCIETY OF Breast Surgeons	**Validation** *A planned early interim analysis of the DCISionRT PREDICT Study, a registry designed to assess the impact of the DCISionRT score (DS) in changing treatment recommendations for women diagnosed with pure DCIS.*	Analyzed the first 197 patients with complete data from 18 sites across the US.	• Demonstrated a significant absolute overall change in RT recommendation based on DCISionRT. • Treatment recommendations were changed post-assay for 51% of women for RT and 13% of women for HT. • Integration of DCISionRT impacts the clinical decision process as clinicians and patients consider strategies aimed at reducing overtreatment and minimizing undertreatment.
Whitworth, PW et al. ASBS; Poster: Interim Analysis of the DCISionRT PREDICT Study: Clinical Utility of a Biologic Signature Predictive of Radiation Therapy Benefit in Patients with DCIS			
CLINICAL CANCER RESEARCH	**Validation** *A biological signature that calculates an individualized Decision Score (DS) was developed and cross-validated in 526 DCIS patients treated with BCS ± RT. The relationship was assessed between DS and 10-year risk of invasive breast cancer (IBC) or any ipsilateral breast event (IBE), including IBC or DCIS. RT benefit was evaluated by risk group and as a function of DS.*	The study was conducted on archived tissue samples in collaboration with Uppsala University Hospital and Västmanland County Hospital, Sweden (UUH), the University of Massachusetts, Worcester (UMass). Patients were included consecutively between 1986 and 2004 at UUH and between 1999 and 2008 at UMass. Treatment decisions were neither randomized nor strictly rules-based.	• The DS was significantly associated with IBC and IBE risk, HR (per 5 units) of 4.2 and 3.1, respectively. • For patients treated without RT, DS identified a Low Group with 10-year IBC risk of 4% (7% IBE) and an Elevated Risk Group with IBC risk of 15% (23% IBE). • In analysis of DS and RT by group, the Elevated Risk Group received significant RT benefit, HR of 0.3 for IBC and IBE. • In a clinicopathologically low-risk subset, DS reclassified 42% of patients into the Elevated Risk Group. • In an interaction analysis of DS and RT, patients with elevated DS had significant RT benefit over baseline.
Bremer, TM et al. A biologic signature for breast ductal carcinoma in situ to predict radiation therapy (RT) benefit and assess recurrence risk, Clinical Cancer Research 2018, Published Online 12/01/2018			

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SAN ANTONIO BREAST CANCER SYMPOSIUM	**Validation** *Validation of predictive biologic profile*	**A Modern Observational Cohort** 584 patients. Randomized to BCS or BCS+RT. Prospective-retrospective randomized clinical trial.	• Predicted RT benefit: Absolute invasive risk reduction. • Low group = 1% (HR 0.8, p=NS) • Elevated group = 9% (HR 0.2, p=0.01).
	Wärnberg, F et al. A validation of DCIS biological risk profile in a randomised study for radiation therapy with 20 year follow-up (SweDCIS), SABCS 2017; Abstract: 851741		
Miami Breast Cancer CONFERENCE	**Validation** *The utility of a novel biologic risk profile was compared with weighted clinicopathologic factors.*	The biologic risk profile was developed in two large female patient cohorts treated with or without radiation therapy (RT) after BCS and subsequently validated in an independent Kaiser Permanente Northwest (KPNW) population treated with BCS and optionally RT.	• The Biological Risk Profile outperformed clinicopathologic factors for assessing total IBE risk. • The patients with the highest DCIS Risk Profiles tended to have higher risk clinicopathologic factors. • The Biological Risk Profile reclassified 59% of patients with multiple low risk clinico–pathologic factors to elevated total risk. • The Biological Risk Profile reclassified 27% of patients with multiple high risk • clinicopathologic factors to low total risk.
	Bremer, TM et al. MBCC 2017; Abstract: Utility of the DCIS Biological Risk Profile for Predicting Recurrence Risk Compared to Standard Clinicopathologic Factors		
Miami Breast Cancer CONFERENCE	**Comparison** *Comparison of biologic risk profile to MSKCC*	999 patients. Biologic risk profile vs. MSKCC weighted clin/path risk.	• Biologic Risk Profile reclassified 59% of the clin/path low risk group and 27% of the clin/path high risk group.
	Bremer, TM et al. MBCC 2017; Poster: Utility of the DCIS Biological Risk Profile for Predicting Recurrence Risk Compared to Standard Clinicopathologic Factors		
SAN ANTONIO BREAST CANCER SYMPOSIUM	**Development** *Early Validation of biologic profile*	650 patients. BCS & BCS+RT patients.	• 10-yr total risk after BCS: Low group = 1%, Elevated group = 25%. • 10-yr total risk after BCS+RT: Low group = 9%, Elevated group = 13%.
	Bremer, TM et al. SABCS 2016; Publication Number: S5-01 – AACR; Cancer Res 2017;77(4 Suppl):Abstract nr S5-01		
ASCO	**Development** *A multi-biomarker prognostic risk assessment was developed using cross-validation modeling within two large patient cohorts treated with and without RT after BCS.*	Patients were from Uppsala University Hospital (UUH), diagnosed 1986-2004, and University of Massachusetts (UMass), diagnosed 1999-2008, had been treated with BCS with (56%) or without (44%) adjuvant RT.	• The biomarker-based risk stratification identified patients at risk for invasive ipsilateral breast events in cross-validation. • Patients with low biomarker based risk had a 10-year invasive recurrence risk without RT that is low and similar to that with RT.
	Bremer, TM et al. A multi-marker test for invasive risk post DCIS treated with BCS +/- RT, ASCO 2016; Abstract 1019		
Miami Breast Cancer CONFERENCE	**Development** *Biomarkers (p16/INK4A, Ki-67, COX-2, PgR, HER2, FOXA1, SIAH2) were assessed using IHC in FFPE tissue by board certified pathologists.*	Two recurrence risk signatures were developed, one for invasive and another for overall ipsilateral breast events (IBEs).	• Over 2/3 of patients had a low risk invasive signature. • Over 1/3 of patients had a low risk signature for ipsilateral breast events. • The 10-year recurrence risk was substantially lower for patients with low risk signatures (p<.001, invasive and overall). • Both algorithms maintained significance when adjusted for nuclear grade, tumor size, age, necrosis and margin status. • Invasive and overall IBE risks were similar regardless of RT in low risk patients. • Patients whose risk signatures were not low and had RT had less than half the 10-year recurrence risk of those without RT.
	Bremer, TM et al. A multi-marker test for recurrence risk after BCS +/- RT for DCIS, MBCC 2016; Abstract 364		

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SAN ANTONIO BREAST CANCER SYMPOSIUM	**Development** *To develop and blindly validate a multi-marker risk stratification test in DCIS patients treated with BCS.*	Separate models to predict DCIS and invasive event risk were developed using statistical pattern recognition and modeling methods on UUH patients treated with BCS in the absence of adjuvant therapy (n=200). In addition, an "overall" risk model was created by combining the DCIS and invasive models.	• This study indicates that the present approach to risk stratification modeling can accurately identify patients at risk for DCIS or invasive events after a primary DCIS diagnosis. • The models presented here were the basis of a comprehensive multi-marker panel undergoing formal validation.
	Linke, SP et al. Validation of a multi-marker test that predicts recurrence in patients diagnosed with ductal carcinoma in situ (DCIS) treated with breast-conserving surgery (BCS), SABCS 2014; Abstract 851032		
JNCI	**Development** *Development of biologic profiles*	329 Patients. BCS & BCS+RT	• Algorithm identified a low risk group with 8% total recurrence risk at 8 years. • Phase 1 of risk algorithm development identifies patients at increased risk of invasive breast cancer.
	Kerlikowske, K et al. Biomarker Expression and Risk of Subsequent Tumors After Initial Ductal Carcinoma In Situ Diagnosis J Natl Cancer Inst 2010; 102(9)627-37		
Cancer Cell	**Discovery** *Discovery of biologic profile*	70 patients.	• Assessment of Rb & cellular stress response pathways allow early prediction of recurrence. • Cell line investigation of DCIS progression/recurrence mechanisms.
	Gauthier, ML et al. Abrogated Response to Cellular Stress Identifies DCIS Associated with Subsequent Tumor Events and Defines Basal-like Breast Tumors, Cancer Cell 2007; 12(5)471		