Clinicopathological Risk Factors Poorly Stratified Baseline Risk and RT Benefit Compared to DCISionRT in Patients with Ductal Carcinoma in Situ

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Background

- Traditional clinicopathological factors have limited capability to risk stratify DCIS patients and predict benefit of Radiation therapy (RT).
- Thus, leading to over and under treatment of DCIS patients.
- DCISionRT (PreludeDx, Laguna Hills, CA) is a biologic signature that provides a validated score to assess the 10-year risk of recurrence and RT benefit after breast conserving surgery (BCS) using individual tumor biology in conjunction with clinical and pathologic risk factors.
- Herein, we present a prospective validation analysis of 3 cohorts of patients using DCISionRT score plus a novel residual risk subtype (RRt) and assessed the stratification of ipsilateral breast recurrence (IBR) risk and RT benefit by clinicopathology.

Materials and Methods

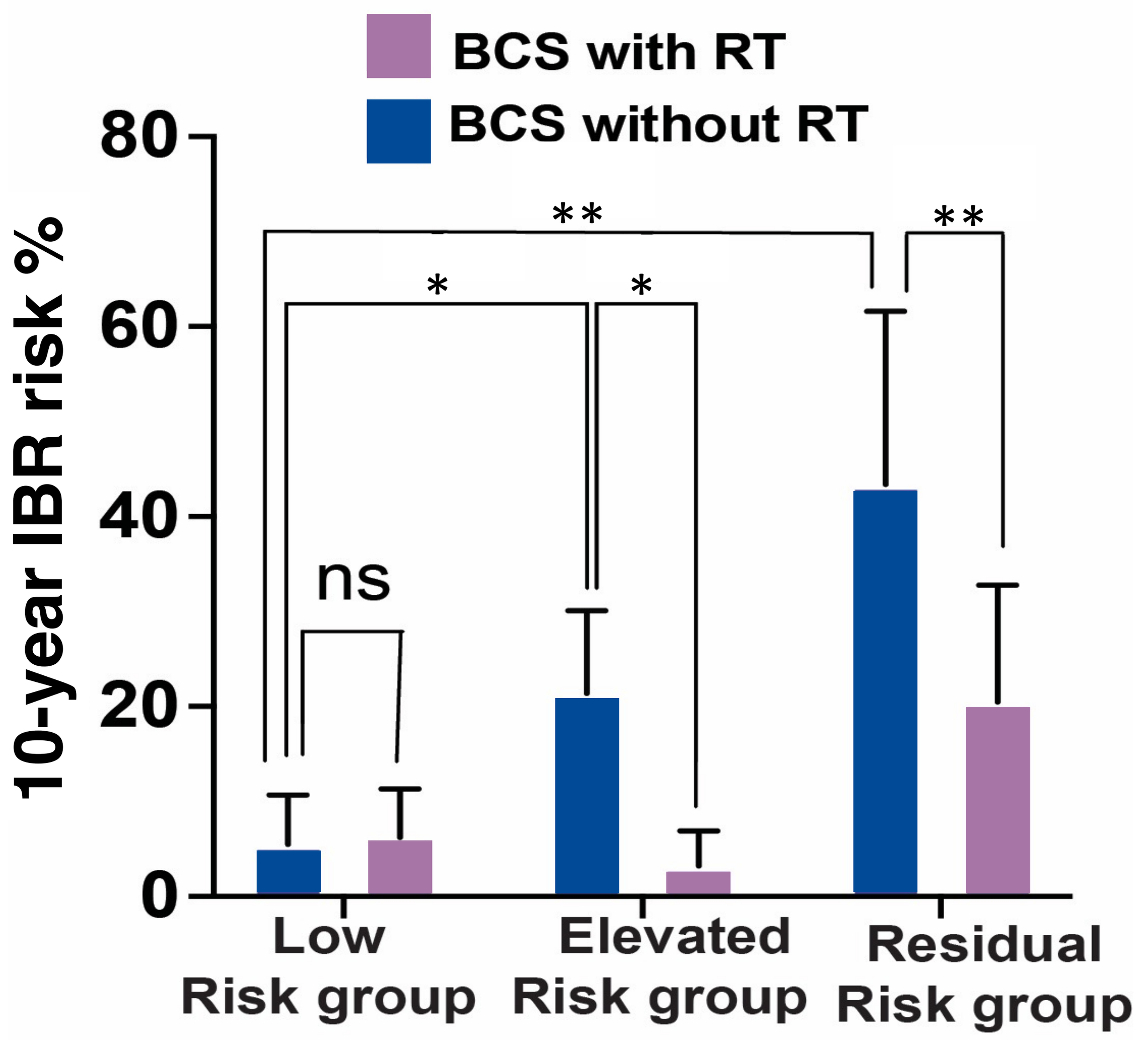
- DCISionRT and its RRt was evaluated in 493 patients from 3 cohorts (Uppsala University Hospital, Sweden (1986-2004), University of Massachusetts, Worcester, MA (1999-2008), and Royal Melbourne Hospital, Australia (2006-2011) at a CLIA lab (PreludeDx, Laguna Hills, CA)
- Central pathology review and biosignature testing was performed on formalin-fixed paraffin embedded tissue at a CLIA-certified lab (Laguna Hills, CA), providing a unique "decision score" for each specimen based on a risk score(DS) 1-10 and RRT yes/no.
- DCISionRT/RRt Risk groups were assessed for 10-yr total (invasive and in situ) IBR risk by survival analysis (Kaplan Meier and Cox proportional Hazard analysis).
- DCISionRT/RRt classified patients into three groups, a) Low Risk (DS≤2.8), b) Elevated Risk (DS>2.8 without RRt) and c) Residual Risk (DS>2.8 with RRt).

Results

- The biosignature classified patients into Low (DS≤2.8, n=173), Elevated (DS>2.8 without RRt, n=209) and Residual (DS>2.8 with RRt, n=111) Risk groups
- Patients had increased 10-yr IBR risk in Elevated (21.4%, p<0.001) and Residual (43.4%, p<0.001) Risk groups without RT, and benefited from RT (Elevated HR=0.15, p=0.002; Residual HR=0.27, p=0.004) vs. Low Risk group (5.5%, RT HR=1.28, p=0.7). The Residual vs. Elevated Risk group had increased 10-yr IBR risk after RT (20.5% vs. 3.2%, p=0.008).
- Clinicopathologic features (age, grade, size, palpability, necrosis) were not associated with 10-yr IBR risk in multivariable analysis including DCISionRT and treatment.
- The distribution of clinicopathologic features varied between biosignature Risk groups; the Residual Risk group had a higher proportion of patients with nuclear grade 3 (71% vs. 31%, p<0.001), necrosis (89% vs. 56%, p<0.001), and size >1 cm (54% vs. 35%, p<0.001) when compared with Low and Elevated Risk groups but no significant change was noted in the distribution between DCISionRT Risk groups for age.

- Traditional clinicopathologic features did not identify patient groups who need RT after BCS
- DCISionRT identified a Low Risk group that had no added benefit of RT after BCS
- DCISionRT identified a Residual Risk group that had high 10-yr IBR despite RT after BCS

Figure 1: 10-year IBR risk with and without RT by Biosignature Risk groups



* p<0.01; ** p<0.001

Table 1: 10-year IBR risk reduction with RT by Biosignature Risk groups

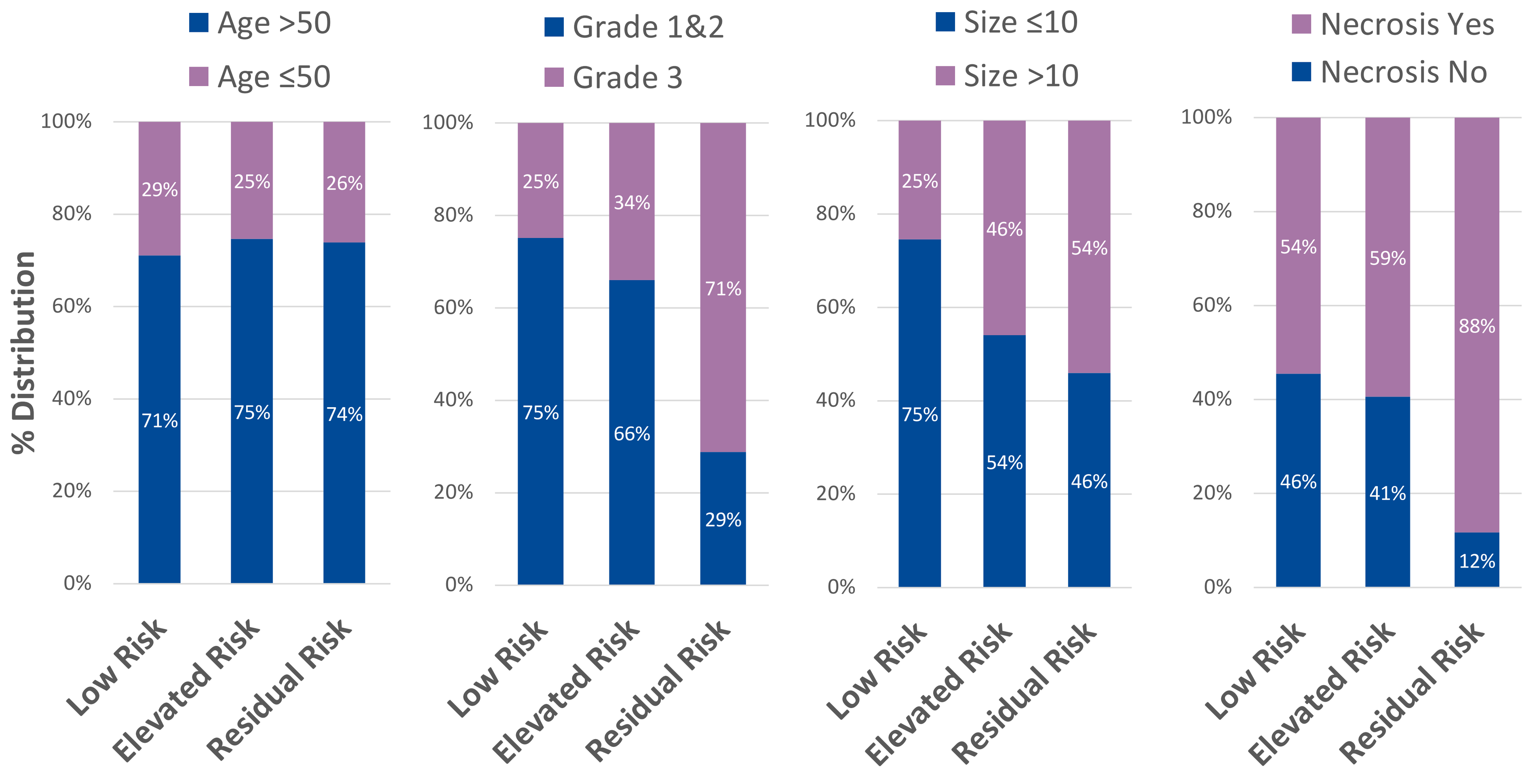
Risk Group	RT HR (CI 95%)
Low Risk DS≤2.8	1.28 (0.34 – 4.8)
Elevated Risk DS>2.8 without RRt	0.15 (0.04-0.51)
Residual Risk DS>2.8 with RRt	0.27 (0.11-0.65)

RRt: Residual Risk Subtype
DS: Decision Score

Table 2. Clinicopathological feature distribution by biosignature risk groups

	DS Low n (%)	DS Elevated n (%)	DS Residual n (%)	p-value
All	173	209	111	
Age ≤50 years	50 (28.9%)	53 (25.4%)	29 (26.1%)	p=0.72
Age >50 years	123 (71.1%)	156 (74.6%)	82 (73.9%)	
Nuclear Grade 1 or 2	130 (75.1%)	138 (66.0%)	32 (28.8%)	p<0.001
Nuclear Grade 3	43 (24.9%)	71 (34.0%)	79 (71.1%)	
Size ≤ 10 mm	129 (74.6%)	113 (54.1%)	51 (45.9%)	p<0.001
Size > 10 mm	44 (25.4%)	96 (45.9%)	60 (54.1%)	
Necrosis No	66 (45.5%)	67 (40.6%)	11 (11%)	p<0.001
Necrosis Yes	79 (54.5%)	98 (59.4%)	89 (89%)	

Figure 2. Clinicopathological feature distribution by biosignature risk groups



Conclusions

- DCISionRT with integrated Residual Risk subtype classified patients into three groups with distinct risk and RT benefit profiles
- Residual Risk group had highest 10-yr IBR risk without RT and significantly elevated IBR risk after RT.
- The distribution of clinicopathological features varied between biosignature Risk groups but were not significantly associated with 10-yr IBR risk, accounting for DCISionRT risk groups and treatment.

 Corresponding Author: Troy Bremer, PhD tbremer@preludedx.com I For further information about PreludeDx, contact Cory Dunn, cdunn@preludedx.com I Miami Breast Cancer Conference – March 3-6, 2022