Identification of DCIS patients with low-risk clinicopathology who benefit from radiation therapy with and without endocrine therapy after breast-conserving surgery assessed with the 7-gene biosignature

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Background

- Ductal carcinoma in situ (DCIS) accounts for 20% of breast cancers.
- For most patients with DCIS, the standard treatment involves breast-conserving surgery (BCS) followed by radiotherapy (RT).
- Adjuvant endocrine therapy (ET) is typically recommended for hormone receptor-positive disease.
- However, prospective trials have failed to identify a low-risk CP group not benefitting from RT with respect to ipsilateral breast recurrence (IBR), with no modern trials evaluating ET.
- We utilized the 7-gene predictive DCIS biosignature to assess the effects of RT and/or ET on 10yr IBR in women with low-risk CP DCIS.

Methods

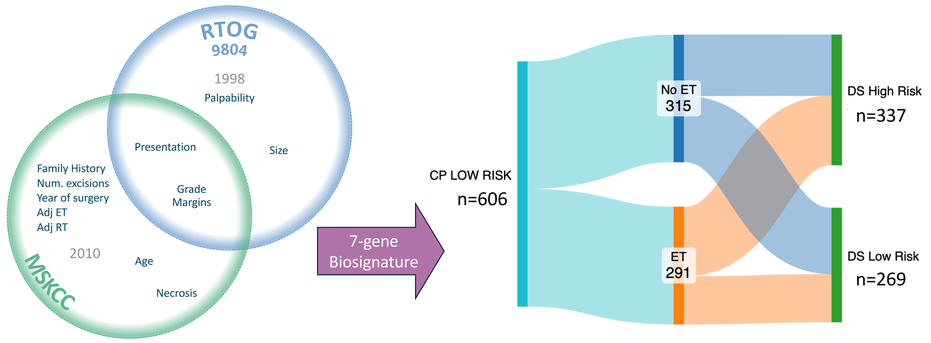
- Women (n = 926) from four DCIS cohorts treated with BCS had tissue samples analyzed at a CLIA lab (Laguna Hills, CA).
- Low-risk CP was defined with RTOG 9804-like criteria (margin negative by no-ink on tumor) or MSKCC-like criteria using nomogram-weighted factors (low-risk score < 220, excluding the number of re-excisions, using negative margins, and RT treatment).
- Women with either low-risk CP criteria were classified as molecular Low Risk (DS ≤ 2.8) or High Risk (DS > 2.8 ± Residual Risk subtype, RRt) using the 7-gene DCIS biosignature.
- Ten-year IBR Kaplan-Meier rates and Cox proportional hazard ratios (HR) were calculated for ET and RT.

Results

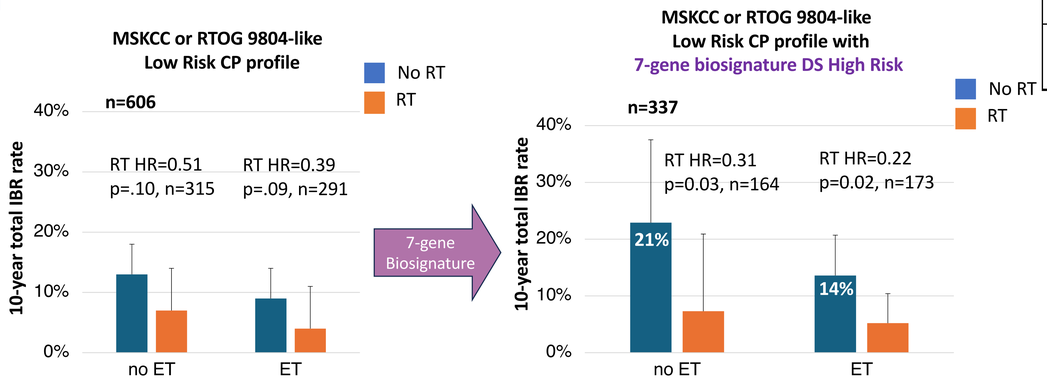
- Overall, 66% of 926 women were classified as low risk by one of the CP criteria and benefited from RT (HR=0.44, n=606, p=.01).
- Patients with low-risk CP treated without ET (n = 315) had 10yr IBR rates of 13% after BCS without RT and 7% with RT (HR = 0.51, p = .10), while those treated with ET (n = 291) had 10yr IBR rates of 9% after BCS without RT and 4% with RT (HR = 0.39, p = .09).
- Overall, 37% of women were classified as low risk (n = 338) by the biosignature and had a 10yr IBR rate of 5.6% after BCS with no significant ET (HR = 0.66, p = .41) or RT benefit (HR = 0.88, p = .78) in multivariable analysis.
- Of patients with low-risk CP, 53% were re-classified as High Risk by the biosignature. Those treated without ET had elevated 10yr IBR rates without RT (21%) and a substantial RT benefit (HR = 0.31, p = .03, n = 164).

- DCIS patients with low-risk clinicopathology who were re-classified as DS High Risk and were prescribed ET still benefited significantly from RT
- Biosignature identified a DS Low Risk group of patients with DCIS with no significant benefit from ET or RT after breast conserving surgery
- ET benefit appears to be restricted to patients classified as DS High Risk and who failed to receive RT

Methods: Defining low-risk using clinicopatholgic criteria and re-classified by the 7-gene biosignature



Results: 10-year IBR rates for low-risk clinicopathology reclassified to DS High Risk by the 7-gene biosignature



Results, continued

- 59% of those treated with ET after BCS were classified by the biosignature as High Risk and had elevated 10yr IBR rates without RT (14%) and a substantially lower IBR rate (5%) with RT (HR = 0.22, p = .02, n = 173).
- Patients with concordant low-risk CP and biosignature Low Risk (n = 269) had a 5.5% 10yr IBR rate after BCS and no significant RT (HR = 1.10, 95% CI 0.33 to 3.7, p = .87) or ET benefit (HR = 0.44, 95% CI 0.1 to 1.6, p = .22) in multivariable analysis.

Results: Low risk clinicopathology and DS low risk by the 7-gene biosignature

		No ET		ET	
	n	no RT	RT	no RT	RT
CP low-risk & DS Low Risk	269	5.5% (1.8-16.2%)	7.3% (3.3-15.8%)	3.6% (0.5-22.8%)	2.8% (0.7-10.9%)
DS Low Risk	338	6.6% (2.8-15.2%)	6.0% (2.8-12.3%)	3.6% (0.5-22.8%)	2.7% (0.7-10.3%)

		RT Effect		ET Effect	
	n	HR	p-value	HR	p-value
CP low-risk & DS Low Risk	269	1.1	0.87	0.44	0.22
DS Low Risk	388	0.88	0.78	0.66	0.41

Conclusions

- Importantly, the biosignature classified over half of women with low-risk CP treated with ET as High Risk.
- The 7-gene biosignature provided better identification of patients with low 10yr IBR rates and no significant RT benefit compared to using CP low-risk criteria.
- This group received substantial benefit from RT, while those with biosignature Low Risk did not.