Impact on Radiation Therapy Recommendation and Treatment Modality for Patients With Ductal Carcinoma In Situ Using the 7-Gene Biosignature: Analysis of the PREDICT Study

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Background

- Breast-conserving surgery (BCS) followed by adjuvant radiotherapy (RT) has been a mainstay in the treatment of DCIS based on multiple randomized trials demonstrating a local recurrence benefit with RT.
- However, these studies have failed to identify subsets of patients who did or did not benefit from adjuvant RT after BCS, raising concerns regarding both over and under-treatment.
- Thus, better prognostic and predictive tools are needed to appropriately risk stratify patients and understand their benefit from RT.
- The 7-gene predictive DCIS biosignature provides a validated score (DS) for women undergoing BCS to assess their 10-year risk of in-breast and invasive recurrence with and without adjuvant RT.

Methods

- The PREDICT study is a prospective, multi-institutional trial for patients who received DCISionRT testing as part of their routine care.
- The registry includes females 26 and older who are diagnosed with DCIS, are candidates for BCS, and eligible for RT.
- Treating physicians completed treatment recommendation forms before and after receiving test results to capture surgical, radiation and hormonal treatment (RT) recommendations and patient preferences.
- Analysis was performed in 2,012 treated patients treated at 63 clinical sites.

Results

- Median age was 62 years old with 32% grade 3 and 9% size 2.5 cm or greater.
- Post-test, RT recommendation changed for 40% of patients (p<0.001), with a net reduction of 20% in patients recommended to receive RT (p<0.001).
- The DCISionRT test results had the greatest impact (OR 26.2, 95%CI 19.1-36.4, when analyzed categorically using DS=3 cut-off; 2.3 per DS, 95%CI 2.1-2.6, when evaluated continuously on post-test RT recommendation in multivariable analysis when compared to all other factors including patient preference, patient clinical and tumor pathological factors, patient race/ethnicity, treatment facility, physician specialty.
- The post-test RT recommendation rate increased with increasing DS (0-2.4, 2.4-4, 4-10) on a categorical basis, with odds ratios of 6.8 DS (2-4 vs 0-2), and 35.0 for DS (4-10 vs 0-2).
- After DCISionRT test result, patient preference was the second most important factor in post-test RT recommendation.
- There was also a significant change in the modality of RT recommended to 34% of those patients recommended RT pre-test and post-test by radiation oncologists (n=97), with intensified RT modality for higher DS (p<0.001) and de-escalation for lower DS (p<0.001).

Conclusions

- This analysis of over 2,000 patients demonstrates significant changes in recommendations to add or omit RT based on 7-gene predictive. The integration of DCISionRT into clinical decision processes has substantial impact on recommendations aimed at optimal management to prevent over- or under-treatment.

TABLE 1. Impact of the 7-gene predictive biosignature on adjuvant radiation recommendation overall and by clinicopathologic factors

<table>
<thead>
<tr>
<th>Clinical Factor</th>
<th>N</th>
<th>Pre-test (%)</th>
<th>Post-test (%)</th>
<th>Net change (%)</th>
<th>Overall change</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Overall</td>
<td></td>
<td>1027</td>
<td>571</td>
<td>45</td>
<td>38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤ 50</td>
<td>339</td>
<td>80</td>
<td>45</td>
<td>-35</td>
<td>15</td>
<td>38, 44</td>
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<tr>
<td>&gt; 50</td>
<td>1673</td>
<td>69</td>
<td>45</td>
<td>-24</td>
<td>19</td>
<td>38, 43</td>
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<tr>
<td>1 or 2</td>
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<td>64</td>
<td>45</td>
<td>-19</td>
<td>31</td>
<td>38, 42</td>
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<tr>
<td>3</td>
<td>652</td>
<td>87</td>
<td>62</td>
<td>-25</td>
<td>30</td>
<td>38, 42</td>
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<tr>
<td>≤ 2.5 cm</td>
<td>1796</td>
<td>69</td>
<td>49</td>
<td>-20</td>
<td>31</td>
<td>39, 41</td>
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<tr>
<td>&gt; 2.5 cm</td>
<td>193</td>
<td>90</td>
<td>69</td>
<td>-21</td>
<td>28</td>
<td>38, 39</td>
</tr>
</tbody>
</table>

- **Gain**
  - 'Good Risk'
  - 'Bad Risk'

- RT Chirag S. Shah1, Pat W. Whitworth2, Steven C. Shivers3, Karuna Mittal1, Troy Bremer3, and Charles E. Cox4

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Figure 1. RT Recommendation Pre- and Post DCISionRT Test Results

Figure 2. DCISionRT Decision Impact on RT Recommendation

Conclusions

- This analysis of over 2,000 patients demonstrates significant changes in recommendations to add or omit RT based on 7-gene predictive. The integration of DCISionRT into clinical decision processes has substantial impact on recommendations aimed at optimal management to prevent over- or under-treatment.