

# Use of Molecular Profiling using Oncotype Dx<sup>(R)</sup> in decision making for adjuvant chemotherapy in breast cancer - the largest single practice Australian experience

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## BACKGROUND:

Molecular profiling to estimate the degree of additional benefit of adjuvant chemotherapy (CT) over and above adjuvant hormone therapy for patients with hormone positive early breast cancer (EBC) is entering routine clinical practice, with over 70% of eligible patients in USA being tested. In Australia, many clinicians use Adjuvant on line (AOL)<sup>(R)</sup> as a decision making tool, but this has not been updated since 2006 and does not include prognostic factors such as Her2 status. Oncotype DX<sup>(R)</sup> is a commercially available 21 gene signature which has been retrospectively validated as a predictive tool for distant recurrence and CT benefit, in node positive and negative EBC<sup>1</sup>. Currently, prospective evaluation is occurring in the TAILORx trial<sup>2</sup>, although only patients with an intermediate with recurrence score (RS) are being randomised to CT+ hormones v hormones alone, reflecting the sentiment that it would be unethical to randomise either those with a low or high RS.

## METHOD:

This audit presents data on 32 Oncotype Dx<sup>(R)</sup> tests performed on 31 patients (one with bilateral tumours) with ER/PR positive EBC in a working practice between Nov 2006- Sep 2009, to assess the impact of the result on the decision about type of adjuvant therapy. The test was discussed with patients where the clinician felt that there was a borderline benefit for CT, or where the patient was very keen to either have or avoid CT but the clinician felt otherwise. The test was self funded by all patients. All patients received adjuvant hormone therapy. Data was extracted from the e-medical record S4S Audit 4<sup>(R)</sup>.

## RESULTS:

Table 1: Patient characteristics (n= 31)

Age range:	35-69
Peri/Premenopausal:	
Postmenopausal:	
Nodal status:	
Positive	11
negative	22
Grade:	
1	1
2	21
3	10
Her 2 FISH/SISH	
Negative	29
equivocal	2
positive	0

Table 2: Oncotype Dx Recurrence Score (RS)

Range	3-52
Standard Oncotype Dx range:	
Low (RS 0-18)	18
Intermediate (RS 19-31)	12
High (RS >32)	2
TAILORx Oncotype Dx range:	
Low (RS 0-10)	3
Intermediate (RS 11-25)	24
High (RS >25)	5

Figure 1: Range of RS (patients 1-22 are node negative, 23-32 are node positive)

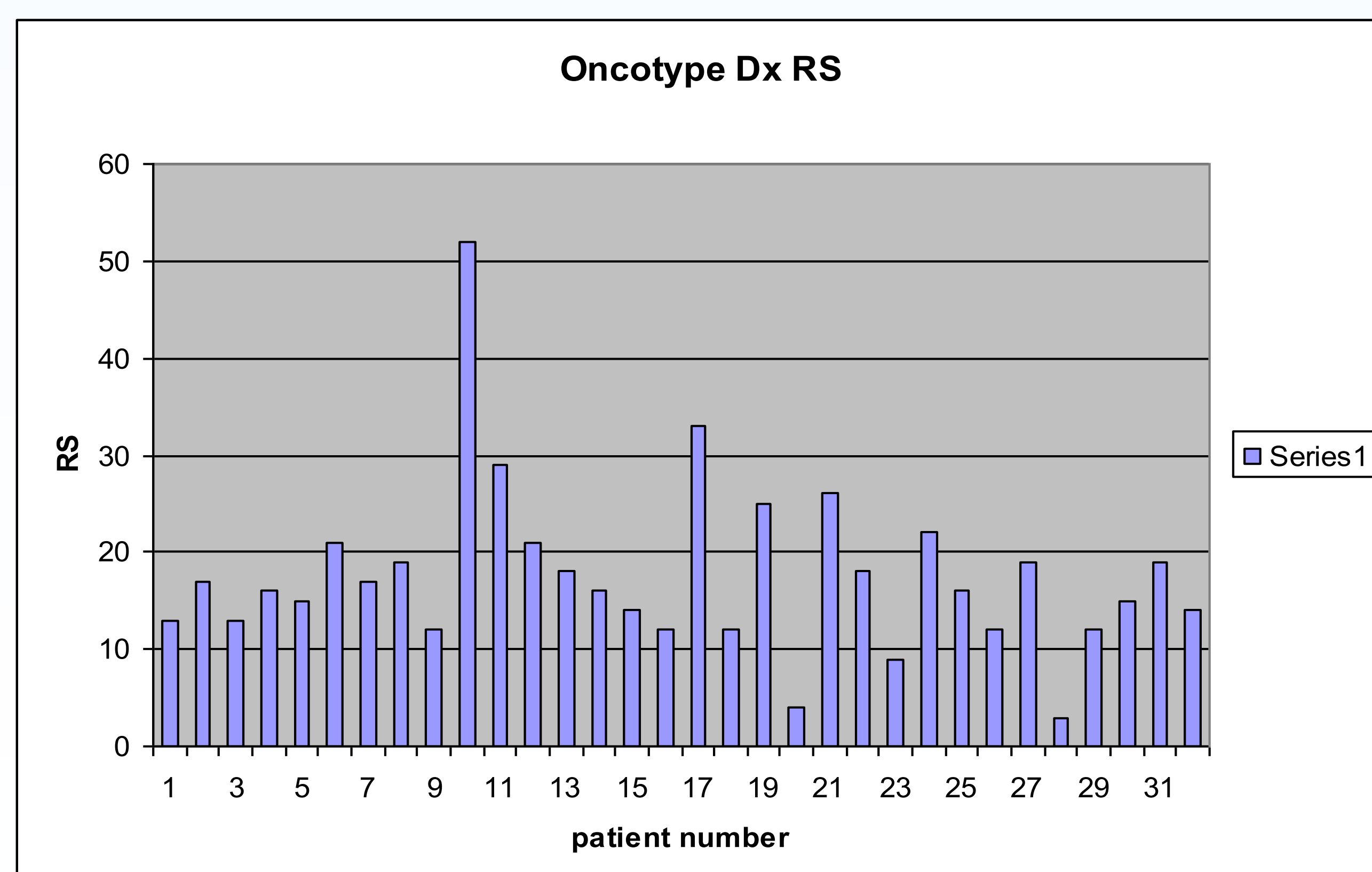


Table 3: Reason to perform Oncotype Dx

Reason for Oncotype	No. of patients
"uncertain" recommendation	8
wanted to avoid chemo++	17
anxious that should have chemo	6

Table 4: Adjuvant chemotherapy v RS

Low (RS 0-18)	0
Intermediate (RS 19-31)	2
High (RS >32)	2

## Oncotype Dx v MDT recommendation

26 patients had been discussed at the SVH breast MDT. Recommendations were listed as 'recommend adjuvant chemotherapy', 'should be discussed' or 'no adjuvant chemotherapy'. RS were interpreted as 'no adjuvant chemotherapy' for low and intermediate RS and 'chemotherapy' for RS high. All patients with intermediate scores had chemotherapy discussed but only 2 of 24 patients elected for treatment (RS of 25 and 26). The two patients with high RS (both node negative) had been given an MDT recommendation of "discuss".

Table 5: MDT recommendation (n=29) v RS recommendation

1 patient had 2 tumours but only 1 recommendation; 1 patient not discussed.

	RS = no chemo	RS = yes chemo
MDT= yes chemo	9	0
MDT = no chemo	4	0
MDT = "discuss"	14	2

## Oncotype Dx v Adjuvant on line

For patients where AOL estimated additional survival benefit of CT to hormone therapy to be 0-3%, RS were L/I/H in 9/4 /1 patients; where AOL benefit estimated to be 3.1-5.0%, RS were L/I/H in 2/3 /1 patients; where AOL benefit estimated to be >5.1%, RS were L/I/H in 3/2/0 patients (6 patients unsuitable for AOL).

Table 6: Adjuvant on line estimate\* v RS

	RS = no chemo (L or I)	RS = yes chemo (H)
AOL 0-3% benefit	13	1
AOL 3.1-5.0% benefit	5	1
AOL >5.1% benefit	5	0

\*Additional benefit of chemotherapy over and above benefit of hormone therapy

Conversely, of the 15 tumours with a low RS, the projected survival benefit of CT over and above hormone therapy estimated by AOL version 8 ranged from 0.9-8.8%; for intermediate RS (n=8), AOL CT benefit: 0.4-5.9%; for RS high (n=2), AOL CT benefit was 2.9 and 5.4% (7 tumours unsuitable for AOL).

Table 7: RS results by AOL estimated survival benefit of CT (additional to HT)

	AOL estimate 0- 3.0%	3.1-5.0%	>5.1%
RS low	7	3	5
RS intermediate	3	1	4
RS high	1	0	1

Table 8: AOL predicted CT benefit by RS.

	RS = L (n=15)	RS = I (n=8)	RS = H (n=2)
AOL chemo benefit	0.9 -10.4%	0.4-9.4%	2.2-5.4%

## CONCLUSION:

The utility of Oncotype DX is unlikely to be prospectively tested for patients with low or high RS, whilst results for intermediate RS are being tested in the current TAILORx trial. Oncotype Dx appears to be a useful test in real life practice in helping patients and clinicians assess the potential benefit of adjuvant CT in addition to hormone therapy, and is unrelated to prediction from AOL. Oncotype Dx testing resulted in less chemotherapy being administered than is recommended by our current MDT. This is consistent with findings from other studies. Long term relapse and survival data is awaited.

## REFERENCES:

- <http://www.oncotypedx.com>
- <http://www.clinicaltrials.gov/ct2/results?term=TAILORx>
- [www.asco.org.au](http://www.asco.org.au) 2010 meeting abstracts

