

## **Discordance between Oncotype DX Recurrence Score and RSPC for predicting residual risk of recurrence of ER-positive breast cancer**

### **FIGURES AND TABLES**

#### **Table 1.**

Patient demographics and tumour characteristics. Percentages indicate the proportions of patients for age, menopausal status and number of involved nodes; for tumour size and grade percentages they are the proportions of cases. NPI, RS% and RSPC distributions for the whole study and for each centre individually are also given.

#### **Figure 1 (combined figure)**

*Chart.* The histogram shows cross-classification of cases by RS% and RSPC to each risk category. Case numbers were similar for RS% and RSPC with respect to intermediate-risk; however, the number of cases in the low-risk category was very noticeably higher when RS% was used to assign the risk compared to RSPC, and concomitantly, the number designated as high-risk very noticeably lower.

*Table.* Contingency table for risk category assignment. Agreement data are shown for all cases in the study and individually for centre-specific cases.

#### **Figure 2.**

Composite figure comprising three scatterplots showing the position of each patient with regard to their RS% and RSPC scores.

(a) shows patients for whom the recommendation was for endocrine treatment alone, indicated by blue circles at the intersection of the RS% and RSPC scores for that patient's tumour.

(b) shows patients in whom the recommendation was for the addition of chemotherapy to endocrine treatment, indicated by red circles.

(c) this scatterplot overlays both sets of cases as shown (a) and (b).

In all plots the green lines indicate boundaries between low-risk and intermediate-risk categories, while the red lines indicate those between intermediate-risk and high-risk; solid lines are applicable to RS% scores, dotted-lines to RSPC scores. The grey dotted line indicates the line of equality. The numbers in each sector are number of patients (note that due to overlying data points the number of points in the sector may not appear to agree with the figure shown).

**Table 2.**

Treatment recommendation according to RS%-designated risk category. Data are presented for the whole study and individually for each centre. A total of 149/174 (85.6%) patient's data were available for analysis (19 patients no treatment recommendation recorded, 6 were excluded for other reasons as detailed in the Results section); centre-specific case availability data are presented in Supplementary Table S1. Endo = endocrine treatment only, Chemo = endocrine treatment plus chemotherapy.

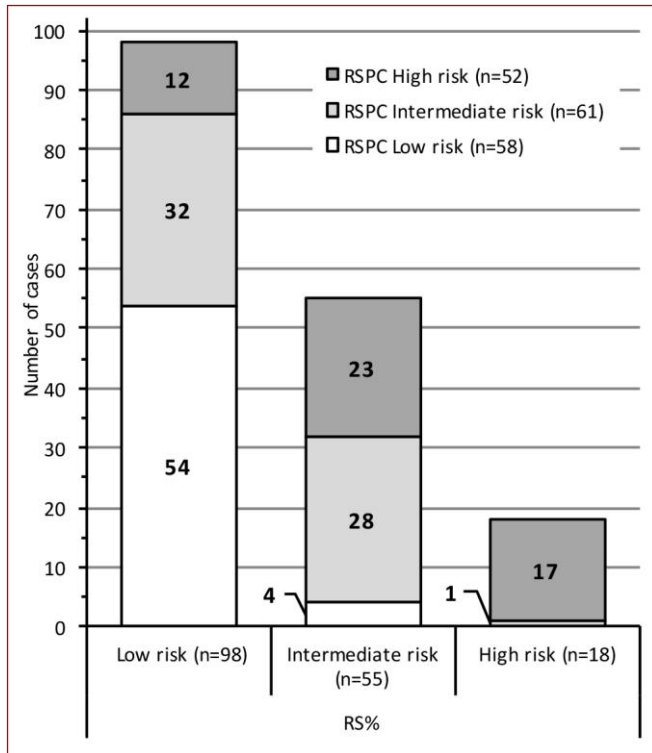
**Table 3.**

Cross-tabulation table for treatment recommendations according to RS% and RSPC designated risk category. A total of 149/174 (85.6%) patient's data were available for analysis (19 patients no treatment recommendation recorded, 6 were excluded for other reasons as detailed in the Results section); centre-specific case availability data are presented in Supplementary Table S1. Figures highlighted in red indicate cases that might be considered to represent the risk-category discrepant cases that have the most potential clinical impact.

## Discordance between RS and RSPC for predicting risk of recurrence in ER+ breast cancer

	All centres	Centre 1	Centre 2	Centre 3	Centre 4
<i>Gender</i>	<i>N patients (%)</i>				
Female	171 (98.3%)	37 (100.0%)	19 (95.0%)	92 (97.9%)	23 (100.0%)
Male	2 (1.1%)	0 (0%)	1 (5.0%)	1 (1.1%)	0 (0%)
Unknown	1 (0.6%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)
<i>Age at surgery (years)</i>	<i>Median (Range)</i>				
Age at surgery (years)	53 (24-78)	49 (33-74)	51 (37-72)	56 (24-78)	54 (38-74)
Unknown (N patients (%))	1 (0.6%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)
<i>Menopausal status</i>	<i>N patients (%)</i>				
Pre-menopausal	81 (46.6%)	24 (64.9%)	8 (40.0%)	38 (40.4%)	11 (47.8%)
Post-menopausal	86 (49.4%)	13 (35.1%)	10 (50.0%)	51 (54.3%)	12 (52.2%)
Peri-menopausal	2 (1.1%)	0 (0%)	1 (5.0%)	1 (1.1%)	0 (0%)
Not applicable (male)	2 (1.1%)	0 (0%)	1 (5.0%)	1 (1.1%)	0 (0%)
Unknown	3 (1.7%)	0 (0%)	0 (0%)	3 (3.2%)	0 (0%)
<i>Number of involved nodes</i>	<i>N patients (%)</i>				
N = 0	165 (94.8%)	35 (94.6%)	20 (100.0%)	88 (93.6%)	22 (95.6%)
N ≥1	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	1 (4.3%)
Micro-metastasis	7 (4.0%)	2 (5.4%)	0 (0%)	5 (5.3%)	0 (0%)
Unknown	1 (0.6%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)
<i>Tumour diameter (mm)</i>	<i>Median (Range)</i>				
Tumour diameter	23 (6-120)	18 (6-70)	25.5 (9-42)	25 (10-120)	20 (6-56)
	<i>N cases (%)</i>				
<10mm	6 (3.4%)	3 (8.1%)	1 (5.0%)	0 (0%)	2 (8.7%)
10 to 19	46 (26.0%)	20 (54.1%)	4 (20.0%)	16 (17.0%)	6 (26.1%)
20 to 29	62 (35.0%)	9 (24.3%)	8 (40.0%)	34 (36.2%)	11 (47.8%)
30 to 39	27 (15.3%)	2 (5.4%)	6 (30.0%)	16 (17.0%)	3 (13.0%)
40 to 49	17 (9.6%)	3 (8.1%)	1 (5.0%)	12 (12.8%)	1 (4.3%)
≥50	18 (10.2%)	2 (5.4%)	0 (0%)	15 (16.0%)	1 (4.3%)
Unknown	1 (0.6%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)
<i>Tumour Grade</i>	<i>Median (Range)</i>				
Tumour Grade	2 (1-3)	2 (2-3)	2 (2-3)	2 (1-3)	2 (2-3)
	<i>N cases (%)</i>				
Grade 1	2 (1.1%)	0 (0%)	0 (0%)	2 (2.1%)	0 (0%)
Grade 2	103 (58.2%)	23 (59.0%)	11 (55.0%)	53 (56.4%)	15 (65.2%)
Grade 3	71 (40.1%)	16 (41.0%)	9 (45.0%)	38 (40.4%)	8 (22.7%)
Unknown	1 (0.6%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)
<i>Prognostic Indices</i>	<i>Median (Range)</i>				
NPI	4.0 (2.4-5.4)	3.8 (3.1-4.9)	3.7 (3.4-4.8)	4.1 (2.4-5.4)	3.7 (3.1-4.7)
RS%	11% (3-34%)	11% (4-34%)	10% (3-30%)	11% (3-34%)	9% (5-23%)
RSPC	15% (4-63%)	14% (4-63%)	14% (5-33%)	18% (5-51%)	13 (6-31%)

TABLE 1.



**FIGURE 1. CHART (combine with Table to form single figure).**

		Risk assigned by RS%			Totals
		Low	Intermediate	High	
Risk assigned by RSPC	<i>All cases</i>				
	Low	<b>54 (31.6%)</b>	4 (2.3%)	0 (0%)	58 (33.9%)
	Intermediate	32 (18.7%)	<b>28 (16.4%)</b>	1 (0.6%)	61 (35.7%)
	High	12 (7.0%)	23 (13.5%)	<b>17 (9.9%)</b>	52 (30.4%)
	Totals	98 (57.3%)	55 (32.2%)	18 (10.5%)	171 (100%)
	<i>Centre 1</i>				
	Low	<b>15 (40.5%)</b>	2 (5.4%)	0 (0%)	17 (45.9%)
	Intermediate	5 (13.5%)	<b>6 (16.2%)</b>	0 (0%)	11 (29.7%)
	High	2 (5.4%)	3 (8.1%)	<b>4 (10.8%)</b>	9 (24.3%)
	Totals	22 (59.5%)	11 (29.7%)	4 (10.8%)	37 (100%)
	<i>Centre 2</i>				
	Low	<b>8 (40.0%)</b>	0 (0%)	0 (0%)	8 (40.0%)
	Intermediate	6 (30.0%)	<b>3 (15.0%)</b>	0 (0%)	9 (45.0%)
	High	0 (0%)	0 (0%)	<b>3 (15%)</b>	3 (15.0%)
	Totals	14 (70.0%)	3 (15.0%)	3 (15.0%)	20 (100%)
	<i>Centre 3</i>				
Low	<b>23 (25.3%)</b>	2 (2.2%)	0 (0%)	25 (27.5%)	
Intermediate	16 (17.6%)	<b>13 (14.3%)</b>	1 (1.1%)	30 (33.0%)	
High	9 (9.9%)	18 (19.8%)	<b>9 (9.9%)</b>	36 (39.6%)	
Totals	48 (52.7%)	33 (36.3%)	10 (11%)	91 (100%)	
<i>Centre 4</i>					
Low	<b>8 (34.8%)</b>	0 (0%)	0 (0%)	8 (34.8%)	
Intermediate	5 (21.7%)	<b>6 (26.1%)</b>	0 (0%)	11 (47.8%)	
High	1 (4.3%)	2 (8.7%)	<b>1 (4.3%)</b>	4 (17.4%)	
Totals	14 (60.9%)	8 (34.8%)	1 (4.3%)	23 (100%)	

FIGURE 1. TABLE (combine with Chart to form a single figure).

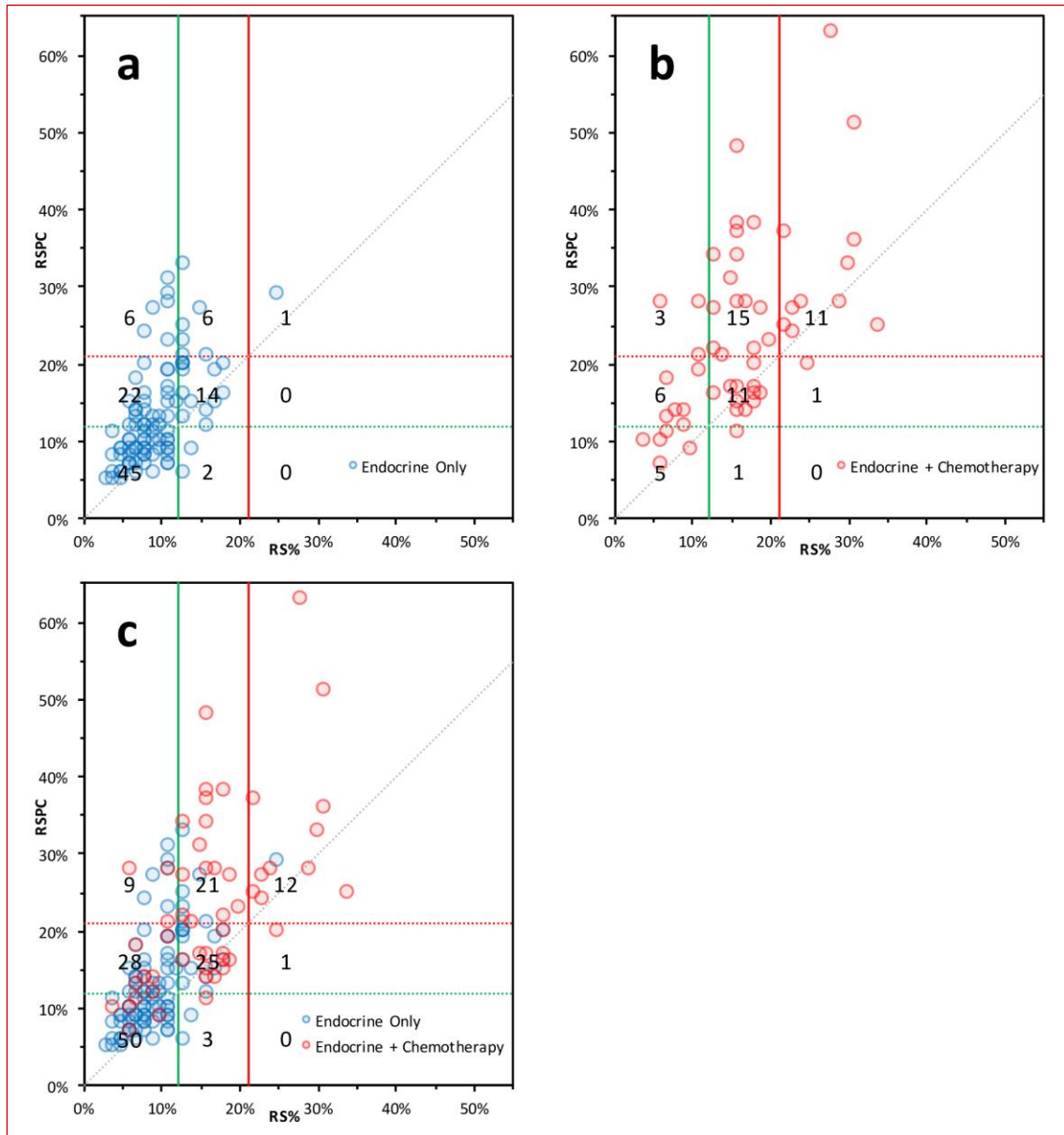


FIGURE 2.

Discordance between RS and RSPC for predicting risk of recurrence in ER+ breast cancer

Risk assigned using RS%	All patients			Centre 1			Centre 2			Centre 3			Centre 4		
	Endo	Chemo	Totals	Endo	Chemo	Totals	Endo	Chemo	Totals	Endo	Chemo	Totals	Endo	Chemo	Totals
Low	73 (49.0%)	14 (9.4%)	87 (58.4%)	20 (57.1%)	0 (0%)	20 (57.1%)	14 (70.0%)	0 (0.0%)	14 (70.0%)	28 (38.4%)	13 (17.8%)	41 (56.2%)	11 (52.4%)	1 (4.8%)	12 (57.1%)
Intermediate	22 (14.8%)	27 (18.1%)	49 (32.9%)	4 (11.4%)	7 (20.0%)	11 (31.4%)	0 (0.0%)	3 (15.0%)	3 (15.0%)	13 (17.8%)	14 (19.2%)	27 (37%)	5 (23.8%)	3 (14.3%)	8 (38.1%)
High	1 (0.7%)	12 (8.1%)	13 (8.7%)	0 (0%)	4 (11.4%)	4 (11.4%)	1 (5.0%)	2 (10.0%)	3 (15.0%)	0 (0%)	5 (6.8%)	5 (6.8%)	0 (0%)	1 (4.8%)	1 (4.8%)
Totals	96 (64.4%)	53 (35.6%)	149 (100%)	24 (68.6%)	11 (31.4%)	35 (100%)	15 (75.0%)	5 (25.0%)	20 (100%)	41 (56.2%)	32 (43.8%)	73 (100%)	16 (76.2%)	5 (23.8%)	21 (100%)

TABLE 2.



Discordance between RS and RSPC for predicting risk of recurrence in ER+ breast cancer

		Risk assigned by RS%						Totals	
		Low		Intermediate		High			
		Endo	Chemo	Endo	Chemo	Endo	Chemo	Endo	Chemo
Risk assigned by RSPC	<i>All patients</i>								
	Low	45 (30.2%)	5 (3.4%)	2 (1.3%)	1 (0.7%)	0 (0%)	0 (0%)	47 (31.5%)	6 (4.0%)
	Intermediate	<b>22 (14.8%)</b>	6 (4.0%)	14 (9.4%)	11 (7.4%)	0 (0%)	1 (0.7%)	36 (24.2%)	18 (12.1%)
	High	<b>6 (4.0%)</b>	3 (2.0%)	6 (4.0%)	15 (10.1%)	1 (0.7%)	11 (7.4%)	13 (8.7%)	29 (19.5%)
	Totals	73 (49.0%)	14 (9.4%)	22 (14.8%)	27 (18.1%)	1 (0.7%)	12 (8.1%)	96 (64.4%)	53 (35.6%)
	<i>Centre 1</i>								
	Low	13 (37.1%)	0 (0%)	2 (5.7%)	0 (0%)	0 (0%)	0 (0%)	15 (42.9%)	0 (0%)
	Intermediate	<b>5 (14.3%)</b>	0 (0%)	2 (5.7%)	4 (11.4%)	0 (0%)	0 (0%)	7 (20%)	4 (11.4%)
	High	<b>2 (5.7%)</b>	0 (0%)	0 (0%)	3 (8.6%)	0 (0%)	4 (11.4%)	2 (5.7%)	7 (20%)
	Totals	20 (57.1%)	0 (0%)	4 (11.4%)	7 (20%)	0 (0%)	4 (11.4%)	24 (68.6%)	11 (31.4%)
	<i>Centre 2</i>								
	Low	8 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (40%)	0 (0%)
	Intermediate	<b>6 (30%)</b>	0 (0%)	0 (0%)	3 (15%)	0 (0%)	0 (0%)	6 (30%)	3 (15%)
	High	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5%)	2 (10%)	1 (5%)	2 (10%)
	Totals	14 (70%)	0 (0%)	0 (0%)	3 (15%)	1 (5%)	2 (10%)	15 (75%)	5 (25%)
	<i>Centre 3</i>								
Low	16 (21.9%)	5 (6.8%)	0 (0%)	1 (1.4%)	0 (0%)	0 (0%)	16 (21.9%)	6 (8.2%)	
Intermediate	<b>9 (12.3%)</b>	5 (6.8%)	7 (9.6%)	3 (4.1%)	0 (0%)	1 (1.4%)	16 (21.9%)	9 (12.3%)	
High	<b>3 (4.1%)</b>	3 (4.1%)	6 (8.2%)	10 (13.7%)	0 (0%)	4 (5.5%)	9 (12.3%)	17 (23.3%)	
Totals	28 (38.4%)	13 (17.8%)	13 (17.8%)	14 (19.2%)	0 (0%)	5 (6.8%)	41 (56.2%)	32 (43.8%)	
<i>Centre 4</i>									
Low	8 (38.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (38.1%)	0 (0%)	
Intermediate	<b>2 (9.5%)</b>	1 (4.8%)	5 (23.8%)	1 (4.8%)	0 (0%)	0 (0%)	7 (33.3%)	2 (9.5%)	
High	<b>1 (4.8%)</b>	0 (0%)	0 (0%)	2 (9.5%)	0 (0%)	1 (4.8%)	1 (4.8%)	3 (14.3%)	
Totals	11 (52.4%)	1 (4.8%)	5 (23.8%)	3 (14.3%)	0 (0%)	1 (4.8%)	16 (76.2%)	5 (23.8%)	

**TABLE 3.**