Screening women at genetic risk of breast cancer using DCE-MRI: the effect of gene mutation status on detection sensitivity, specificity and cancer characteristics

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Introduction Women with a high risk of breast cancer due to a family history of breast cancer, or a known breast cancer gene mutation, such as BRCA1 or BRCA2, have a 45% - 65% chance of developing breast cancer by the age of 70, and approximately a 2-3% risk of developing cancer per annum between the ages of 35 and 50, compared with a normal population risk of about 0.1%. Recently a number of studies have reported that MRI is more sensitive than X-ray mammography (XRM) in women in such high risk groups, with an overall sensitivity of 71% (1) or 77% (2,3) for MRI compared with 40% (1,3) or 36% (2) for XRM. MRI has shown sensitivities of 81% when double read in a large multicentre study (3), 91% in a single centre study (2) or 95% in a six centre study (1). Combining MRI with XRM 86% (2), 89% (1) or 94% (3). These findings are leading to health providers considering provision of a screening service in high risk groups. Such decisions require consideration of which groups would benefit from such provision. In this study we present the evaluation of MRI and XRM sensitivity in three specific risk groups: tested BRCA1 mutation carriers, tested BRCA2 mutation carriers and women who did not test positive for either mutation.

Method Women were drawn from the MARIBS study, screened annually and assessed in accordance with the study protocol (3), with both MRI and XRM being double read blinded within and between modalities. All women were followed up for a minimum of one year. Women who had not previously been mutation tested provided blood samples such that they could not be linked or identified by those caring for the women. These were tested by Myriad in all cases were a cancer was detected in the study.

Results The results of the analysis, and the calculated sensitivities and specificities are detailed in the table, together with confidence limits and p-values for comparison of MRI with XRM. Data on the size, stage, receptor status and nodal status show differences between each of the groups.

Result	Cancers	Non-cancers	Sensitivity %	Specificity %	Sensitivity excl. DCIS* %	No. DCIS excluded
BRCA1						1
MRI +	12	76	92 (64-100)	79 (75-83)	100 (74-100)	
XRM +	3	30	23 (5-54)	92 (88-94)	25 (5.5-57)	
P-value for MRI vs XRM			P=0.004	P<0.0001		
Either MRI or XRM +	12	95	92 (64-100)	74 (69-78)		
BRCA2						3
MRI +	7	41	58 (28-84)	82 (77-87)	67 (30-93)	
XRM +	6	13	50 (21-79)	94 (91-97)	33 (7.5-70)	
P-value for MRI vs XRM			P=1.0	P=0.0001	P=0.45	
Either MRI or XRM +	11	51	92 (62-100)	78 (72-83)		
BR/OV FH						0
MRI +	8	1022	80 (44-97)	82 (80-84)		
XRM +	5	1171	50 (19-81)	94 (92-95)		
P-value for MRI vs XRM			P=0.45	P=0.0001		
Either MRI or XRM +	10	967	100	77 (75-80)		

Discussion and Conclusion MRI was most sensitive in women with BRCA1 mutations, where XRM led to no additional cases of cancer being detected. In this group XRM had a sensitivity of only 23%. Cancer in BRCA2 mutation carriers was less readily detected by by MRI, but MRI detected different lesions to those detected by XRM, and combined analysis led to an overall sensitivity of 92%. Some of the additional sensitivity of XRM was due to the higher level of DCIS in this group. BRCA2 tumours were oestrogen and progesterone receptor positive, the reverse of the receptor status in BRCA1 tumours. MRI was more sensitive in those women who tested negative to both BRCA1 and BRCA2, compared with those who were BRCA2 positive. Again MRI detected tumours not seen by XRM, and the comnbined sensitivity was 100%.
MRI is most sensitive in BRCA1 carriers, but for both other groups MRI detects tumours not seen by XRM, and in all cases a combined examination provides a sensitivity between 92% and 100%.

References

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