

Rapid HTA: Can Magnetic Resonance Imaging be Used to Screen Women at High Risk for Breast Cancer?

• service
• education
• research



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Introduction

Breast cancer has been the most common malignancy and the leading cause of cancer death among Singaporean women for the past 30 years. Currently, it accounts for 29.7% of all female cancers, with an age-standardized rate of 54.9 per 100,000 per year in 2006¹. Given that treatment at an early stage of the disease is effective and lead to better outcomes, there is a strong emphasis on breast screening in Singapore. Women at high risk of familial breast cancer tend to present at a younger age (mean age: early 40s). For them with a higher breast density it is difficult to detect lesions with X-ray mammography (XRM). The aggressive tumor growth rate requires a more sensitive screening regimen. We evaluate the evidence for using adjunctive MRI to XRM for the screening of high risk patients.

Objective

The objective of this rapid HTA is to evaluate the evidence for and against the use of adjunctive MRI to XRM for the screening of patients at high risk of breast cancer.

Population	Women with a BRCA gene mutation, a strong family history of breast cancer, or personal history of breast / ovarian cancer
Intervention	MRI+XRM
Comparison	XRM
Outcomes	sensitivity, specificity, cost-effectiveness

Results

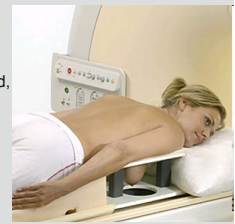
14 prospective studies, 1 systematic review, 6 reviews and 3 cost evaluation analyses were found. No RCTs were found. The systematic review, based on 11¹² of the 14 prospective studies, reported that MRI+XRM was the most sensitive method of detecting cancer in women at familial risk of breast cancer, with a higher sensitivity compared to XRM alone (80% – 100% vs 25% – 59%). However, the specificity of MRI+XRM appeared to be lower than XRM (73% – 93% vs 91% – 100%). It also performed some subgroup meta-analysis based on 10 of the prospective studies, which showed when a BI-RADS score of 3 or higher was used as the definition of positive, MRI+XRM was associated with the highest sensitivity (94% [95% CI: 90-97%]), compared with that of 84% (95% CI: 70-97%) for BI-RADS score of 4 or higher. The specificity for MRI+XRM was 77.2% (CI: 74.7-79.7%) and 95.2% (CI: 93.7-96.6%), respectively, compared with 86.3% (CI: 80.9-91.7%) and 96.1% (CI: 94.8-97.5%) for XRM alone. The 3 cost evaluation analyses¹⁶⁻¹⁸ showed the cost increased with lower risk level due to lower specificity (see Table 1). Table 1 also summarized 3¹³⁻¹⁵ of the 14 prospective studies, which were not included in the systematic review. The 6 reviews¹⁹⁻²⁴ shared the similar conclusion that despite its moderate specificity and high cost, MRI+XRM can be a valuable, sensitive and cost-effective tool for screening high risk women.

Methodology

A systematic search was conducted through PubMed, Medline, Embase and bibliographies of published articles.

Search Terms: [Magnetic Resonance Imaging / MRI] AND [Breast Cancer] AND [Screen*]

Inclusion criteria: Available in English and published from January 1995 to October 2009



Source: <http://myblip.files.wordpress.com/2009/12/breast-mri.jpg>

Ref.	Type of Study	Methodology	Population (N)	Results	Conclusion
Griebsch et al. (2006) ¹⁶	Cost-effectiveness analysis	• Perspective: the UK National Health Services • The measure of effectiveness: number of cancers detected, derived directly from a separate prospective multi-centre cohort study ⁶ • The measure of cost: direct cost based on mean costs and resources utilized from the effectiveness study ⁶	Women aged 35-49 at high genetic risk of breast cancer (N=649)	MRI+XRM resulted in an additional cost of £28284 per additional cancer detected compared to XRM alone. Based on the same data, MRI+XRM has an incremental cost per quality-adjusted life-year (QALY) saved compared to XRM ranging from £7003 to £48189, depending on the ages selected for MRI screening and the specific BRCA mutation.	MRI+XRM had a 67% probability of being cost-effective, when assuming a willingness-to-pay of £30000 per cancer detected.
Plevritis et al. (2006) ¹⁷	Cost-effectiveness analysis	• A computer model that simulates the life histories of individual BRCA1/2 mutation carriers, incorporating the effects of mammographic and MRI screening was used. • Both effectiveness and costs data were estimated on a combination of published literature and Medicare payments for 2005	--	The cost per QALY gained for women 35-54 years old was US\$55420 for BRCA1 mutation carriers and US\$130695 for BRCA2. MRI+XRM has a cost per QALY gained ranging from less than US\$45,000 to more than US\$700,000, depending on the ages selected for MRI and the specific BRCA mutation.	MRI+XRM is more cost-effective for BRCA1 than BRCA2 mutation carriers, where the extent varies greatly by age.
Taneja et al. (2009) ¹⁸	Cost-effectiveness analysis	• A model was developed to depict the lifetime consequences of screening with MRI and/or XRM	Cohorts of 10,000 women with BRCA1/2 mutations and women with other high-risk characteristics.	Compared with XRM alone, cost per QALY gained with MRI+XRM for women with BRCA1/2 mutations was US\$25,277. Among other high-risk women, cost per QALY gained with MRI+XRM varied depending on the prevalence of breast cancer, ranging from US\$45,566 (300 cases) to US\$310,616 (50 cases).	MRI+XRM, in women with BRCA1/2 mutations is cost effective compared with XRM alone. In women with other high-risk characteristics, MRI+XRM may also be cost effective, depending on the expected prevalence of undiagnosed breast cancer at the time of screening.
Weinstein et al. (2009) ¹⁵	Prospective comparative study	• Prospectively compare cancer detection of digital mammography (DM), whole-breast ultrasound (WBUS), and contrast-enhanced MRI in a high-risk screening population previously screened negative by film screen mammogram (FSM).	Asymptomatic high-risk women with nonactionable FSM examinations presented (N=609)	The cancer yield was 1.0% for FSM (6 of 597 women), 1.2% for DM (7 of 569 women), 0.53% for WBUS (3 of 567 women), and 2.1% for MRI (12 of 571 women). Of the 20 cancers detected, some were only detected on one modality (FSM: 1; DM: 3; WBUS: 1; MRI: 8)	The addition of MRI to mammography in the high-risk group has the greatest potential to detect additional mammographically occult cancers. The incremental cancer yield of WBUS and DM is much less.
Rubinstein et al. (2006) ¹⁴	Prospective pilot study	• Prospectively evaluated the addition of 0.5 Tesla MRI to conventional XRM	High risk women 25-49 years with dense breasts (N=30)	Medium-strength MRI detected 1 early breast tumor that was mammographically undetectable	MRI can enhance surveillance by XRM alone for young high-risk women with dense breasts
Podo et al. (2002) ¹³	Multi-centre, non-randomised, prospective study	• Prospectively evaluated the effectiveness of MRI, XRM and ultrasound (US) in a cohort of women at high risk.	High risk women aged 25-77 years (N=105)	All cancers (8/8) were identified by MRI, while XRM and US correctly classified only one. MRI had one false positive case, XRM and US none.	MRI is a very useful tool to screen subjects at high genetic risk with a low probability of false positive cases.

Conclusion

Despite the lack of RCT studies, current evidence strongly supports the addition of MRI to XRM for screening women at high risk of familial breast cancer, because of the early disease onset and breast density in this group. However, lower specificity can result in higher cost particularly in the lower risk group. There is however little information from longitudinal studies on the impact of the combined modality on survival.

References

1. Singapore Cancer Registry Report. Trends in Cancer Incidence in Singapore 2000-2006. National Registry of Diseases Office. 2. Hogen, A., Kristof, A., Maehle, L., Holman, M., Aasen, H., Stry, B. et al. (2007). Sensitivity of MRI versus conventional mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 3. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 4. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 5. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 6. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 7. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 8. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 9. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 10. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 11. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 12. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 13. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 14. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 15. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 16. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 17. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 18. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 19. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 20. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 21. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 22. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 23. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 24. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 25. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 26. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 27. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 28. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 29. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 30. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 31. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 32. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 33. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 34. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 35. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 36. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 37. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 38. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 39. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 40. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 41. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 42. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 43. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 44. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 45. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 46. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 47. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 48. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 49. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 50. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 51. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 52. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 53. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 54. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 55. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 56. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 57. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 58. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 59. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 60. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 61. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 62. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 63. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 64. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 65. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 66. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 67. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 68. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 69. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 70. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 71. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 72. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 73. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 74. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 75. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 76. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 77. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 78. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*, 16(2), 174-180. doi: 10.1054/breast.2007.012003. 79. Hogen, A., Kristof, A., Holman, M., Aasen, H., Stry, B., Wille, B., et al. (2007). Sensitivity of MRI versus mammography in the diagnosis of BRCA-associated breast cancer in a national population-based series. *Breast*