



EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Directorate F - Health, Consumers & Reference Materials (Ispra)
Health in Society

European Commission Initiative on Breast Cancer (ECIBC): European guidelines on breast cancer screening and diagnosis Evidence profile

| | |
|----------------------------|---|
| Healthcare question | Should tailored screening with magnetic resonance imaging, in addition to digital mammography vs. digital mammography alone be used for early detection of breast cancer in asymptomatic women with high mammographic breast density in organised screening programmes? |
| Date | January 2020 |
| Authors | Guideline Development Group (GDG): Guideline Development Group (GDG): Mariangela Autelitano, Bettina Borisch, Mireille Broeders, Xavier Castells, Edoardo Colzani, Jan Daneš, Stephen Duffy, Patricia Fitzpatrick, Markus Follmann, Livia Giordano, Paolo Giorgi Rossi, Axel Gräwingholt, Solveig Hofvind, Lydia Ioannidou-Mouzaka, Susan Knox, Miranda Langendam, Annette Lebeau, Helen McGarrigle, Lennarth Nyström, Elsa Pérez Gómez, Cecily Quinn, Holger Schünemann, Alberto Torresin, Ruben Van Engen, Cary Van Landsveld-Verhoeven, Sue Warman, Kenneth Young. Systematic Review team: Carlos Canelo-Aybar, Jessica Beltran, Ingrid Arévalo-Rodríguez, Ignacio Ricci, Ivan Solá, Nieves Plana, Margarita Posso, David Rigau, Pablo Alonso-Coello. JRC Healthcare Quality team: Zuleika Saz-Parkinson, Elena Parmelli |
| Abbreviations | CI: Confidence interval RR: Risk ratio |

| Certainty assessment | | | | | | | Nº of patients | | Effect | | Certainty | Importance |
|---|------------------------------------|------------------------|----------------------|--------------------------|--------------------------|----------------------|--|---------------------------|-------------------------------------|---|-------------|------------|
| Nº of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Tailored screening with magnetic resonance imaging (MRI), in addition to mammography | Digital mammography alone | Relative (95% CI) | Absolute (95% CI) | | |
| Breast cancer detection - incremental (all lesions) | | | | | | | | | | | | |
| 7 1,2,3,4,5,6,7 | observational studies ^a | not serious | serious ^b | serious ^c | not serious | none | 1,819 more per 100,000 examinations (95% CI 1,012 more to 2,837 more). Population 9,876 exams | | | ⊕⊕○○ LOW | CRITICAL | |
| Breast cancer detection - incremental (invasive) | | | | | | | | | | | | |
| 6 1,3,4,5,6,7 | observational studies ^a | not serious | not serious | serious ^c | not serious | none | 1,323 more per 100,000 examinations (95% CI 1,073 more to 1,596 more). Population 8,153 exams. | | | ⊕⊕⊕○ MODERATE | CRITICAL | |
| Adverse effects (False positive recall - incremental) | | | | | | | | | | | | |
| 7 1,2,3,4,5,6,7 | observational studies | not serious | serious ^b | serious ^c | not serious | none | 9,972 more per 100,000 exams (95%CI 6,533 more to 14,032 more). Population 9,709. | | | ⊕⊕○○ LOW | CRITICAL | |
| Interval cancer - Per protocol (undergone MRI) | | | | | | | | | | | | |
| 3 ^{1,2,6} | observational studies ^e | serious ^{d,f} | not serious | serious ^{c,g} | not serious ^h | none | 6/6046 (0.1%) | 178/34320 (0.5%) | RR 0.19 (0.09 to 0.43) ⁱ | 420 fewer per 100,000 (from 472 fewer to 296 fewer) | ⊕⊕○○ LOW | CRITICAL |
| Serious adverse effects (During or immediately after MRI) | | | | | | | | | | | | |
| 1 ¹ | randomised trials ^j | not serious | not serious | not serious ^g | serious ^k | none | 104 more per 100,000 MRI examinations (0 more to 200 more) (5/4783) ^l | | | ⊕⊕⊕○ MODERATE | CRITICAL | |
| Provision of chemotherapy - not measured | | | | | | | | | | | | |
| - | - | - | - | - | - | - | | | | - | CRITICAL | |
| Breast cancer mortality - not measured | | | | | | | | | | | | |
| - | - | - | - | - | - | - | | | | - | CRITICAL | |
| Breast cancer stage - not measured | | | | | | | | | | | | |
| - | - | - | - | - | - | - | | | | - | CRITICAL | |
| Mastectomy - not measured | | | | | | | | | | | | |
| - | - | - | - | - | - | - | | | | - | CRITICAL | |

Explanations

- a. Cohort diagnostic studies that provided incremental information on participants with negative mammography. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool.
- b. Relevant unexplained heterogeneity across studies
- c. Included studies recruited participants that had additional risk factors and/or were younger than the average participant in a organized screening program. None of the participants from the included study had personal history of breast cancer or were BRCA mutation carriers.
- d. Cohort diagnostic studies, with a paired assessment. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool.
- e. The reading of index tests were blinded from each other. No information about the previous readers experience (Kriege 2006, Berg 2012)
- f. Imprecise estimates due to low number of events.
- g. One RCT (FaMRIsc) compared annual MRI plus annual breast clinical examination (BCE) + biennial mammography Vs. annual breast clinical examination (BCE) + annual mammography. Participants had familiar history of breast cancer. The RR for BCDR was 2.14 (95% CI 1.09 to 4.20) (Saadatmand 2019)
- h. The estimated absolute number of events are imprecise for this outcome.
- i. One RCT (FaMRIsc) compared annual MRI plus annual breast clinical examination (BCE) + biennial mammography Vs. annual breast clinical examination (BCE) + annual mammography. Participants had familiar history of breast cancer. The RR for FPR was 1.61 (95% CI 1.37 to 1.90) (Saadatmand 2019)
- j. Cohort diagnostic studies, with a paired assessment and one study with random allocation of the index tests. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool.
- k. In one study, the 40% of participants allocated to the MRI arm did not accepted the intervention (Bakker 2019)
- l. One study included only patients with extremely dense breast tissue, which roughly represents the 10% of the population (Bakker 2019)
- m. Imprecise estimates due to low number of events, but the range of possible absolute events is below the clinical decision threshold.
- n. One RCT (FaMRIsc) compared annual MRI plus annual breast clinical examination (BCE) + biennial mammography Vs. annual breast clinical examination (BCE) + annual mammography. Participants had familiar history of breast cancer. The RR for ICR was 0.71 (95% CI 0.06 to 7.88) (Saadatmand 2019)
- o. A diagnostic study with random allocation of the index tests. The risk of bias was assessed using an ad-hoc modified QUADAS-2 tool.
- p. Low number of events in each arms.
- q. The RCT estimated the outcomes as incremental events in the MRI arm. The baseline number of events in the mammography arm were not reported.

References

- 1. Bakker MF, de Lange SV, Pijnappel RM, Mann RM, Peeters PHM, Monninkhof EM, Emaus MJ, for the DENSE Trial Study Group. Supplemental MRI Screening for Women with Extremely Dense Breast Tissue. NEJM; 2019.
- 2. M, Kriege. Factors affecting sensitivity and specificity of screening mammography and MRI in women with an inherited risk for breast cancer. Breast Cancer Res Treat; 2006.
- 3. Kuhl CK, Schrading S, Strobel K, Schild HH, Hilgers RD, Bieling HB. Abbreviated Breast Magnetic Resonance Imaging (MRI): First Postcontrast Subtracted Images and Maximum-Intensity Projection-A Novel Approach to Breast Cancer Screening With MRI. J Clin Oncol; 2014.

4. Chen SQ, Huang M, Shen YY, Liu CL, Xu CX. Application of Abbreviated Protocol of Magnetic Resonance Imaging for Breast Cancer Screening in Dense Breast Tissue. Acad Radiol; 2017.
5. Kuhl CK, Strobil K, Bieling H, Leutner C, Schild HH, Schradingb S. Supplemental Breast MR Imaging Screening of Women with Average Risk of Breast Cancer. Radiology; 2017.
6. Berg WA, Zhang Z, Lehrer D, Jong RA, Pisano ED, Barr RG, et al. Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. JAMA ; 2012.
7. Strahle D, Pathak D, Sierra A, Saha S, Strahle C, Devisetty K. Systematic development of an abbreviated protocol for screening breast magnetic resonance imaging. Breast Cancer Res Treat; 2017.