



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

QUESTION	
Should additional magnetic resonance imaging vs. no additional magnetic resonance imaging be used in women with histologically confirmed ductal carcinoma in situ for preoperative planning?	
POPULATION:	women with histologically confirmed ductal carcinoma in situ (DCIS)
INTERVENTION:	additional magnetic resonance imaging
COMPARISON:	no additional magnetic resonance imaging
MAIN OUTCOMES:	MRI triggered treatment change (from breast conservative to mastectomy or from unilateral to bilateral mastectomy rate); Initial breast conservative surgery (BCS); Proportion of re-operation after BCS (re-excision or conversion to mastectomy); Proportion of positive margins after BCS; Mastectomy; Disease-free survival (inferred from loco-regional recurrence); Quality of life; Direct adverse events.
SETTING:	European Union
PERSPECTIVE:	Population (National Health System)
BACKGROUND:	<p>Ductal carcinoma in situ (DCIS) is the most common form of non-invasive breast cancer. DCIS of the breast represents a heterogeneous group of malignant cells confined within the basement membrane of the ductal epithelium (1). In the last years detection of DCIS has increased, mostly attributed to the widespread use of screening mammography, as this type of lesions accounts nowadays for 20 to 25 percent of new breast cancer diagnosis (2).</p> <p>After detection, breast conservative surgery (BCS) has been adopted as a treatment option for patients with small, screen detectable lesions (3). Also, the addition of adjuvant radiation or hormonal therapy after BCS has been shown to reduce the risk of invasive recurrence (3). Given the number of options of surgical and adjuvant treatments, there is a growing interest in a better assessment of the disease extension to adequately tailor the treatment of the patients.</p> <p>Theoretically, the use of additional magnetic resonance imaging (MRI) after standard mammography may improve the definition of DCIS extension during the preoperative planning and potentially reducing the need for additional surgery after BCS, especially in the context of extensive microcalcification. Nevertheless, the role of MRI in management of DCIS remains unclear, while some studies show high sensitivity compared to mammography other studies suggest that MRI has no advantages for local control of DCIS or even might overestimate the extent of disease leading to an increase in the number of unnecessary surgical biopsies (4)(5) or mastectomies.</p> <p>Thus, whether the use of preoperative MRI in these patients translates to clinical advantages or to a positive balance between benefits and harms remains unclear.</p>

CONFLICT OF INTEREST:	<p><u>Management of Conflicts of Interest (Col):</u> Cols for all Guidelines Development Group (GDG) members were assessed and managed by the Joint Research Centre (JRC) following an established procedure in line with European Commission rules. GDG member participation in the development of the recommendations was restricted, according to Col disclosure. Consequently, for this particular question, the following GDG members were recused from voting: Axel Gräwingholt. Edoardo Colzani, Markus Follman, and Kenneth Young were not allowed to vote because they didn't fill in the Dol for this specific question. Miranda Langendam was not allowed to vote due to the established rules for external experts.</p> <p>For more information please visit https://healthcare-quality.jrc.ec.europa.eu/discover-ecibc/governance/ecibc-working-groups</p>
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ASSESSMENT

Problem







Is the problem a priority?




JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know 	<p>Ductal carcinoma in situ (DCIS) is the most common form of non-invasive breast cancer. DCIS of the breast represents a heterogeneous group of malignant cells confined within the basement membrane of the ductal epithelium (1). In the last years detection of DCIS has increased, mostly attributed to the widespread use of screening mammography, as this type of lesions accounts nowadays for 20 to 25 percent of new breast cancer diagnosis (2).</p> <p>Thus, whether the use of preoperative MRI in these patients translates to clinical advantages or to a positive balance between benefits and harms remains unclear.</p>	The GDG prioritized this question for the ECIBC.

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE					ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know 	Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	<p>The GDG agreed that the desirable outcomes are: MRI triggered treatment change (from breast conservative to mastectomy or from unilateral to bilateral mastectomy rate); Initial breast conservative surgery (BCS); Disease-free survival (inferred from loco-regional recurrence); Quality of life.</p> <p>The GDG judged that the desirable effects are trivial.</p> <p>The results of the surgical and clinical outcomes were complemented with data on accuracy (detection of lesions, size correlation, or under/oversize estimation) reported in the same included studies.</p> <p>We did not found studies reporting in QoL. But a</p>
	Initial BCS - RCT	80	⊕○○○	RR 1.05	<div>Risk with no additional magnetic resonance imaging</div> <div>Risk difference with additional magnetic resonance imaging</div>	

	(1 RCT) ¹	VERY LOW ^{a,b,c}	(0.77 to 1.42)	659 per 1000	33 more per 1000 (151 fewer to 277 more)	<p>judgement about this outcome might be inferred from initial BCS, total mastectomy and loco-regional recurrence estimates.</p> <p>The included randomized clinical trials (RCT) were not designed to assess the clinical question of interest. The extracted data come from subgroups of the reported results and thus are highly imprecise and subject to selection bias.</p> <p>The body evidence includes results from observational studies (cohorts) given the limitations of the identified RCTs.</p> <p>The certainty of evidence was very low, there was no data to support a potential benefit from the intervention.</p>
Initial BCS - Cohorts	3991 (7 observational studies) ^{2,3,4,5,6,7,8}	 VERY LOW ^{d,e,f}	OR 0.45 (0.27 to 0.76)	Study population		
				759 per 1000	173 fewer per 1000 (299 fewer to 54 fewer)	
Proportion of positive margins after BCS - RCT	91 (1 RCT) ⁹	 VERY LOW ^{b,c,g}	RR 1.58 (0.85 to 2.92)	Study population		
				250 per 1000	145 more per 1000 (38 fewer to 480 more)	
Proportion of positive margins after BCS - Cohorts	3212 (6 observational studies) ^{10,11,2,5,8}	 VERY LOW ^{d,e,f}	OR 0.95 (0.67 to 1.35)	Study population		
				185 per 1000	8 fewer per 1000 (53 fewer to 50 more)	
Proportion of re-operation after BCS (Re-operation rate) - RCT	55 (1 RCT) ¹	 VERY LOW ^{b,c}	RR 1.44 (0.79 to 2.64)	Study population		
				370 per 1000	163 more per 1000 (78 fewer to 607 more)	
Proportion of re-operation after BCS (Re-operation rate) - Cohorts	1654 (10 observational studies) ^{11,12,2,3,6,7,8}	 VERY LOW ^{d,e,f}	OR 0.97 (0.63 to 1.48)	Study population		
				237 per 1000	5 fewer per 1000 (73 fewer to 78 more)	
Mastectomy (total mastectomy rate) - RCT	80 (1 RCT) ¹	 VERY LOW ^{b,c}	RR 0.79 (0.48 to 1.31)	Study population		
				488 per 1000	102 fewer per 1000 (254 fewer to 151 more)	

Mastectomy (total mastectomy rate) - Cohorts	1283 (4 observational studies) ^{11,2,3,7,8}	 VERY LOW ^{d,e,f}	OR 1.59 (0.90 to 2.81)	Study population	
				235 per 1000	93 more per 1000 (18 fewer to 228 more)
Disease free survival (inferred from locoregional recurrence) - Cohorts	2347 (2 observational studies) ^{10,13}	 VERY LOW ^{h,i,j}	OR 1.17 (0.79 to 1.73)	Study population	
				82 per 1000	13 more per 1000 (16 fewer to 52 more)
MRI triggered treatment change - Cohort	750 (6 observational studies) ^{14,15,16,17,18,3}	 LOW	-	The pooled proportion of treatment change was 19% (95% CI 13% to 24%; I2 67%). (n/N= 127/750).	
Quality of Life - not reported	-	-	-	-	-
Direct adverse events - not reported	-	-	-	-	-

1. Peters NH, van Esser S, van den Bosch MA, Storm RK, Plaisier PW, van Dalen T, Diepstraten SC, Weits T, Westenend PJ, Stapper G, Fernandez-Gallardo MA, Borel Rinkes IH, van Hillegersberg R, Mali WP, Peeters PH.. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: the MONET - randomised controlled trial. Eur J Cancer; 2011.
2. Vos, E. L., Voogd, A. C., Verhoef, C., Siesling, S., Obdeijn, I. M., Koppert, L. B.. Benefits of preoperative MRI in breast cancer surgery studied in a large population-based cancer registry. Br J Surg; Dec 2015.
3. Pilewskie M, Kennedy C, Shappell C, Helenowski I, Scholtens D, Hansen N, Bethke K, Jeruss J., Karstaedt, P., Khan, S. A.. Effect of MRI on the management of ductal carcinoma in situ of the breast. Ann Surg Oncol; 2013.
4. Onega T, Weiss JE, Goodrich ME, Zhu W, DeMartini WB, Kerlikowske K, Ozanne E, Tosteson A. N. A., Henderson, L. M., Buist, D. S. M., Wernli, K. J., Herschorn, S. D., Hotaling, E., O'Donoghue, C., Hubbard, R.. Relationship between preoperative breast MRI and surgical treatment of non-metastatic breast cancer. J Surg Oncol; 2017.
5. Itakura K, Lessing J, Sakata T, Heinzerling A, Vriens E, Wisner D, Alvarado M, Esserman L, Ewing C, Hylton N, Hwang ES.. The impact of preoperative magnetic resonance imaging on surgical treatment and outcomes for ductal carcinoma in situ. Clin Breast Cancer; 2011.
6. Hajaj, M., Karim, A., Pascaline, S., Noor, L., Patel, S., Dakka, M.. Impact of MRI on high grade Ductal Carcinoma In situ (HG DCIS) management, are we using the full scope of MRI?. Eur J Radiol; Oct 2017.
7. Davis, K. L., Barth, R. J., Jr., Gui, J., Dann, E., Eisenberg, B., Rosenkranz, K.. Use





	<p>of MRI in preoperative planning for women with newly diagnosed DCIS: risk or benefit?. Ann Surg Oncol; Oct 2012.</p> <ol style="list-style-type: none"> 8. Allen, L. R., Lago-Toro, C. E., Hughes, J. H., Careaga, E., Brown, A. T., Chernick, M., Barrio, A. V., Frazier, T. G.. Is there a role for MRI in the preoperative assessment of patients with DCIS?. Ann Surg Oncol; Sep 2010. 9. Turnbull, L. W., Brown, S. R., Olivier, C., Harvey, I., Brown, J., Drew, P., Hanby, A., Manca, A., Napp, V., Sculpher, M., Walker, L. G., Walker, S.. Multicentre randomised controlled trial examining the cost-effectiveness of contrast-enhanced high field magnetic resonance imaging in women with primary breast cancer scheduled for wide local excision (COMICE). Health Technol Assess; Jan 2010. 10. Pilewskie, M., Olcese, C., Eaton, A., Patil, S., Morris, E., Morrow, M., Van Zee, K. J.. Perioperative breast MRI is not associated with lower locoregional recurrence rates in DCIS patients treated with or without radiation. Ann Surg Oncol; May 2014. 11. Kropcho, L. C., Steen, S. T., Chung, A. P., Sim, M. S., Kirsch, D. L., Giuliano, A. E.. Preoperative breast MRI in the surgical treatment of ductal carcinoma in situ. Breast J; Mar-Apr 2012. 12. So, A., De La Cruz, L. M., Williams, A. D., Bahng, J., Liao, G., McDonald, E. S., Fisher, C. S., Czerniecki, B. J., Sataloff, D., Tchou, J.. The impact of preoperative magnetic resonance imaging and lumpectomy cavity shavings on re-excision rate in pure ductal carcinoma in situ-A single institution's experience. J Surg Oncol; Mar 2018. 13. Vapiwala N, Hwang WT, Kushner CJ, Schnall MD, Freedman GM, Solin LJ.. No impact of breast magnetic resonance imaging on 15-year outcomes in patients with ductal carcinoma in situ or early-stage invasive breast cancer managed with breast conservation therapy. Cancer; 2017. 14. Pettit, K., Swatske, M. E., Gao, F., Salavaggione, L., Gillanders, W. E., Aft, R. L., Monsees, B. S., Eberlein, T. J., Margenthaler, J. A.. The impact of breast MRI on surgical decision-making: are patients at risk for mastectomy?. J Surg Oncol; Dec 1 2009. 15. Obdeijn IM, Tilanus-Linthorst MM, Spronk S, van Deurzen CH, de Monye C, Hunink MG, Menke MB.. Preoperative breast MRI can reduce the rate of tumor-positive resection margins and reoperations in patients undergoing breast-conserving surgery. AJR Am J Roentgenol; 2013. 16. Lee, J., Jung, J. H., Kim, W. W., Hwang, S. O., Kim, H. J., Park, J. Y., Chae, Y. S., Yang, J. D., Park, H. Y.. The role of preoperative breast magnetic resonance (MR) imaging for surgical decision in patients with triple-negative breast cancer. J Surg Oncol; Jan 2016. 17. Hlubocky, J., Bhavnagri, S., Swinford, A., Mitri, C., Rebner, M., Pai, V.. Does the use of pretreatment MRI change the management of patients with newly diagnosed breast cancer?. Breast J; Nov 5 2017. 18. Duygulu G, Oktay A, Bilgen IG, Kapkaç M, Zekioğlu O.. The role of breast MRI in planning the surgical treatment of breast cancer. Diagn Interv Radiol; 2012. <ol style="list-style-type: none"> a. Downgraded due that initial BCS is not an end outcome, as later women might have received re-excision or a mastectomy depending on the status of operative margins. b. The number of events from the patients recruited in each arm is much lower than the minimum required to have adequate power. c. The intervention (preoperative MRI) was not feasible to be blinded which originated a performance high risk of bias which might have impacted on the surgeon initial planning decision. d. In some cohort studies, the comparison was between arms over different periods of time (no overlapping), and thus potentially introducing a high risk of secular bias. 	
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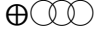




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| | <ul style="list-style-type: none">e. The majority of studies reported measurement of association as crude estimates or it had to be calculated from crude numbers.f. There is a high heterogeneity in the estimated effect across the included studies ranging from significant benefit to harm.g. The definition of positive margins was variable across the different clinical centres included (distance from operative margins) this might have introduced a misclassification bias.h. Downgraded due to be a surrogate outcome of disease-free survival.i. A proportion of patients had breast MRI performed after lumpectomy or at re-excision stage which does not directly apply to the clinical pathway of interest.j. The confidence interval of the effect size ranged from significant benefit to harm. | |
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Accuracy results from included studies			
Study Id	N patients	Diagnostic outcomes	Clinical outcomes
Pilewskie 2012*	352	Multifocal abnormality seen: MM: 15.3%; MRI: 32.6%	
		Bilateral abnormality seen: MM: 6.5%; MRI: 25.7%	Initial BCS: OR 0.71 (0.45 to 1.14).
			Re-excision rate: OR 0.67 (0.38 to 1.18).
		Accurate size estimation: MM: 52.1%; MRI: 41.1%	Total mastectomy rate: OR 1.52 (0.95 to 2.41)
		Size underestimation by 1 cm or more: MM: 13.2%; MRI: 15%	Treatment change: 15% (11% to 21%)
Hajaj 2017*	122	MRI showed a better histological size correlation compared to MM.	Size overestimated by 1 cm or more: MM: 34.7%; MRI: 43.9%
			Initial BCS: OR 0.04 (0.01 to 0.17).
Davis 2012	218	Identification of additional lesions: 26/154 (16.9%; 10 were biopsy-confirmed and 8 lead to wider lumpectomy).	Re-excision rate: OR 0.55 (0.19 to 1.62).
			Initial BCS: OR 0.88 (0.42 to 1.84).
			Re-excision rate: OR 0.92 (0.48 to 1.78).
		Detection of invasive contralateral lesions: 4.5% (2 invasive, 5 DCIS)	Total mastectomy rate: OR 1.27 (0.64 to 2.49)
*the comparison was not made over the same samples as the MRI arm is made of about 60% of the subjects included in the mammography arm.			

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE						ADDITIONAL CONSIDERATIONS
<div>○ Large</div> <div>● Moderate</div> <div>○ Small</div> <div>○ Trivial</div> <div>○ Varies</div> <div>○ Don't know</div>	Outcomes	Nº of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		
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					185 per 1000	8 fewer per 1000 (53 fewer to 50 more)	
The GDG agreed that the undesirable outcomes are: Proportion of re-operation after BCS (re-excision or conversion to mastectomy); Proportion of positive margins after BCS; Mastectomy; Direct adverse events.							
The GDG judged that the undesirable effects are moderate.							
A systematic review about the role of preoperative MRI versus no-MRI in all breast cancer histology suggested an unfavourable harm-benefit ratio for routine use of preoperative MRI in the management of breast cancer (MRI significantly increased mastectomy rates - adjusted OR, 1.51, <i>P</i> < 0.001-) (Houssami 2013).							

	Proportion of re-operation after BCS (Re-operation rate) - RCT	55 (1 RCT) ¹	 VERY LOW ^{b,c}	RR 1.44 (0.79 to 2.64)	Study population	
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	Quality of Life - not reported	-	-	-	-	-
	Direct adverse events - not reported	-	-	-	-	-

1. Peters NH, van Esser S, van den Bosch MA, Storm RK, Plaisier PW, van Dalen T, Diepstraten SC, Weits T, Westenend PJ, Stapper G, Fernandez-Gallardo MA, Borel Rinkes IH, van Hillegersberg R, Mali WP, Peeters PH.. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: the MONET - randomised controlled trial. *Eur J Cancer*; 2011.
2. Vos, E. L., Voogd, A. C., Verhoef, C., Siesling, S., Obdeijn, I. M., Koppert, L. B.. Benefits of preoperative MRI in breast cancer surgery studied in a large population-based cancer registry. *Br J Surg*; Dec 2015.
3. Pilewskie M, Kennedy C, Shappell C, Helenowski I, Scholtens D, Hansen N, Bethke K, Jeruss J., Karstaedt, P., Khan, S. A.. Effect of MRI on the management of ductal carcinoma in situ of the breast. *Ann Surg Oncol*; 2013.
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12. So, A., De La Cruz, L. M., Williams, A. D., Bahng, J., Liao, G., McDonald, E. S., Fisher, C. S., Czerniecki, B. J., Sataloff, D., Tchou, J.. The impact of preoperative magnetic resonance imaging and lumpectomy cavity shavings on re-excision rate in pure ductal carcinoma in situ-A single institution's experience. *J Surg Oncol*; Mar 2018.
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	<p>2009.</p> <ol style="list-style-type: none"> 15. Obdeijn IM, Tilanus-Linthorst MM, Spronk S, van Deurzen CH, de Monye C, Hunink MG, Menke MB.. Preoperative breast MRI can reduce the rate of tumor-positive resection margins and reoperations in patients undergoing breast-conserving surgery. <i>AJR Am J Roentgenol</i>; 2013. 16. Lee, J., Jung, J. H., Kim, W. W., Hwang, S. O., Kim, H. J., Park, J. Y., Chae, Y. S., Yang, J. D., Park, H. Y.. The role of preoperative breast magnetic resonance (MR) imaging for surgical decision in patients with triple-negative breast cancer. <i>J Surg Oncol</i>; Jan 2016. 17. Hlubocky, J., Bhavnagri, S., Swinford, A., Mitri, C., Rebner, M., Pai, V.. Does the use of pretreatment MRI change the management of patients with newly diagnosed breast cancer?. <i>Breast J</i>; Nov 5 2017. 18. Duygulu G, Oktay A, Bilgen IG, Kapkaç M, Zekioğlu O.. The role of breast MRI in planning the surgical treatment of breast cancer. <i>Diagn Interv Radiol</i>; 2012. <ol style="list-style-type: none"> a. Downgraded due that initial BCS is not an end outcome, as later women might have received re-excision or a mastectomy depending on the status of operative margins. b. The number of events from the patients recruited in each arm is much lower than the minimum required to have adequate power. c. The intervention (preoperative MRI) was not feasible to be blinded which originated a performance high risk of bias which might have impacted on the surgeon initial planning decision. d. In some cohort studies, the comparison was between arms over different periods of time (no overlapping), and thus potentially introducing a high risk of secular bias. e. The majority of studies reported measurement of association as crude estimates or it had to be calculated from crude numbers. f. There is a high heterogeneity in the estimated effect across the included studies ranging from significant benefit to harm. g. The definition of positive margins was variable across the different clinical centres included (distance from operative margins) this might have introduced a misclassification bias. h. Downgraded due to be a surrogate outcome of disease-free survival. i. A proportion of patients had breast MRI performed after lumpectomy or at re-excision stage which does not directly apply to the clinical pathway of interest. j. The confidence interval of the effect size ranged from significant benefit to harm. 	
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Accuracy results from included studies			
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		Bilateral abnormality seen: MM: 6.5%; MRI: 25.7%	Initial BCS: OR 0.71 (0.45 to 1.14).
			Re-excision rate: OR 0.67 (0.38 to 1.18).
		Accurate size estimation: MM: 52.1%; MRI: 41.1%	Total mastectomy rate: OR 1.52 (0.95 to 2.41)
		Size underestimation by 1 cm or more: MM: 13.2%; MRI: 15%	Treatment change: 15% (11% to 21%)
Hajaj 2017*	122	Size overestimated by 1 cm or more: MM: 34.7%; MRI: 43.9%	
		MRI showed a better histological size correlation compared to MM.	Initial BCS: OR 0.04 (0.01 to 0.17).
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			Re-excision rate: OR 0.92 (0.48 to 1.78).
		Detection of invasive contralateral lesions: 4.5% (2 invasive, 5 DCIS)	Total mastectomy rate: OR 1.27 (0.64 to 2.49)
*the comparison was not made over the same samples as the MRI arm is made of about 60% of the subjects included in the mammography arm.			

Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Very low ○ Low ○ Moderate ○ High ○ No included studies 		The overall certainty of the evidence of effects is very low.

Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes 	No research evidence was identified	The GDG judged that there may be important uncertainty or variability in how much women would value the main outcomes. Better mastectomy and reconstructive surgery may change the values placed on it, but conservative surgery will be preferred by others, depending on the availability of post-surgical radiation therapy.

Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Favors the comparison ● Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know 		The GDG judged that the balance of effects probably favours the comparison.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS																												
<div><div>○ Large costs</div><div>● Moderate costs</div><div>○ Negligible costs and savings</div><div>○ Moderate savings</div><div>○ Large savings</div><div>○ Varies</div><div>○ Don't know</div></div>	<div><div>Median cost of diagnostic/preopeartive workup* for women with Stage 0 Breast Cancer.</div><div><table><thead><tr><th>Study ID</th><th>Country</th><th>Year-value</th><th>With MRI</th><th>Without MRI</th><th>Increment</th><th>Quality</th></tr></thead><tbody><tr><td colspan="7">Median cost of diagnostic/preoperative workup* (Medicare) US Dollars</td></tr><tr><td colspan="6"></td><td>Low^a</td></tr><tr><td>Onega2016</td><td>USA</td><td>2004–2010</td><td>\$2627</td><td>\$1524</td><td>\$1103</td><td></td></tr></tbody></table></div><div><div>MRI: Magnetic Resonance Imaging. *The time between the initial breast imaging or biopsy within 60 days prior to diagnosis and the primary surgical treatment was defined as the diagnostic/preoperative window. 1) the diagnostic period was defined as 60 days prior to, and including, the diagnosis date; 2) the preoperative period was defined as post diagnosis date to initial surgery date.</div><div>^a The quality is low due to high risk of bias and indirectness. The study was a retrospective analysis performed in the USA. Medicare data and costs may not be representative of the European setting.</div><div>The study cohort included women aged 66 yrs. or older at the time of an incident breast cancer diagnosis in 2005–2009 who were enrolled in Medicare for one year before and six months after breast cancer diagnosis (N = 71,193; Stage 0 = 8,533).</div><div>Reference:</div><div>(6) Onega T, et al. Costs of diagnostic and preoperative workup with and without breast MRI in older women with a breast cancer diagnosis. BMC Health Serv Res. 2016; 16: 76.</div></div></div>	Study ID	Country	Year-value	With MRI	Without MRI	Increment	Quality	Median cost of diagnostic/preoperative workup* (Medicare) US Dollars													Low ^a	Onega2016	USA	2004–2010	\$2627	\$1524	\$1103		<div>The GDG judged that the costs are moderate.</div>
Study ID	Country	Year-value	With MRI	Without MRI	Increment	Quality																								
Median cost of diagnostic/preoperative workup* (Medicare) US Dollars																														
						Low ^a																								
Onega2016	USA	2004–2010	\$2627	\$1524	\$1103																									

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ● Low ○ Moderate ○ High ○ No included studies 		<p>The GDG judged that the certainty of the evidence of the required resources is low.</p> <p>US study, representativeness questionable.</p>

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Favors the comparison ● Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies 	No relevant economic evaluations were identified.	<p>In the UK, for all breast cancers -not particularly for DCIS - 12 months after initial surgery there was no statistically significant difference in HRQoL, as measured by the EQ-5D, between women who underwent MRI vs. no MRI. Also, the economic evaluation did suggest that the MRI arm had a larger mean cost (2010 value) per patient (£5508.40 compared with £5213.50), although the difference was not statistically significant (7)</p> <p>Net harm, so no cost-effectiveness.</p> <p>Reference:</p> <p>(7)Turnbull LW, et al. Multicentre randomised controlled trial examining the cost-effectiveness of contrast-enhanced high field magnetic resonance imaging in women with primary breast cancer scheduled for wide local excision (COMICE). Health Technol Assess 2010; 14(1).</p>

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know 	No research evidence was identified	The GDG judged that equity would probably be reduced because not everybody can have easy access to MRI and the cost is not always covered by health insurance.

Acceptability		
Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input checked="" type="radio"/> Varies <input type="radio"/> Don't know	No research evidence was identified	The GDG judged that acceptability varies. Public payers will probably not accept MRI.

Feasibility		
Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input checked="" type="radio"/> Varies <input type="radio"/> Don't know	No research evidence was identified	The GDG judged that feasibility varies.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			No known undesirable outcomes
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

In women with histologically confirmed ductal carcinoma in situ (DCIS), the ECIBC's Guidelines Development Group (GDG) suggests not using additional magnetic resonance imaging (MRI) for preoperative planning (conditional recommendation, very low certainty of the evidence).

Justification

Overall justification

Voting was conducted as agreement could not be reached by consensus. The GDG voted: 4 GDG members voted for a conditional recommendation against the intervention, 13 GDG members voted for a strong recommendation against the intervention and one GDG member voted for a conditional recommendation for the intervention. **The majority required for a strong recommendation, 80% votes, was not reached according to ECIBC voting procedures.**

The judgment was based mainly on the evidence on desirable and undesirable effects, the moderate costs, and the fact that the intervention is probably no cost-effective and would probably reduce equity.

Detailed justification

Desirable Effects

The GDG judged that the desirable effects are trivial.

Undesirable Effects

The GDG judged that the undesirable effects are moderate.

Resources required

The GDG judged that there are moderate costs associated with the intervention

Cost effectiveness

According to a UK study, MRI is probably no cost-effective.

Equity

The GDG judged that the intervention would probably reduce equity

Subgroup considerations

Utility in very extended, suspect multifocal, or multiple disease could not be investigated, but the rationale for better morphological has been considered stronger in these cases.

Low, intermediate and high-grade DCIS.

Implementation considerations

None identified.

Monitoring and evaluation

Overuse of MRI especially when there is a very small DCIS mammographically, it is not likely to find a very big one in MRI.

Research priorities

The GDG recommends research on other MRI techniques, especially abbreviated protocols. The ideal design would be RCT but there are problems with feasibility because of numbers and long term outcomes; alternatively observational studies.

The possible utility in specific subgroups (extremely extended, suspect multifocal or multiple lesions) should be investigated.

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