Original article

Benefits of preoperative MRI in breast cancer surgery studied in a large population-based cancer registry

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Background: **Although evidence for the benefits of preoperative MRI in breast cancer is lacking, use of MRI is increasing and characterized by large interhospital variation. The aim of the study was to evaluate MRI use and surgical outcomes retrospectively.**

Methods: **Women with invasive breast cancer (pT1–3) or ductal carcinoma *in situ* (DCIS), diagnosed in 2011–2013, were selected from the Netherlands Cancer Registry and subdivided into the following groups: invasive cancer, high-grade DCIS, non-palpable cancer, age 40 years or less, and invasive lobular cancer. Associations between preoperative MRI use and initial mastectomy, resection margin after breast-conserving surgery (BCS), re-excision after BCS, and final mastectomy were analysed.**

Results: **In total, 5514 women were included in the study; 1637 (34·1 per cent) of 4801 women with invasive cancer and 150 (21·0 per cent) of 713 with DCIS had preoperative MRI. Positive resection margins were found in 18·1 per cent women who had MRI and in 15·1 per cent of those who did not (adjusted odds ratio (OR) 1·20, 95 per cent c.i. 1·00 to 1·45), with no differences in subgroups. Re-excision rates were 9·8 per cent in the MRI group and 7·2 per cent in the no-MRI group (adjusted OR 1·33, 1·04 to 1·70), with no differences in subgroups. In the MRI group, 38·8 per cent of patients ultimately underwent mastectomy, compared with 24·2 per cent in the no-MRI group (adjusted OR 2·13, 1·87 to 2·41). This difference was not found for patients aged 40 years or less, or for those diagnosed with lobular cancer.**

Conclusion: **No subgroup was identified in which preoperative MRI influenced the risk of margin involvement or re-excision rate after BCS. MRI was significantly associated with more extensive surgery, except in patients aged 40 years or less and those with invasive lobular cancer. These results suggest that use of preoperative MRI should be more targeted, and that general, widespread use be discouraged.**

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Introduction

The primary goal of breast-conserving surgery (BCS) for breast cancer is to obtain complete tumour excision. If the excision is incomplete, re-excision may be necessary, which will increase healthcare costs, the burden to the patient and the risk of a poor cosmetic result. Obtaining a high complete tumour excision rate is important to the patient, as well as to the many healthcare stakeholders that use the re-excision rate as a quality indicator of breast cancer care.

A meta-analysis[1] has shown that MRI can detect mammographically and clinically occult disease in the ipsilateral breast in around 16 per cent of patients with invasive cancer or ductal carcinoma *in situ* (DCIS). MRI has also been shown[2] to be more accurate than mammography or ultrasonography in determining tumour size and delineating tumour margins. As a consequence, preoperative MRI is believed to improve the surgical planning and likelihood of complete tumour excision at the first attempt. Especially in DCIS with high nuclear grade, MRI complementary to mammography could help improve the ability to diagnose the extent of the DCIS[3,4]. The American College of Radiology guidelines suggest that contrast-enhanced MRI of the breast may be useful to determine both the extent of disease and the presence of multifocality and multicentricity in patients with invasive carcinoma and

DCIS. However, currently there is no convincing evidence that preoperative MRI does improve surgical outcomes, such as the rates of positive margins, re-excision or breast conservation, in the average patient with breast cancer[5–7]. An exception to this is the subgroup of patients with lobular cancer, for whom a significantly reduced rate of re-excision has repeatedly been shown following preoperative MRI[5,6,8,9]. This may support the targeted use of preoperative MRI in particular subgroups of patients with breast cancer, as recommended by the European Society of Breast Cancer Specialists (EUSOMA)[10]. Although multiple studies have suggested that MRI is not beneficial in patients with breast cancer in general, and that subgroups must be identified, studies investigating the benefit of MRI in specific subgroups are lacking.

Owing to lack of evidence of the benefits of preoperative MRI regarding short- and long-term treatment outcomes, the value of MRI is heavily debated. Unlike most European countries, guidelines are available in the Netherlands regarding the use of preoperative MRI in women for whom BCS is being considered. In 2011, preoperative MRI was recommended in patients with a (non)-invasive tumour with poorly defined margins, located in dense breast tissue, or with an extensive intraductal component[11]. Since 2012, MRI has been advised in patients with: an invasive tumour and a discrepancy in size between physical examination, mammography and ultrasound imaging; invasive lobular breast cancer; uncertainty regarding the extent of high-grade DCIS; or suspected (micro)invasive breast cancer in DCIS[12]. Despite these guidelines, extremely wide interhospital variation in the use of preoperative MRI still exists in the Netherlands, with a range of 0–85 per cent for women with invasive cancer[13].

Most studies on the potential benefits of preoperative MRI have described single-centre hospital cohorts, and no European population-based studies have been published. In the present study, the population-based Netherlands Cancer Registry was used to determine the association between preoperative MRI and initial mastectomy rate, surgical margin status after BCS, re-excision rate after BCS, and final mastectomy rate in subgroups of patients with invasive cancer, high-grade DCIS, non-palpable cancer, age 40 years or less, and lobular type of invasive cancer. The aim was to identify subgroups in which the preoperative use of MRI might result in improved surgical outcomes after BCS.

Methods

The population-based Netherlands Cancer Registry (Eindhoven region) registers all new cancer diagnoses in an area of south-east Netherlands that has 2·4 million inhabitants, and ten large community and teaching (but no academic) hospitals. The registry collects data based on notifications from the automated pathology archive (PALGA) according to international guidelines by specially trained personnel, and meets high-quality standards with completeness exceeding 95 per cent[14,15]. It provides detailed information on patient demographics, tumour characteristics and treatment. Since 2011, the registry has included data commissioned by the National Breast Cancer Audit, which includes information on preoperative MRI and the date it was performed[13]. In each hospital, dynamic contrast-enhanced MRI was performed according to local protocol, using various MRI scanners. Breast radiologists read the images using the Breast Imaging Reporting and Data System (BI-RADS). All patients, including their imaging findings, were discussed in preoperative multidisciplinary meetings.

Patients diagnosed with a new invasive breast cancer or DCIS between 1 January 2011 and 1 January 2014 were selected. Exclusion criteria were: male sex, neoadjuvant chemotherapy or hormone therapy, clinical or pathological tumour stage T4, distant metastasis at presentation, unknown pathological tumour stage or T0, and unknown type of surgery or unknown surgical margin status. Clinical and pathological TNM stage was according to the seventh edition of the TNM staging system[16]. Margin status after the initial surgical procedure was registered in detail as negative, focally positive, or more than focally positive for both the non-invasive and invasive component of the tumour separately.

Statistical analysis

Patients with concurrent contralateral cancer or contralateral new primary cancer later in time were eligible for inclusion. The contralateral breast cancer was analysed as a new patient. The study population was divided into a no-MRI group and an MRI group according to preoperative use of MRI. Differences in patient characteristics between the two groups were tested using the Mann–Whitney *U* test for continuous variables and χ^2 test for categorical variables. The association between MRI and time from diagnosis to surgery (in days) was determined with the Mann–Whitney *U* test. Subsequently, the total study population was allocated to none, one or more of the following subgroups: invasive cancer, purely high-grade DCIS (defined as Bloom and Richardson grade 2 or 3), non-palpable invasive cancer, young patients (40 years or less) at time of diagnosis, and lobular type of invasive cancer. A negative margin was defined as 'no

ink on tumour', a focally positive margin as 'tumour at the resection margin over a length of less than 4 mm', and a more than focally positive margin as 'tumour at the resection margin over a length of 4 mm or more'. Univariable and multivariable binary logistic regression analysis was used to test the association between MRI and the following outcomes: initial mastectomy rate (*versus* initial BCS), positive margin rate after BCS (*versus* negative margin after BCS), re-excision rate after BCS (*versus* no re-excision after BCS) and final mastectomy rate (*versus* final BCS). The multivariable model was performed by the enter method and included all variables displayed in *Table 1* that were associated with the outcome of interest in univariable analysis with a *P* value of less than 0·100. Both age and tumour size were included as continuous variables in the univariable and multivariable regression analyses. To study the association between surgical margin status after BCS and MRI in more detail, χ^2 analysis was also performed. Statistical tests were two-sided, and $P < 0{\cdot}050$ was considered statistically significant. SPSS® version 20 (IBM, Armonk, New York, USA) was used for all statistical analyses.

Results

In 2011–2013, a total of 6685 patients with a new diagnosis of invasive breast cancer or DCIS were registered in the Netherlands Cancer Registry (Eindhoven region). After applying the exclusion criteria, 5514 patients were eligible. Invasive cancer was diagnosed in 4801 women (87·1 per cent), of whom 1637 (34·1 per cent) had preoperative MRI; their characteristics are summarized in *Table 1*. Pure DCIS was diagnosed in 713 patients (12·9 per cent), of whom 150 (21·0 per cent) had preoperative MRI. Of the patients with DCIS in the MRI and no-MRI group, 12 (8·0 per cent) and seven (1·2 per cent) respectively were aged 40 years or less, and 60 (40·0 per cent) and 298 (52·9 per cent) were aged 60 years or over ($P < 0{\cdot}001$). Furthermore, of the patients with DCIS in the MRI and no-MRI group, 12 (8·0 per cent) and 82 (14·6 per cent) respectively had differentiation grade 1 disease, 55 (36·7 per cent) and 217 (38·5 per cent) had differentiation grade 2, and 81 (54·0 per cent) and 261 (46·4 per cent) had differentiation grade 3; the grade was unknown in two (1·3 per cent) and three (0·5 per cent) patients respectively ($P = 0{\cdot}089$). In the total study population, the incidence of contralateral invasive breast cancer or DCIS diagnosed within 3 months after diagnosis of the first invasive breast cancer or DCIS was 58 (3·2 per cent) in the MRI group and 45 (1·2 per cent) in the no-MRI group. The time between diagnosis and surgery in the total study population was longer for the MRI group: median (i.q.r.) 34 (24–45) days *versus* 22 (15–30) days in the no-MRI group ($P < 0{\cdot}001$). The median time from MRI to surgery was 24 (15–36) days.

Preoperative MRI and initial mastectomy rate

In the total study population, 1480 patients (26·8 per cent) were initially treated with mastectomy, 651 (36·4 per cent) of the 1787 patients in the MRI group and 829 (22·2 per cent) of the 3727 in the no-MRI group (both unadjusted and adjusted $P < 0{\cdot}001$) (*Table 2*). Likewise, significantly higher initial mastectomy rates were seen in MRI *versus* no-MRI groups in the subgroups of patients with invasive cancer (35·9 *versus* 23·1 per cent respectively), high-grade DCIS (43·4 *versus* 18·2 per cent) and non-palpable cancer (28·8 *versus* 11·8 per cent) (all unadjusted and adjusted $P < 0{\cdot}001$). In contrast, initial mastectomy rates were not significantly different between MRI and no-MRI groups in patients aged 40 years or less (40·4 *versus* 42 per cent), or in patients with lobular type of cancer (41·2 *versus* 40·7 per cent) (all unadjusted and adjusted $P > 0{\cdot}200$) (*Table 2*).

Preoperative MRI and margin status

BCS was performed in 4034 (73·2 per cent) of the total study population. In the MRI group, a focally positive margin was found more frequently than a more than focally positive margin ($P = 0{\cdot}048$) (*Table 3*). However, MRI was not significantly associated with a positive margin after adjustment for possible confounders (odds ratio (OR) 1·20, 95 per cent c.i. 1·00 to 1·45; $P = 0{\cdot}052$) (*Table 2*). In all subgroups, no differences in negative, focally positive, or more than focally positive margin rates were seen between MRI and no-MRI groups in univariable analysis (all $P > 0{\cdot}050$) (*Table 3*). In addition, in multivariable analysis MRI was not associated with a positive surgical margin (all $P > 0{\cdot}050$) (*Table 2*). In patients with lobular type of cancer, preoperative MRI was more frequently associated with a negative margin (75·4 per cent *versus* 73·0 per cent in the no-MRI group), and more rarely with a more than focally positive margin (5·7 and 8·8 per cent respectively) (*Table 3*). However, this difference was not significant in univariable analysis ($P = 0{\cdot}507$) (*Table 3*) or multivariable analysis (OR 0·80, 95 per cent c.i. 0·47 to 1·38; $P = 0{\cdot}419$) (*Table 2*).

Preoperative MRI and re-excision rate

Re-excision after BCS was performed in 111 (9·8 per cent) and 210 (7·2 per cent) patients in the MRI and no-MRI

Table 1 Patient and tumour characteristics of the 4801 patients with invasive breast cancer of the total study population of 5514†

	MRI ($n = 1637$)	No MRI ($n = 3164$)	P§
Age (years)			< 0·001
≤ 40	102 (6·2)	76 (2·4)	
41–59	767 (46·9)	1096 (34·6)	
≥ 60	768 (46·9)	1992 (63·0)	
Palpability			0·120
No	676 (41·3)	1347 (42·6)	
Yes	920 (56·2)	1764 (55·8)	
Unknown	41 (2·5)	53 (1·7)	
Histology			< 0·001
Ductal	1105 (67·5)	2712 (85·7)	
Lobular	449 (27·4)	231 (7·3)	
Other	83 (5·1)	221 (7·0)	
DCIS adjacent to tumour			0·006
No	790 (48·3)	1682 (53·2)	
Yes	846 (51·7)	1480 (46·8)	
Unknown	1 (0·1)	2 (0·1)	
Pathological tumour size (mm)*‡	16 (11–23)	15 (9–21)	< 0·001¶
Tumour category			< 0·001
T1	1126 (68·8)	2397 (75·8)	
T2	474 (29·0)	731 (23·1)	
T3	37 (2·3)	36 (1·1)	
Differentiation grade			< 0·001
1	483 (29·5)	1076 (34·0)	
2	752 (45·9)	1259 (39·8)	
3	355 (21·7)	754 (23·8)	
Unknown	47 (2·9)	75 (2·4)	
Oestrogen receptor status			0·001
Positive	1438 (87·8)	2657 (84·0)	
Negative	184 (11·2)	481 (15·2)	
Unknown	15 (0·9)	26 (0·8)	
Progesterone receptor status			0·007
Positive	1200 (73·3)	2185 (69·1)	
Negative	422 (25·8)	952 (30·1)	
Unknown	15 (0·9)	27 (0·9)	
Her2/Neu receptor status			0·154
Negative	1417 (86·6)	2755 (87·1)	
Positive	189 (11·5)	327 (10·3)	
Unknown	31 (1·9)	82 (2·6)	
Node category			0·004
N0	1155 (70·6)	2292 (72·4)	
N1	348 (21·3)	627 (19·8)	
N2	71 (4·3)	102 (3·2)	
N3	36 (2·2)	49 (1·5)	
Unknown	27 (1·6)	94 (3·0)	

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). †Details of patients with ductal carcinoma *in situ* (DCIS) alone are described in the main text. ‡Tumour size was not known in five patients in the MRI group and eight in the no-MRI group. §χ^2 test, except ¶Mann–Whitney U test.

group respectively (unadjusted OR 1·39, 95 per cent c.i. 1·09 to 1·76; $P = 0·008$), and remained significantly different after adjustment for age and differentiation grade (OR 1·33, 1·04 to 1·70; $P = 0·026$) (*Table 2*). In the subgroup with invasive cancer, re-excision was needed in 9·1 and 5·9 per cent of patients in the MRI and no-MRI group respectively (unadjusted $P = 0·001$), and in those with non-palpable cancer re-excision was required in 7·9 and 5·0 per cent respectively (unadjusted $P = 0·021$). However, these differences were not significant after multivariable analysis (OR 1·27, 0·94 to 1·72, $P = 0·125$, and OR 1·33, 0·83 to 2·13, $P = 0·234$, respectively). The number of re-excisions was not significantly different between the MRI and no-MRI group in patients with high-grade DCIS (21 *versus* 15·1 per cent respectively), patients aged 40 years or less (13 *versus* 8 per cent), and patients with lobular type of cancer (11·0 *versus* 11·7 per cent) (all unadjusted and adjusted $P > 0·200$).

Table 2 Univariable and multivariable logistic regression analysis for initial mastectomy rate, positive margin rate after breast-conserving surgery, re-excision rate after BCS and final mastectomy rate, according to preoperative MRI use

	Total*	MRI*	No MRI*	Unadjusted OR†	Unadjusted *P*	Adjusted OR†	Adjusted *P*
Total study population‡							
Initial mastectomy	1480 of 5514 (26·8)	651 of 1787 (36·4)	829 of 3727 (22·2)	2·00 (1·77, 2·27)	< 0·001	2·18 (1·92, 2·48)	< 0·001
Positive margin	645 of 4034 (16·0)	206 of 1136 (18·1)	439 of 2898 (15·1)	1·24 (1·03, 1·49)	0·020	1·20 (1·00, 1·45)	0·052
Re-excision	321 of 4034 (8·0)	111 of 1136 (9·8)	210 of 2898 (7·2)	1·39 (1·09, 1·76)	0·008	1·33 (1·04, 1·70)	0·026
Final mastectomy	1595 of 5514 (28·9)	693 of 1787 (38·8)	902 of 3727 (24·2)	1·99 (1·76, 2·24)	< 0·001	2·13 (1·87, 2·41)	< 0·001
Invasive cancer							
Initial mastectomy§	1318 of 4801 (27·5)	588 of 1637 (35·9)	730 of 3164 (23·1)	1·87 (1·64, 2·13)	< 0·001	1·80 (1·54, 2·09)	< 0·001
Positive margin¶	548 of 3483 (15·7)	188 of 1049 (17·9)	360 of 2434 (14·8)	1·26 (1·04, 1·53)	0·020	0·98 (0·79, 1·22)	0·882
Re-excision#	239 of 3483 (6·9)	95 of 1049 (9·1)	144 of 2434 (5·9)	1·58 (1·21, 2·08)	0·001	1·27 (0·94, 1·72)	0·125
Final mastectomy§	1406 of 4801 (29·3)	623 of 1637 (38·1)	783 of 3164 (24·7)	1·87 (1·64, 2·12)	< 0·001	1·74 (1·50, 2·03)	< 0·001
High-grade DCIS							
Initial mastectomy**	146 of 614 (23·8)	59 of 136 (43·4)	87 of 478 (18·2)	3·44 (2·28, 5·20)	<0·001	3·18 (2·09, 4·82)	< 0·001
Positive margin‡	90 of 468 (19·2)	18 of 77 (23)	72 of 391 (18·4)	1·35 (0·75, 2·43)	0·314	1·28 (0·70, 2·32)	0·426
Re-excision‡	75 of 468 (16·0)	16 of 77 (21)	59 of 391 (15·1)	1·48 (0·80, 2·73)	0·216	1·38 (0·73, 2·59)	0·320
Final mastectomy**	171 of 614 (27·9)	66 of 136 (48·5)	105 of 478 (22·0)	3·35 (2·25, 5·00)	< 0·001	3·11 (2·07, 4·66)	< 0·001
Non-palpable invasive cancer							
Initial mastectomy††	354 of 2023 (17·5)	195 of 676 (28·8)	159 of 1347 (11·8)	3·03 (2·40, 3·83)	< 0·001	2·68 (2·05, 3·50)	< 0·001
Positive margin‡‡	229 of 1669 (13·7)	74 of 481 (15·4)	155 of 1188 (13·0)	1·21 (0·90, 1·64)	0·209	0·92 (0·66, 1·29)	0·645
Re-excision§§	97 of 1669 (5·8)	38 of 481 (7·9)	59 of 1188 (5·0)	1·64 (1·08, 2·50)	0·021	1·33 (0·83, 2·13)	0·234
Final mastectomy††	380 of 2023 (18·8)	207 of 676 (30·6)	173 of 1347 (12·8)	3·00 (2·38, 3·76)	< 0·001	2·58 (1·99, 3·47)	< 0·001
Age ≤ 40 years							
Initial mastectomy‡	81 of 197 (41·1)	46 of 114 (40·4)	35 of 83 (42)	0·93 (0·52, 1·65)	0·798	0·68 (0·37, 1·27)	0·226
Positive margin¶¶	24 of 116 (20·7)	16 of 68 (24)	8 of 48 (17)	1·54 (0·60, 3·95)	0·371	1·43 (0·55, 3·76)	0·463
Re-excision##	13 of 116 (11·2)	9 of 68 (13)	4 of 48 (8)	1·68 (0·49, 5·80)	0·414	–	–
Final mastectomy‡	90 of 197 (45·7)	52 of 114 (45·6)	38 of 83 (46)	0·99 (0·56, 1·75)	0·981	0·75 (0·41, 1·39)	0·358
Lobular invasive cancer							
Initial mastectomy***	279 of 680 (41·0)	185 of 449 (41·2)	94 of 231 (40·7)	1·02 (0·74, 1·41)	0·898	1·00 (0·68, 1·45)	0·977
Positive margin†††	102 of 401 (25·4)	65 of 264 (24·6)	37 of 137 (27·0)	0·88 (0·55, 1·41)	0·603	0·80 (0·47, 1·38)	0·419
Re-excision#	45 of 401 (11·2)	29 of 264 (11·0)	16 of 137 (11·7)	0·93 (0·49, 1·79)	0·835	0·97 (0·44, 2·12)	0·933
Final mastectomy***	301 of 680 (44·3)	198 of 449 (44·1)	103 of 231 (44·6)	0·98 (0·71, 1·35)	0·903	0·95 (0·65, 1·39)	0·791

Values in parentheses are *percentages and †95 per cent c.i. Adjustment for variables associated with (initial and final) mastectomy, positive resection margin, and re-excision with $P < 0·100$ in univariable analysis: ‡age and differentiation grade, §age, palpability, histology, tumour size, differentiation grade, oestrogen receptor status, progesterone receptor status, Her2/Neu receptor status and regional lymph node status, ¶age, palpability, histology, presence of ductal carcinoma *in situ* (DCIS) component, tumour size, differentiation grade, oestrogen receptor status and regional lymph node status, #age, palpability, histology, presence of DCIS component, tumour size, differentiation grade and regional lymph node status, **age, ††age, histology, presence of DCIS component, tumour size, differentiation grade, oestrogen receptor status, progesterone receptor status, Her2/Neu receptor status and regional lymph node status, ‡‡histology, presence of DCIS component, tumour size, differentiation grade and regional lymph node status, §§histology, presence of DCIS component, tumour size, differentiation grade, progesterone receptor status, Her2/Neu receptor status and regional lymph node status, ¶¶differentiation grade, ##none, ***palpability, tumour size, differentiation grade and regional lymph node status, †††presence of DCIS component, tumour size, Her2/Neu receptor status and regional lymph node status. OR, odds ratio; BCS, breast-conserving surgery.

Preoperative MRI and final mastectomy rate

Including re-excisions, 1595 (28·9 per cent) of the 5514 patients in the total study population finally had a mastectomy: 693 (38·8 per cent) of the 1787 patients in the MRI group and 902 (24·2 per cent) of 3727 in the no-MRI group (both unadjusted and adjusted $P < 0·001$) (*Table 2*). In addition, significantly higher final mastectomy rates were seen in patients with MRI than without MRI in the subgroups of invasive cancer (38·1 *versus* 24·7 per cent respectively), high-grade DCIS (48·5 *versus* 22·0 per cent) and non-palpable cancer (30·6 *versus* 12·8 per cent) (all unadjusted and adjusted $P < 0·001$). However, final mastectomy rates were similar in MRI and no-MRI groups in patients aged 40 years or less (45·6 *versus* 46 per cent respectively) and in those with lobular type of cancer (44·1 *versus* 44·6 per cent) (all unadjusted and adjusted $P > 0·300$).

Discussion

The hypothesis of this retrospective study in patients with invasive or non-invasive breast cancer was that there are subgroups in which the preoperative use of MRI will result in improved surgical outcomes after BCS. In the total study population, patients who underwent MRI had a small, but significantly higher, positive margin rate (18·1 per cent *versus* 15·1 per cent in those who did not have MRI). However, this does not imply a clinically relevant difference, and in multivariable analysis the difference was no

Table 3 Surgical resection margin after breast-conserving surgery according to preoperative use of MRI

Surgical resection margin	MRI	No MRI	*P**
Total study population	*n* = 1136	*n* = 2898	0·048
Negative	930 (81·9)	2459 (84·9)	
Focally positive	147 (12·9)	326 (11·2)	
More than focally positive	59 (5·2)	113 (3·9)	
Invasive cancer	*n* = 1049	*n* = 2434	0·062
Negative	861 (82·1)	2074 (85·2)	
Focally positive	135 (12·9)	264 (10·8)	
More than focally positive	53 (5·1)	96 (3·9)	
High-grade DCIS	*n* = 77	*n* = 391	0·396
Negative	59 (77)	319 (81·6)	
Focally positive	12 (16)	55 (14·1)	
More than focally positive	6 (8)	17 (4·3)	
Non-palpable invasive cancer	*n* = 481	*n* = 1188	0·312
Negative	407 (84·6)	1033 (87·0)	
Focally positive	52 (10·8)	117 (9·8)	
More than focally positive	22 (4·6)	38 (3·2)	
Age ≤ 40 years	*n* = 68	*n* = 48	0·638
Negative	52 (76)	40 (83)	
Focally positive	11 (16)	6 (13)	
More than focally positive	5 (7)	2 (4)	
Lobular invasive cancer	*n* = 264	*n* = 137	0·507
Negative	199 (75·4)	100 (73·0)	
Focally positive	50 (18·9)	25 (18·2)	
More than focally positive	15 (5·7)	12 (8·8)	

Values in parentheses are percentages. DCIS, ductal carcinoma *in situ*. *χ^2 test.

longer significant ($P = 0{\cdot}052$). Preoperative MRI was associated with neither improved resection margins nor lower re-excision rates after BCS in any of the subgroups studied. However, MRI was associated with higher initial and final mastectomy rates, except in the subgroup of younger patients (aged 40 years or less) and in patients with lobular type of invasive breast cancer.

This is a large, multicentre, population-based analysis of the effect of preoperative MRI on surgical outcomes in Europe. Multivariable analyses were performed, adjusting for multiple patient, tumour and treatment characteristics associated with each outcome separately, which is one of the strengths of the study. Another strength is the large number of patients, which made it possible to focus on patient subgroups, which so far have been studied insufficiently.

The association between preoperative MRI and resection margins after BCS has not been studied in detail before. Contradictory results have been found in multiple small, single-centre studies that have focused on the surgical outcomes of BCS in patients with invasive breast cancer[17–22]. Similar to the findings in the present study, in the only other population-based study, by Fortune-Greeley and colleagues[6], preoperative MRI was not associated with improved surgical outcomes. Only small, single-centre studies with contradictory results have reported on preoperative MRI in patients with pure DCIS[23–27]. In line with the present findings, the only population-based study, performed by Wang and co-workers[7], showed no association between preoperative MRI and positive resection margin and re-excision rates after BCS. To date, only the MONET trial[28] has focused on patients with non-palpable invasive cancer. In contrast to the present findings, the MONET trial (based on 149 patients) found that the addition of preoperative MRI to routine clinical care was associated with an increased re-excision rate.

It is clear from the present findings, and has also been shown frequently in the literature[1,5], that there is a strong association between MRI and mastectomy in all subgroups, except for patients aged 40 years or less and those with invasive lobular breast cancer. A weakness of the study is its retrospective design, and thus the inherent lack of information, such as the presence of multifocality or multicentricity, the indication for performing MRI, the result of the MRI and whether it changed the surgical plan. Recommendations in the Dutch breast cancer guidelines regarding the preoperative use of MRI, described above, can, however, shed some light on the decision-making process underlying the results of this study. The retrospective, non-randomized design of the study also explains the differences in patient characteristics, such as patients

undergoing MRI having larger tumours and being more likely to have a DCIS component adjacent to the invasive tumour (*Table 1*). It is known that these factors increase the risk of incomplete excision, and this could have been the reason for performing MRI and thus be a source of selection bias. Even though factors associated with mastectomy were adjusted for in the multivariable analysis, residual confounding may be present owing to factors not taken into consideration. It must also be noted that the study did not include data from university hospitals, and it is therefore likely that MRI was used for surgical planning rather than screening purposes. The median (i.q.r.) time between MRI and surgery was 24 (15–36) days, supporting the assumption that MRI was used for surgical planning. In addition, the lack of information regarding the incidence of additional occult disease in the ipsilateral breast (estimated to be 16 per cent) detected by MRI prevents firm conclusions from being drawn[1]. The detection rate for contralateral breast cancer by preoperative MRI has been estimated to be 4·1 per cent[29]. In the present study, the incidence of contralateral breast cancer diagnosed within 3 months after diagnosis of the first tumour was 3·2 per cent in patients who had MRI and 1·2 per cent in those who did not. This difference might be larger in patients with lobular cancer and older patients, owing to the higher absolute risk of contralateral breast cancer in these subgroups[30]. Whether preoperative MRI reduces the risk of local and distant recurrence is still a matter of debate[31,32]. Because the cancer registry has included information on preoperative MRI only since 2011, long-term outcomes could not be studied. It can be expected, however, that residual disease in the breast results in positive resection margins that will be treated by re-excision, regardless of the preoperative MRI. It has been shown previously that overall survival is similar in women who have a re-excision and those who do not[33]. Moreover, long-term prognosis has proved to be similar in women having BCS and those undergoing mastectomy[34], and preoperative MRI is therefore unlikely to influence prognosis. Thus, short-term surgical outcomes remain important endpoints for studying the benefits of MRI.

Overall, MRI was used with a relatively high frequency of 32·4 per cent, compared with rates in the above-mentioned population-based studies. In these studies[6,7], which used the US SEER–Medicare-linked database, 6·6–12·2 per cent of patients underwent MRI. The greater use of MRI in the Netherlands could be explained by the more recent time interval, compared with the periods covered in previous studies. It could also be explained by the fact that preoperative staging by MRI has been advised for invasive lobular cancer by the Dutch breast cancer guideline since 2012[12], and by the EUSOMA working group since 2010[10]. There is also a growing body of evidence that the targeted use of MRI in this subgroup improves surgical planning[5,6,8,9]. In the present study, MRI was used in 449 (66·0 per cent) of the 680 patients with invasive lobular breast cancer, and all surgical outcomes were similar for patients with and without MRI. At least these results indicate that MRI is unlikely to have a negative effect in this subgroup. The third explanation for the more widespread use of MRI in the Netherlands, in comparison with values reported by the studies based on the SEER–Medicare database, could be the younger age of the population. The SEER–Medicare database contains data only for patients aged 65 years or more, whereas the present study included women of all ages, making it the first population-based study to include patients aged less than 65 years. Interestingly, the subgroup analysis of patients aged 40 years or less showed that MRI was significantly associated with neither more extensive surgery (initial and final mastectomy rates) nor the other surgical outcomes studied. However, considering the small number of patients in this subgroup (197), there is a risk of a type II error, and thus the results need to be interpreted with caution. The finding is merely an observation of statistical association and does not provide evidence for a causative relationship.

The present study has shown in a population-based retrospective cohort that preoperative MRI does not result in improved surgical outcomes after BCS, but instead leads to more extensive surgery in patients with breast cancer in general, a finding in line with previous studies. An exception could be in patients aged 40 years or less, and those with invasive lobular breast cancer. Furthermore, MRI may cause a delay in treatment. Large prospective studies are needed urgently to define patient subgroups in which preoperative MRI is of value in short- and long-term outcomes.

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Snapshot quiz

Snapshot quiz 15/12

Answer: The forceps is not holding anything. Rather, the appendix is being tented up by magnetic attraction between intraluminal magnets and the instrument's handle. A teenager underwent minilaparotomy to remove swallowed magnets, which were arrested in the right lower quadrant on serial radiographs. To minimize procedural morbidity, the magnetic attraction between the intraluminal foreign bodies and an extraluminal metal instrument was exploited. Thus, the magnets were dragged from the right colon back into the appendix. From this point, simple appendicectomy allowed easy and clean removal of the magnets. The patient was discharged the following day.