



Attending the breast screening programme after breast cancer treatment: A population-based study

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ABSTRACT

Introduction: In the Netherlands, breast cancer patients are treated and followed at least 5 years after diagnosis. Furthermore, all women aged 50–74 are invited biennially for mammography by the nationwide screening programme. The relation between the outpatient follow-up (follow-up visits in the outpatient clinic for 5 years after treatment) and the screening programme is not well established and attending the screening programme as well as outpatient follow-up is considered undesirable. This study evaluates potential factors influencing women to attend the screening programme during their outpatient follow-up (overlap) and the (re-)attendance to the screening programme after 5 years of outpatient follow-up.

Methods: Data of breast cancer patients aged 50–74 years, treated for primary breast cancer between 1996 and 2007 were selected from the Netherlands Cancer Registry and linked to the National Breast Cancer Screening Programme in the Northern region. Cox regression analyses were used to study women (re-)attending the screening programme over time, possible overlap with the outpatient follow-up and factors influencing this.

Results: In total 11 227 breast cancer patients were included, of whom 19% attended the screening programme after breast cancer treatment, 4.4% within 5 years and 15.4% after more than 5 years. Factors that independently influenced attendance within 5 years as well as more than 5 years after treatment were: interval tumours (HR 0.77; 95%CI 0.61–0.97 and HR 0.69; 95%CI 0.53–0.88, ref: screen-detected tumours), receiving adjuvant radiotherapy (HR 0.65; 95%CI 0.47–0.90 and HR 0.66; 95%CI 0.47–0.93; ref: none) and diagnosis of in situ tumours (HR 1.67; 95%CI 1.25–2.23 and HR 1.39; 95%CI 1.05–1.85; ref: stage I tumours). Non-screen related tumours (HR 0.41; 95%CI 0.29–0.58) and recent diagnosis (HR 0.89 per year; 95%CI 0.86–0.92) were only associated with attendance within 5 years after treatment.

Conclusion: The interrelation between outpatient follow-up and screening should be improved to avoid overlap and low attendance to the screening programme after outpatient follow-up. Breast cancer patients should be informed that attending the screening programme during the outpatient follow-up is not necessary.

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1. Introduction

Breast cancer is the most common type of cancer in women in the Netherlands, with an incidence of 16 000 new cases in 2011 (www.cancerregistry.nl) [1]. In the Netherlands a population-based breast cancer screening programme has been fully

implemented since 1996. Women aged 50–74 (70–74 since 1999) are invited biennially for mammography [2]. Due to the implementation of this screening programme, breast cancer is diagnosed at an earlier stage. Together with improved treatment options, this has led to an increasing number of women surviving 5 years and more after diagnosis. Although the optimal follow-up after breast cancer treatment is still unknown, women frequently attend scheduled outpatient follow-up visits (follow-up visits in the outpatient clinic for 5 years after treatment), including mammography [3–10].

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Women attending outpatient follow-up after breast cancer diagnosis aged 50–74 can also attend the screening programme which is considered undesirable. In the guideline for breast cancer, recommendations are given about outpatient follow-up after treatment of breast cancer for the first 5 years [11]. These visits focus on wound healing, adverse effects of the treatment, the need for psychosocial care and the early detection of second primary tumours. From the revision of 2008 onwards, the Dutch guideline for breast cancer states that breast cancer patients treated with mastectomy could, after 5 years of outpatient follow-up and then 60–74 years of age, be referred to the screening programme [12]. Nevertheless, little is known about the relation between the outpatient follow-up and the attendance to the screening programme after treatment for breast cancer, and which factors influence the screening participation.

The objective of this population-based study was to determine whether breast cancer patients attended the screening programme during their outpatient follow-up (overlap) and the (re-)attendance to the screening programme after more than 5 years of outpatient follow-up, and which factors (method of detection, tumour characteristics and primary and adjuvant treatment) influenced this attendance.

2. Patients and methods

2.1. Patients

Women with breast cancer were selected from the population-based Netherlands Cancer Registry (NCR) of the Comprehensive Cancer Centre the Netherlands (IKNL). The NCR contains data on patient and tumour characteristics, stage and treatment of all newly diagnosed malignancies [13]. The National Breast Cancer Screening Programme invites women 50–74 years of age (70–74 since 1999). All women aged 50–74 at the time of their first invasive or in situ breast cancer between 1996 and 2007 were selected ($N = 12\,010$). Women with metastases at diagnosis ($N = 497$) and women without primary treatment ($N = 46$) were excluded, as well as women with bilateral mastectomy ($N = 240$). In total 11 227 women were included in this study. For the analyses of women attending the screening programme after more than 5 years of outpatient follow-up, women aged 50–69, diagnosed between 1996 and 2004, not attending screening within 5 years after treatment were included ($N = 6251$).

2.2. Relation to screening

Data of the NCR were merged with the data of the National Breast Cancer Screening Programme, region North, covering an area of 3.3 million inhabitants comprising 1.6 million women. Thereafter only data from the NCR covering the same area as the screening programme were selected, to ensure that all breast cancer patients had the chance to be invited by the National Breast Cancer Screening Programme, region North. Dutch legislation states that the breast screening programme is obliged to invite all women aged 50–74 (70–74 since 1999), even after breast cancer treatment. Women do have the option to return a non-attender form on which they can state that they are in follow-up after breast cancer treatment in the hospital. The data of the screening programme include the date of attendance and the screening result. Three groups were defined: the first group comprised of women with a suspect mammography by breast cancer screening who were subsequent diagnosed with breast cancer within 12 months (“screen-detected tumour”). The second group comprised of women who developed breast cancer within 24 months after a normal mammogram by breast screening (“interval tumour”). The third group comprised of women with breast cancer without a

relation to the screening programme (“non-screen related tumours”). This group included women who never attended the screening programme before their breast cancer diagnosis and women diagnosed with breast cancer more than 24 months after the last biennial screening mammography. Data until 31 December 2009 were available.

2.3. Statistical analysis

Chi-squared analysis was used to compare categorical variables. The time period between diagnosis and attendance to the screening programme was defined as the date of pathological confirmation and the first screen mammography afterwards. Patients were censored at the date of a new primary breast tumour, death, date when a woman reached the age of 75, or end of the study period (31 December 2009). The percentage of women attending the screening programme was calculated using Kaplan Meijer analysis. Multivariable Cox regression analyses were used to identify independent prognostic factors for the chance of attending the screening programme. Factors considered were: age, year of diagnosis, stage, type of surgery and adjuvant therapy (radio-, chemo- and/or endocrine). Analyses were performed using the STATA software package, version 12.0 for Windows (Stata Corporation LP, College Station, TX, USA).

3. Results

3.1. Attendance to the screening programme within 5 years after treatment

In total 11 227 breast cancer patients were included in the study and tumour and treatment characteristics are shown in Table 1. In total 19% attended the screening programme after breast cancer treatment. Of 11 227 breast cancer patients, 4.4% attended the screening programme within 5 years after treatment. Of the screen-detected cases, 5.2% attended the screening programme within 5 years. Furthermore, 4.0% of women with an interval tumour and 2.7% of women with a non-screen related tumour attended the screening programme within 5 years after treatment. Fig. 1a shows the results of multivariable analysis for attending screening within 5 years after treatment. Breast cancer patients with interval and non-screen related cancer attended the screening programme after breast cancer treatment less often than breast cancer patients with screen-detected tumours (HR 0.77; 95%CI 0.61–0.97 and 0.41; 95%CI 0.29–0.58 resp.; Table 2), as well as later year of diagnosis (HR 0.89 per year; 95%CI 0.86–0.92) and breast cancer patients who received adjuvant radiotherapy (HR 0.65; 95%CI 0.47–0.90 compared to patients without adjuvant radiotherapy). Breast cancer patients with in situ tumours (HR 1.67; 95%CI 1.25–2.23) were more likely to attend the screening programme than patients with stage I tumours.

3.2. Attendance to the screening programme after more than 5 years after treatment

Of 6251 women, 15.4% attended the screening programme more than 5 years after treatment. Of women with screen-detected tumours 15.4% of patients attended the screening programme more than 5 years after treatment, compared to 13.0% and 18.3% women with an interval tumour and women with a non-screen related tumour, respectively. In multivariable analysis for attending screening more than 5 years after treatment, breast cancer patients with interval tumours attended the screening programme after breast cancer treatment less often than breast cancer patients with screen-detected tumours (HR 0.69; 95%CI 0.53–0.88; Table 2; Fig. 1b). Furthermore, breast cancer patients who received

Table 1
Characteristics of the total study population.

	Total (N=11 227)	
	N	%
Detection		
Screen-detected	6002	53.5
Interval	3328	29.6
Non-screen related ^a	1897	16.9
Age at diagnosis		
50–54	2595	23.1
55–59	2310	20.6
60–64	2222	19.8
65–69	2117	18.9
70–74	1983	17.7
Year of diagnosis		
1996–1998	1757	15.6
1999–2001	2831	25.2
2002–2004	2926	26.1
2005–2007	3213	28.6
Stage		
Stage I	4772	42.5
Stage II	4303	38.3
Stage III	969	8.6
In situ	1183	10.5
Surgery		
BCS	6315	56.2
Mastectomy	4706	41.9
Other	206	1.8
Radiotherapy		
No	3953	35.2
Yes	7274	64.8
Chemotherapy		
No	8922	79.5
Yes	2305	20.5
Endocrine therapy		
No	7630	68.0
Yes	3597	32.0

^a Non-screen related tumours include women who never attended the screening programme, and women diagnosed with breast cancer more than 24 months after the last screen; BCS, breast conserving surgery.

adjuvant radiotherapy attended less often than patients without adjuvant radiotherapy (HR 0.66; 95%CI 0.47–0.93). Breast cancer patients with in situ tumours (HR 1.39; 95%CI 1.05–1.85) were more likely to attend the screening programme more than 5 years after treatment than patients with stage I tumours.

4. Discussion

Of the breast cancer patients, 4.4% attended the breast screening programme within 5 years after breast cancer treatment, followed by another 15.4% of patients attending the programme more than 5 years after treatment. Factors associated with a lower attendance to the screening programme within 5 years after treatment were interval tumours and non-screen related tumours (compared to screen-detected tumours), higher age, later year of diagnosis, and receiving adjuvant radiotherapy (compared to none). Diagnosis with in situ tumours was related to a higher attendance to the screening programme compared to women with stage I tumours. Breast cancer patients with interval tumours and patients who received adjuvant radiotherapy were also less likely to attend the screening programme more than 5 years after treatment, patients with in situ tumours were more likely to attend.

Breast cancer patients with screen-detected tumours were more likely to return to the screening programme, which may be caused by more trust in the programme. Women with in situ tumours were also more likely to attend the screening programme. It is known that these women have a lower risk of local recurrence [14]. Due to this lower risk, specialists might be more willing to refer these patients to the screening programme. Breast cancer patients with an interval tumour, which either did not exist at the time of the screening or was undetected, may have been disappointed and therefore reluctant to re-enter the programme.

Breast cancer patients receiving adjuvant radiotherapy were less likely to attend the screening programme. A study by Grandjean et al. revealed that women who had received

Table 2
Hazard ratios (HR) and associated 95% confidence intervals (CI) for attending screening within 5 years after breast cancer treatment and more than 5 years after treatment.

	Attending screening < 5 years				p-Value	Attending screening ≥ 5 years				
	N	HR	95%CI			N	HR	95%CI		p-Value
Detection					<0.001					0.014
Screen-detected	6002	Ref.				3353	Ref.			
Interval	3328	0.77	0.61	0.97	0.026	1862	0.69	0.53	0.88	0.004
Non-screen related	1897	0.41	0.29	0.58	<0.001	1036	0.91	0.70	1.18	0.478
Age										
By year	11 227	0.99	0.97	1.00	0.133	6251	1.01	0.99	1.03	0.227
Year of diagnosis										
By year	11 227	0.89	0.86	0.92	<0.001	6251	1.00	0.95	1.05	0.882
Stage					0.002					0.015
Stage I	4772	Ref.				2584	Ref.			
Stage II	4303	1.17	0.87	1.56	0.300	2567	0.76	0.57	1.02	0.065
Stage III	969	1.69	1.01	2.82	0.044	480	0.82	0.40	1.67	0.582
In situ	1183	1.67	1.25	2.23	0.001	620	1.39	1.05	1.85	0.021
Surgery					0.413					0.095
BCS	6315	Ref.				3400	Ref.			
Mastectomy	4706	0.90	0.65	1.25	0.539	2731	0.79	0.56	1.11	0.175
Other	206	1.37	0.68	2.78	0.381	120	0.15	0.02	1.12	0.065
Radiotherapy										
No	3953	Ref.				2248	Ref.			
Yes	7274	0.65	0.47	0.90	0.009	4003	0.66	0.47	0.93	0.017
Chemotherapy										
No	8922	Ref.				4959	Ref.			
Yes	2305	0.96	0.69	1.34	0.798	1292	0.72	0.49	1.07	0.107
Endocrine therapy										
No	7630	Ref.				4356	Ref.			
Yes	3597	0.88	0.67	1.17	0.389	1895	1.14	0.85	1.54	0.391

BCS, breast conserving surgery.

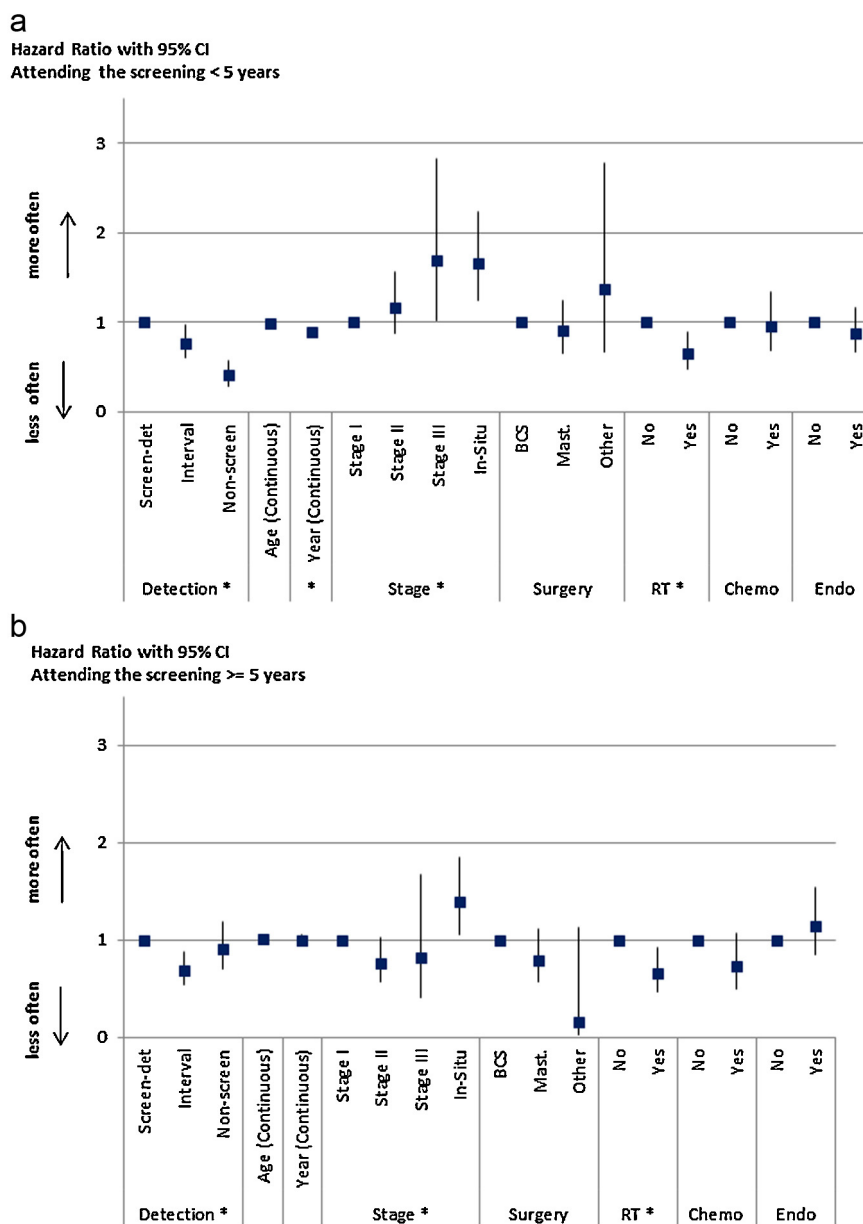


Fig. 1. Factors influencing the attendance to the screening programme for (a) attending screening < 5 year after treatment and (b) attending screening ≥ 5 year after treatment, multivariable Cox regression analyses.

radiotherapy had follow-up by both the surgeon and the radiation oncologist and therefore received more outpatient follow-up than recommended by the guidelines [15]. This might reduce the urge for women to attend the regular screening programme.

Besides the specialists in the hospital, the patient's needs and preferences are important factors. These factors should be taken into account when discussing follow-up. De Bock et al. studied the needs of patients during follow-up and showed that patients have widely different needs and preferences [16]. Furthermore, there is an ongoing debate about the effectiveness of routine follow-up including an annual mammography. De Bock et al. showed that still 40% of recurrences were detected in an asymptomatic stage during routine follow-up visits or tests. A simulation study found that patients aged 50 years with standard follow-up examinations had only 2 months gain in life expectancy compared to patients without follow-up examinations. For older patients the benefit was even less [17]. On the other hand, several studies reported that most patients prefer frequent follow-up visits for a long, even a life-long period [3,6,10]. Patients indicated that the main benefit

attending follow-up visits was the perceived reassurance they gained [18,19]. This might be an important reason why women will attend the screening programme when invited, while still attending outpatient follow-up.

After breast cancer diagnosis and treatment, women frequently attend scheduled outpatient follow-up visits [11]. According to guidelines, in the first year the breast cancer patients are seen four times, in the second year twice, and thereafter once a year. During these visits women receive a physical examination, and annually a mammography. Until 2008, after a follow-up of 5 years, annual or biennial mammography was recommended, and the optimal length of follow-up given was to be decided individually by the specialist and the breast cancer patient. In specific situations, depending on age and treatment, the option was to be referred to the screening programme after 10 years of follow-up [20,21]. As no explicit recommendations were made about referral to the screening programme, this might resulted in the low percentage of breast cancer patients attending the screening programme after treatment. In 2008 the Dutch guideline for breast cancer was

revised and since then a clear recommendation is given about referral to the screening programme after curative treatment: after 5 years outpatient follow-up, female patients over 60 years of age and treated with mastectomy should be referred to the screening programme [11,12,22]. This might result in more women attending the screening programme after treatment. However, surgeons and radiologists might not be willing to refer a patient to the screening programme for many different reasons.

Furthermore, screen radiologists are probably not so eager to include breast cancer patients who underwent BCS in the screening programme, as these mammographies are more difficult to analyse. After surgery and/or radiotherapy the women's breast will change in appearance and density. On mammography scar tissue from the operation and radiotherapy may have an appearance similar to a second breast tumour [23]. For the screen radiologist a comparison is difficult, as he has only the screen mammographies made before diagnosis or none at all. Therefore, screen radiologists are more likely to refer the women for further diagnostics. In the future it may become more feasible to exchange digital images from hospitals to the screening programme, enabling screen radiologists in interpreting mammographies over time.

To reduce overlap, breast cancer patients should be informed by their specialist that attending the screening programme in the first 5 years of follow-up is unnecessary and the interrelation between the outpatient follow-up and the screening programme should be improved. The recommendation in the national guideline that breast cancer patients can be referred to the screening programme 5 years after mastectomy is the first step in creating a more efficient follow-up. The effect of this recommendation should be seen in the forthcoming years.

In conclusion, 4.4% of the breast cancer patients attended the breast screening programme within 5 years after breast cancer treatment, followed by another 15.4% of patients attending the programme after 5 years after treatment. Women with screen-detected breast cancer, in situ tumours, and women treated without adjuvant radiotherapy were more likely to return to the screening programme. In the future, improving the interrelation between the outpatient follow-up and the screening programme is desirable to avoid overlap and low attendance to the screening programme after outpatient follow-up. Breast cancer patients should be informed by their specialist that attending the screening programme during the outpatient follow-up is not necessary.

Conflict of interest statement

None declared.

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References

- [1] Comprehensive Cancer Centre the Netherlands. <http://www.cancerregistry.nl> [accessed 26.08.13].
- [2] Fracheboud J, de Koning HJ, Boer R, Groenewoud JH, Verbeek AL, Broeders MJ, et al. Nationwide breast cancer screening programme fully implemented in the Netherlands. *Breast* 2001;10:6–11.
- [3] de Bock GH, Bonnema J, van der Hage J, Kievit J, van de Velde CJH. Effectiveness of routine visits and routine tests in detecting isolated locoregional recurrences after treatment for early-stage invasive breast cancer: a meta-analysis and systematic review. *J Clin Oncol* 2004;22:4010–8.
- [4] Grunfeld E, Levine MN, Julian JA, Coyle D, Szechtman B, Mirsky D, et al. Randomized trial of long-term follow-up for early-stage breast cancer: a comparison of family physician versus specialist care. *J Clin Oncol* 2006;24:848–55.
- [5] Montgomery DA, Krupa K, Cooke TG. Follow-up in breast cancer: does routine clinical examination improve outcome? A systematic review of the literature. *Br J Cancer* 2007;97:1632–41.
- [6] Kimman ML, Voogd AC, Dirksen CD, Falger P, Hupperets P, Keymeulen K, et al. Follow-up after curative treatment for breast cancer: why do we still adhere to frequent outpatient clinic visits? *Eur J Cancer* 2007;43:647–53.
- [7] Sheppard C. Breast cancer follow-up: literature review and discussion. *Eur J Oncol Nurs* 2007;11:340–7.
- [8] Grunfeld E. Optimizing follow-up after breast cancer treatment. *Curr Opin Obstet Gynecol* 2009;21:92–6.
- [9] Kimman ML, Bloebaum MM, Dirksen CD, Houben RM, Lambin P, Boersma LJ. Patient satisfaction with nurse-led telephone follow-up after curative treatment for breast cancer. *BMC Cancer* 2010;30(10):174.
- [10] van Hezewijk M, Ranke GMC, van Nes JGH, Stiggelbout AM, de Bock GH, van de Velde CJH. Patients' needs and preferences in routine follow-up for early breast cancer; an evaluation of the changing role of the nurse practitioner. *Eur J Surg Oncol* 2011;37:765–73.
- [11] National Breast Cancer Organization of the Netherlands. Guideline breast cancer 2008; 2008. <http://www.oncoline.nl> [accessed 04.04.12].
- [12] National Breast Cancer Organization of the Netherlands. Guideline breast cancer 2012; 2012. <http://www.oncoline.nl> [accessed 20.10.12].
- [13] de Munck L, Schaapveld M, Siesling S, Wesseling J, Voogd AC, Tjan-Heijnen VCG, et al. Implementation of trastuzumab in conjunction with adjuvant chemotherapy in the treatment of non-metastatic breast cancer in the Netherlands. *Breast Cancer Res Treat* 2011;129:229–33.
- [14] van der Leij F, Elkhuizen PHM, Bartelink H, van de Vijver MJ. Predictive factors for local recurrence in breast cancer. *Semin Radiat Oncol* 2012;22:100–7.
- [15] Grandjean I, Kwast ABG, de Vries H, Klaase J, Schoevers WJ, Siesling S. Evaluation of the adherence to follow-up care guidelines for women with breast cancer. *Eur J Oncol Nurs* 2012;16:281–5.
- [16] de Bock GH, Bonnema J, Zwaan RE, van de Velde CJH, Kievit J, Stiggelbout AM. Patient's needs and preferences in routine follow-up after treatment for breast cancer. *Br J Cancer* 2004;90:1144–50.
- [17] Jacobs HJM, van Dijk JAAM, de Kleijn EMHA, Kiemeny LALM, Verbeek ALM. Routine follow-up examinations in breast cancer patients have minimal impact on life expectancy: a simulation study. *Ann Oncol* 2001;12:1107–13.
- [18] Allen A. The meaning of the breast cancer follow-up experience for the women who attend. *Eur J Oncol Nurs* 2002;6:155–61.
- [19] Kwast ABG, Drossaert CHC, Siesling S. Breast cancer follow-up: from the perspective of health professionals and patients. *Eur J Cancer Care* 2013. <http://dx.doi.org/10.1111/ecc.12094>.
- [20] Otter R. Richtlijnen voor diagnostiek en behandeling van premaligne en maligne aandoeningen in de IKN-regio. Groningen: Integraal Kankercentrum Noord-Nederland, 2003.
- [21] National Breast Cancer Organization of the Netherlands. Guideline breast cancer 2005; 2005. <http://www.oncoline.nl> [accessed 04.04.12].
- [22] Zonderland HM, Tuut MK, den Heeten GJ, van Asperen CJ, de Bock GH, Rutgers EJTh, et al. Richtlijn 'screening en diagnostiek van het mammacarcinoom' (heziening). *Ned Tijdschr Geneesk* 2008;152:2336–9.
- [23] Shaheen R, Schimmelpenninck CA, Stoddart L, Raymond H, Slanetz PJ. Spectrum of diseases presenting as architectural distortion on mammography: multimodality radiologic imaging with pathologic correlation. *Semin Ultrasound CT MRI* 2011;32:351–62.