

# Diagnosis and Treatment of Patients with early and advanced Breast Cancer

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## Early Detection and Diagnosis

# Early Detection and Diagnosis

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- **Versions 2005–2019:**  
**Albert / Blohmer / Fersis / Junkermann /  
Maass / Müller-Schimpfle / Scharl / Schreer**
- **Version 2020**  
**Fallenberg / Maass**

# Early Detection Mammography (normal risk)

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Age	Interval	Oxford		AGO
		LOE	GR	
< 40	na	-	-	--
40–49	12–24	1b	B	+
50–69*	24	1a	A	++
70–74	24	1a	A	++
> 75**	24	4	C	+

\* National Mammography-Screening-Program

\*\* health status + life expectancy more than 10 years

# Early Detection in Asymptomatic Women

## Digital Breast Tomosynthesis

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	Oxford LOE	GR	AGO
<b>Digital Breast Tomosynthesis (DBT alone or in addition to FFDM)*</b>	<b>2a</b>	<b>B</b>	<b>+</b>
<b>Replacing FFDM by synthetic MG in addition to DBT**</b>	<b>3b</b>	<b>B</b>	<b>+</b>

The complete DBT dataset of images has to be available for judgment/reporting, the synthetic mammography only is not sufficient.

\* Sign. higher sensitivity, heterogeneous specificity, and higher costs [machine, evaluation, archiving] in comparison to Full-Field Digital Mammography (FFDM)

\*\* Evaluation for Germany in a current prospective trial (TOSYMA)

# Breast Cancer Mortality Reduction

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## Meta-Analysis

RR 95%CI

### Independent UK Panel, 2012

13-year metaanalysis

0.80 (0.73–0.89)

### Cochrane Review, 2011

Fixed-effect metaanalysis of 9 RCT-trials

0.81 (0.74–0.87)

As above, but excluding women <50 years

0.77 (0.69–0.86)

### Canadian Task Force, 2011

Women aged 50–69 years

0.79 (0.68–0.90)

### Duffy et al, 2012

Review of all trials and age groups

0.79 (0.73–0.86)

# Breast Cancer Mortality Reduction

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## Meta-Analysis

RR 95%CI

### Case-Control Studies

Broeders et al	Screening Mx	0.46 (0.4 – 0.54)
	Corr. for self selection	0.52 (0.42–0.65)
	Invited for screening	0.69 (0.57–0.83)

### Incidence-based Mortality Studies

Broeders et al	Screening Mx	0.62 (0.56–0.69)
	Invited to screening	0.75 (0.69–0.81)

### Randomized Clinical Trials

Gotsche and Jorgenson	Screening Mx	0.81 (0.74–0.87)
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### ECIBC

#### Screening MX

45–49	0.88 (0.76 - 1.02)
50–69	0.77 (0.66 - 0.90)
70–75	0.77 (0.54 - 1.09)

# Breastcancer: incidence and mortality

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- **Annual incidence of breast cancer and mortality in the EU (GLOBOCAN 2012)**

Age	Incidence/1000	Mortality/1000
40 to 44	1,2	0,1
45 to 49	1,7	0,2
50 to 69	2,7	0,5
70 to 74	3,0	0,8

# Mammography-Screening

## Benefit and Harm

### Data background: Breast Cancer Surveillance Consortium Registry Data per 10.000 Women screened over 10 years

Age	40-49	50-59	60-69	70-74
Breast cancer death avoided (CI95%)	3 (0-9)	8 (2-17)	21 (11-32)	13 (0-32)
False-positive (n)	1212	932	808	696
Breast biopsies (n)	164	159	165	175
False-negative (n)	10	11	12	13

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Siu Al on behalf of the USPSTF 2016, 164:279–296



# Early Detection Sonography/MRI

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- **Screening-Breast Sonography alone**
  - **Automated 3D-Sonography**
- **Breast sonography as an adjunct:**
  - **Dense mammogram  
(heterogeneously dense, extremely dense)**
  - **Elevated risk**
  - **Mammographic lesion**
  - **Second-look US (MRI-only detected lesions)**
- **MRI if screening MG is negative and breast  
composition: extremely dense\* 50–75 LJ**

Oxford		
LoE	GR	AGO
5	D	--
3a	C	--
2a	B	++
1b	C	++
2b	B	++
2b	C	++
1b	B	+

\* Definition of extremely dense corresponds to BIRADS-density category D heterogeneously dense categorie C according to ACR BI-RADS-Atlas 5th ed. 2013

# Early Detection Clinical Examination

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## As stand alone procedure

- Self-examination
  - Clinical breast examination (CBE) by health professionals
  - CBE because of mammographic/sonographic lesion
- CBE in combination with imaging

Oxford		
LoE	GR	AGO
1a	A	-*
3b	C	-*
5	D	++
BCP		++

\* May increase breast awareness

# Assessment of Breast Symptoms or Lesions

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- **Clinical examination**
- **Mammography**
  - Tomosynthesis
  - Contrast-enhanced mammography (alone or as adjunct)
- **Sonography**
  - Elastography (shear-wave) \*
  - Automated 3D-sonography
- **Minimally invasive biopsy**
- **MRI\*\***

Oxford		
LoE	GR	AGO
3b	B	++
1b	A	++
2b	B	+
3a	B	+/-
2b	B	++
2b	B	+
3b	B	+/-
1c	A	++
1b	B	+

\* Adjunct assessment

\*\*If clinical examination, mammography and sonography incl. needle biopsy do not allow a definite diagnosis

# Pre-therapeutic Assessment of Breast and Axilla

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- **Clinical examination**
- **Mammography**
  - + Tomosynthesis (DBT)
  - Contrast-enhanced mammography (alone or as adjunct)
- **Sonography (breast and axilla)**
- **MRI\***
- **Minimally invasive biopsy\*\***
- **Breast-CT**

Oxford		
LoE	GR	AGO
5	D	++
2b	B	++
3b	B	+
3a	B	+/-
2b	B	++
1b	B	+
1b	A	++
5	D	-

\* MRI-guided vacuum biopsy is mandatory in case of MRI-detected additional lesions. Individual decision for patients at high familiar risk, with dense breast (density 3-4/diagnostic assessability C-D), lobular invasive tumors, suspicion of multilocular disease. No reduction in re-excision rate.

\*\* Histopathology of lesions if relevant for treatment

# MRI: Preoperative Staging

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- **9 eligible studies  
(2 randomized trials; 7 comparative cohorts)**
- **3112 patients with BC**
- **MRI versus no-MRI:**
  - **Initial mastectomy 16.4% versus 8.1%**  
[OR, 2.22 (P < 0.001); adjusted OR, 3.06 (P < 0.001)]
  - **Re-excision after initial breast conservation 11.6% versus 11.4%**  
[OR, 1.02 (P = 0.87); adjusted OR, 0.95 (P = 0.71)]
  - **Overall mastectomy 25.5% versus 18.2%**  
[OR, 1.54 (P < 0.001); adjusted OR, 1.51 (P < 0.001)]

# MRI: Preoperative Staging in Lobular Invasive Breast Cancer

- **766 patients with invasive lobular cancer (ILC)**
  - **Initial mastectomy: 31.1% versus 24.9%**  
[OR, 1.36 (P = 0.056); adjusted OR, 2.12 (P = 0.008)]
  - **Re-excision after initial breast conservation 10.9% versus 18.0%**  
[OR, 0.56 (P = 0.031); adjusted OR, 0.56 (P = 0.09)]
  - **Overall mastectomy 43.0% versus 40.2%**  
[OR, 1.12 (P = 0.45); adjusted OR, 1.64 (P = 0.034)]

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# MRI and DCIS

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Study	No. Cases	Overall accuracy (%)	Sens. (%)	Spec. (%)
Gilles et al 1995	172	70	95	51
Westerhof et al 1998	63	56	45	72
Bazzocchi et al 2006	112	80	79	68
Kuhl et al 2007	75	-	88	-
Baur et al. 2013	58	-	79,3	

# Sensitivities CESM

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Author	n	MG	CESM	MRI	US	Analyse
Dromain 2011	110	78	92			Per patient
Fallenberg 2014	118	77.9	94.7			Per patient
Mokhtar 2014	60	93.2	97.7			Per patient
Lobbess 2014*	113	96.9	100			Per patient
Perez 2015 ECR	98		78		66	Per lesion
Luczinska 2014	152	91	100			
Jochelson 2012	52	81 59	96 83	96 93		Per patient Per lesion
Fallenberg 2013	80	81	100	97		Per patient
Fallenberg 2016	155	81 55	94 72	95 76		Index Per Lesion
Lalji 2016*	199	93	96,9			Per patient 10 reader
Tennant 2016	100	84	95			
Luczynska 2016	116	90	100		92	

\* Recall from Screening

CESM is comparable to MRI regarding index, a bit inferior for additional lesions



# Pre-therapeutic Staging

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Oxford		
LoE	GR	AGO
5	D	++

## ■ History and clinical examination

**Additional diagnosis for patients with high metastatic potential and/or symptoms (in decision making for chemotherapy and/or anti-HER2-therapy):**

■ CT scan of thorax/abdomen	2a	B	+
■ Bone scan	2b	B	+
■ Chest X-ray	5	C	+/-
■ Liver ultrasound	5	D	+/-
■ In case of suspicious lesions further diagnosis (e.g. liver-MRI, CEUS*, biopsy etc.)	2a	B	+
■ FDG-PET or FDG-PET /CT	3a	C	+/-
■ Whole body MRI	4	C	+/-

\* Contrast enhanced ultrasound