

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 / Fallenberg / Fersis / Junkermann /
Maass / Müller-Schimpfle / Scharl / Schreer**
- **Version 2021**
Fallenberg / Gerber

Early Detection with Mammography

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Age	Interval	Oxford		
		LOE	GR	AGO
< 40	na	-	-	--
40-44	na	1b	B	-
45-49	24-36	1a	B	+#
50-69*	24	1a	A	++
70-74	24	1a	A	+#
> 75**	24	4	C	+/-#

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* National Mammography-Screening-Program

** health status + life expectancy more than 10 years

clear indication necessary

Early Detection and Diagnosis

Early Detection in Asymptomatic Women

Digital Breast Tomosynthesis

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Digital Breast Tomosynthesis (DBT in addition to FFDM or SM)*

Replacing FFDM by synthetic MG in addition to DBT**

	Oxford		
	LOE	GR	AGO
Digital Breast Tomosynthesis (DBT in addition to FFDM or SM)*	1a	B	+
Replacing FFDM by synthetic MG in addition to DBT**	2a	B	++

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

- **Sign. higher sensitivity, heterogeneous specificity, and higher costs [machine, evaluation, archiving] of DBT in comparison to Full-Field Digital Mammography (FFDM)**
- **Dose reduction due to calculated synthetic 2D mammography (SM) instead of FFDM**
- **** Evaluation for Germany in a randomized 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)

Duffy et al, 2020

Review of 549,091 Women (30% eligible Swedish screening population)

0.59 (0.51-0.68) mortality

0.75 (0.66-0.84) advanced BC

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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

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From: <http://gco.iarc.fr/>

Mammography-Screening

Benefit and Harm

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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 and Diagnosis

Early Detection (normal risk) 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 y**

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 to BIRADS-category C according to ACR BI-RADS-Atlas 5th ed. 2013

Early Detection (normal risk)

Clinical Breast Examination (CBE)

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As a stand-alone procedure

- Self-examination
- Clinical breast examination (CBE) by health professionals outside checkup for cancer
- Clinical breast examination (CBE) by health professionals during checkup for cancer
- Medical palpation thru blind/optically disabled persons

CBE because of mammographic/sonographic lesion

CBE in combination with imaging

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

* May increase breast awareness

Assessment of Breast Symptoms or Lesions

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

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

* Adjunct assessment

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

*** replacement of FFDM with SM

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****
 - Axilla CNB, if lymph node is suspect
- **Breast-CT**

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

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

** Histopathology of additional lesions if relevant for treatment

*** replacement of FFDM with SM

Sensitivities CESM

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Author	n	MG	CESM	MRI	US	Analyse
Domain 2011	110	78	92			Per patient
Fallenberg 2014	118	77.9	94.7			Per patient
Mokhtar 2014	60	93.2	97.7			Per patient
Lobbes 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	
Xing 2019	235		91,5	91,5		Per lesion

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

Early Detection and Diagnosis

* Recall from Screening

Pre-therapeutic Staging

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Oxford		
LoE	GR	AGO
5	D	++

History and clinical examination

Additional diagnosis for patients with tumors of high metastatic potential and/or symptoms and/or indication for (neo-)adjuvant chemotherapy and/or antibody-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**	2b	B	+/-
Whole body MRI	4	C	+/-

* Contrast enhanced ultrasound

** especially in patients with high tumor stage(III) if available
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