Symposium I

"Breast cancer screening in Asia.
Should it be different from strategies of western country?"

Breast Cancer Screening in Korea

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Contents

- Epidemiology
- Breast Cancer Screening Program & MQSA in Korea
- Published Data of Screening Mammography in Korea
- Suggested Other or Supplementary Modalities for Breast Cancer Screening

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Basic Principles of Screening

- Earlier detection → Reduce mortality
- Healthy individuals who are screened → Harmless
- The screening test → Widely available and well tolerated
- Cost effectiveness

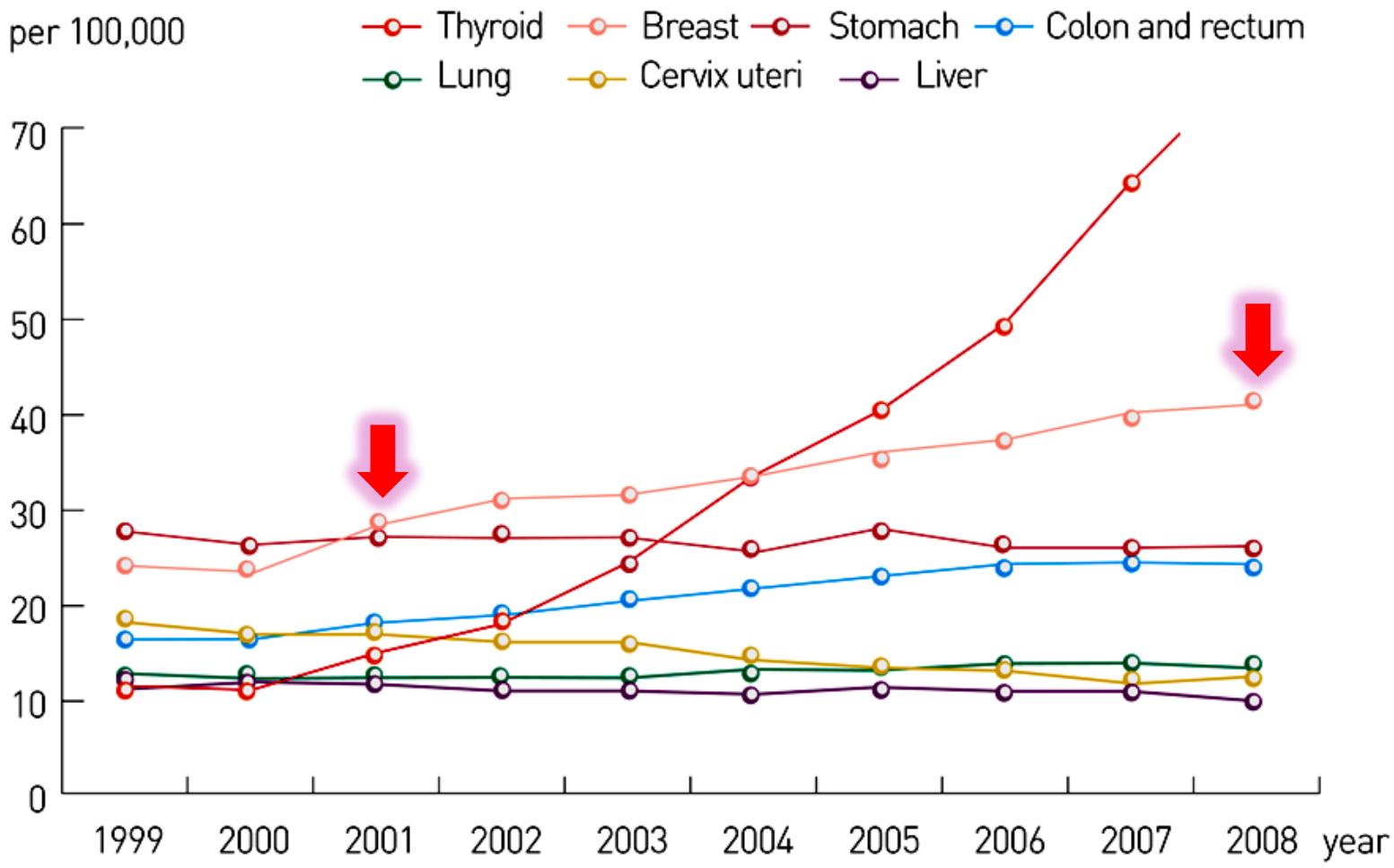
Screening of Cancer

- Information
  - Cancer Incidence
  - Cancer Mortality
  - Changing trends
- Plan and Monitor of the Programs
- Cancer Prevention, early Detection and Treatment

Breast Cancer

- The most common cancer
- The leading cause of cancer death in women worldwide
- In Korea, breast cancer is the most prevalent cancer from 2001

Trends of Age-standardized Incidence Rates in Major Cancers : Female

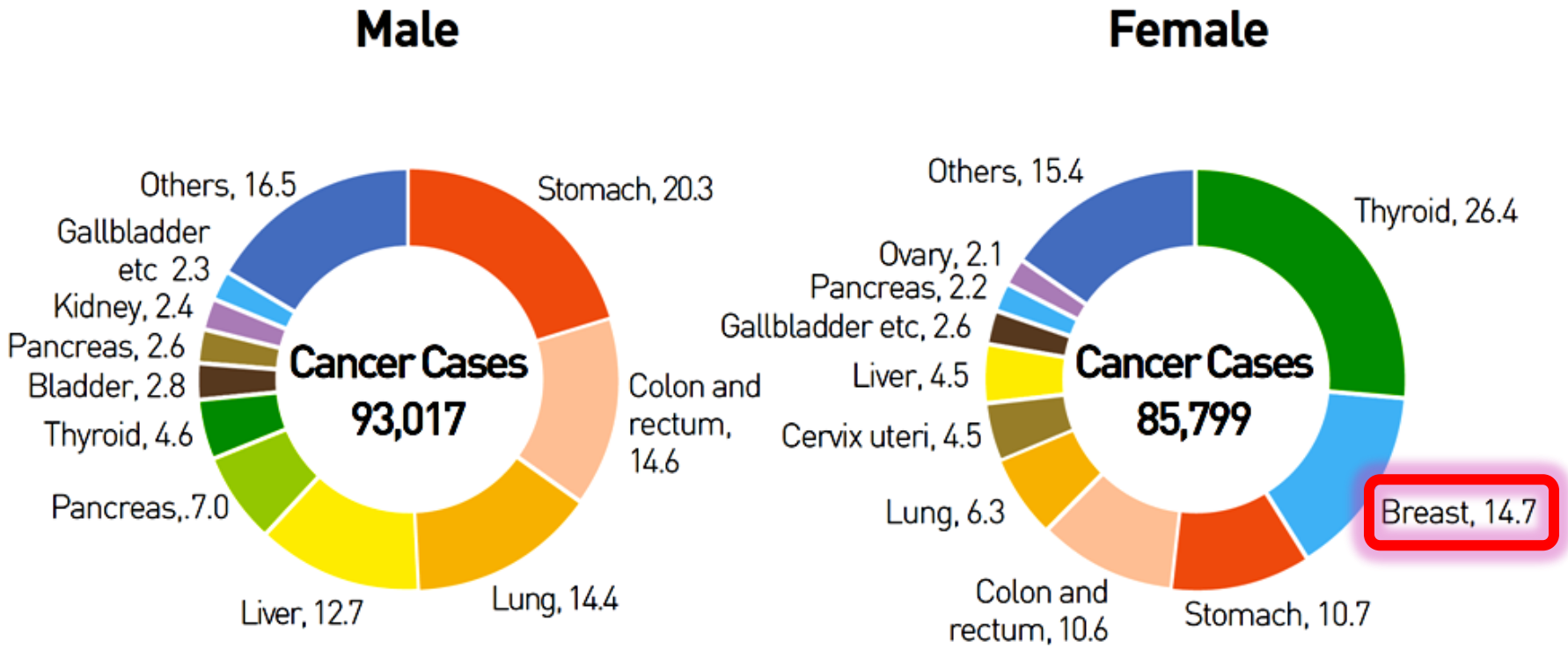


Source) Ministry of Health & Welfare, The Korea Central Cancer Registry, 2010

Note) Age-standardized incidence rate uses "mid-year population in 2000"as standard population.

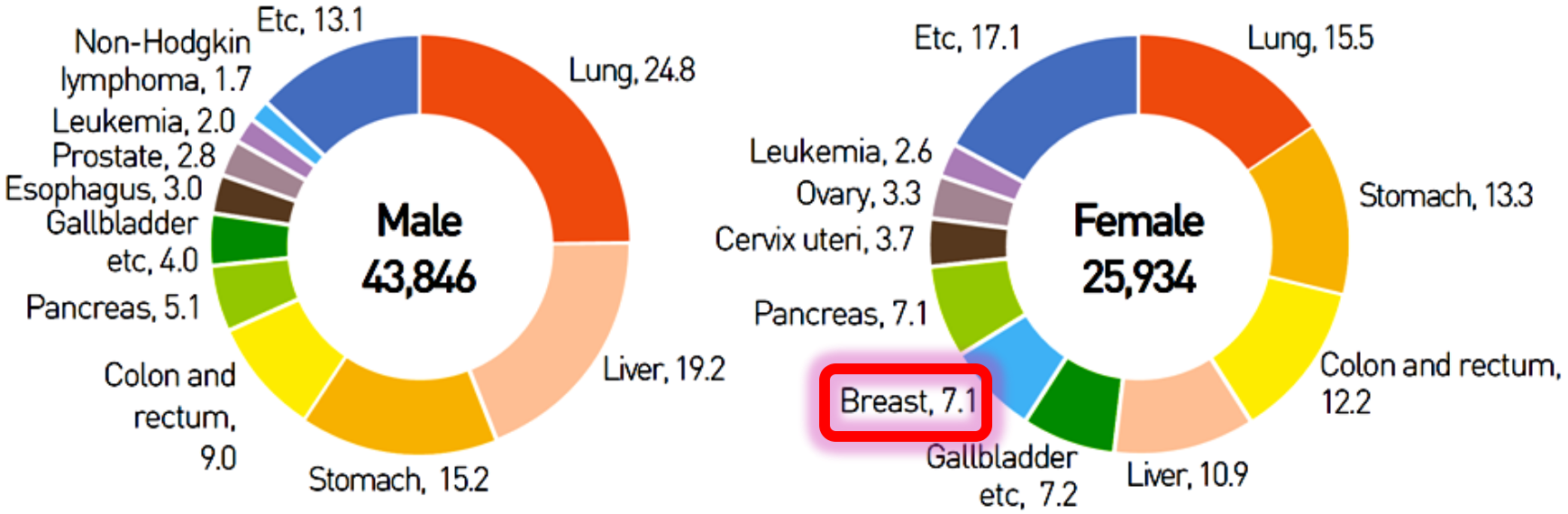
Proportion of Cancer Incidence[2008]

(Unit: %)



Source) Ministry of Health & Welfare, The Korea Central Cancer Registry, 2010

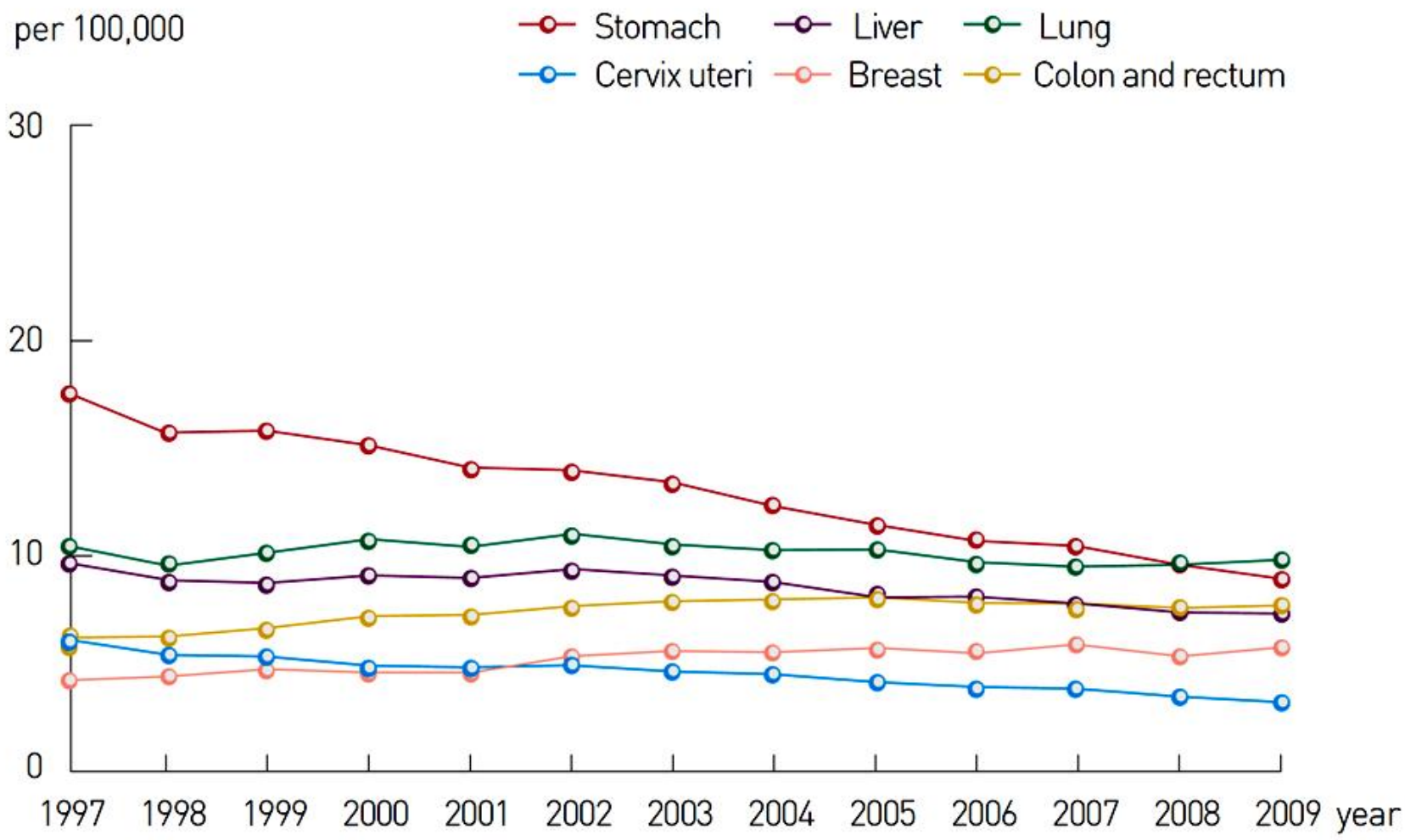
Proportion of cancer death [2009]



Source) STATISTICS KOREA, 2010

Note) Colon and rectum C18-C21 (International Classification of Diseases for Oncology, ICD-10),
Non Hodgkin lymphoma C82-C85 (International Classification of Diseases for Oncology, ICD-10)

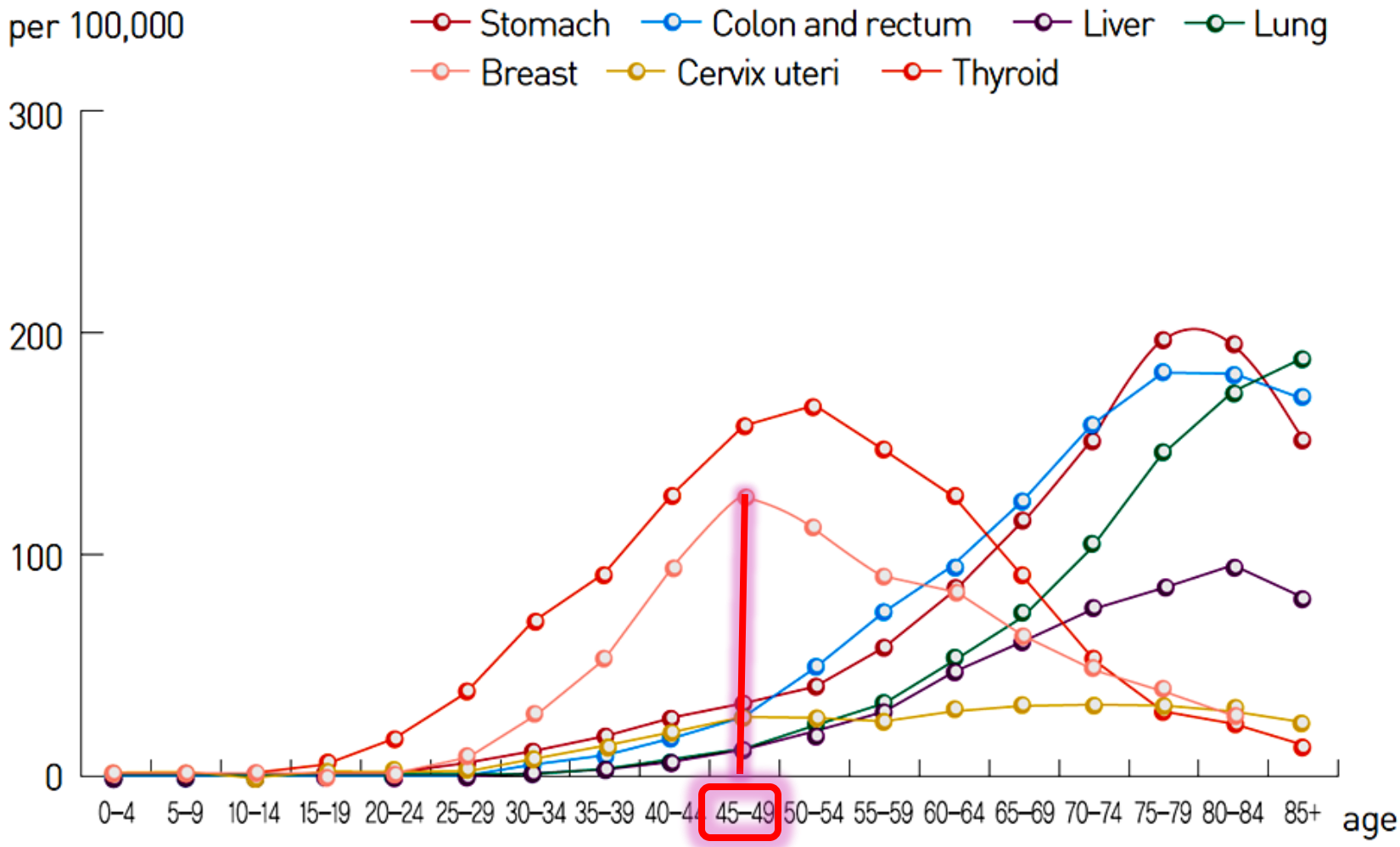
Trends of Age-standardized Mortality Rates in Major Cancers : Female



Source) STATISTICS KOREA, 2010

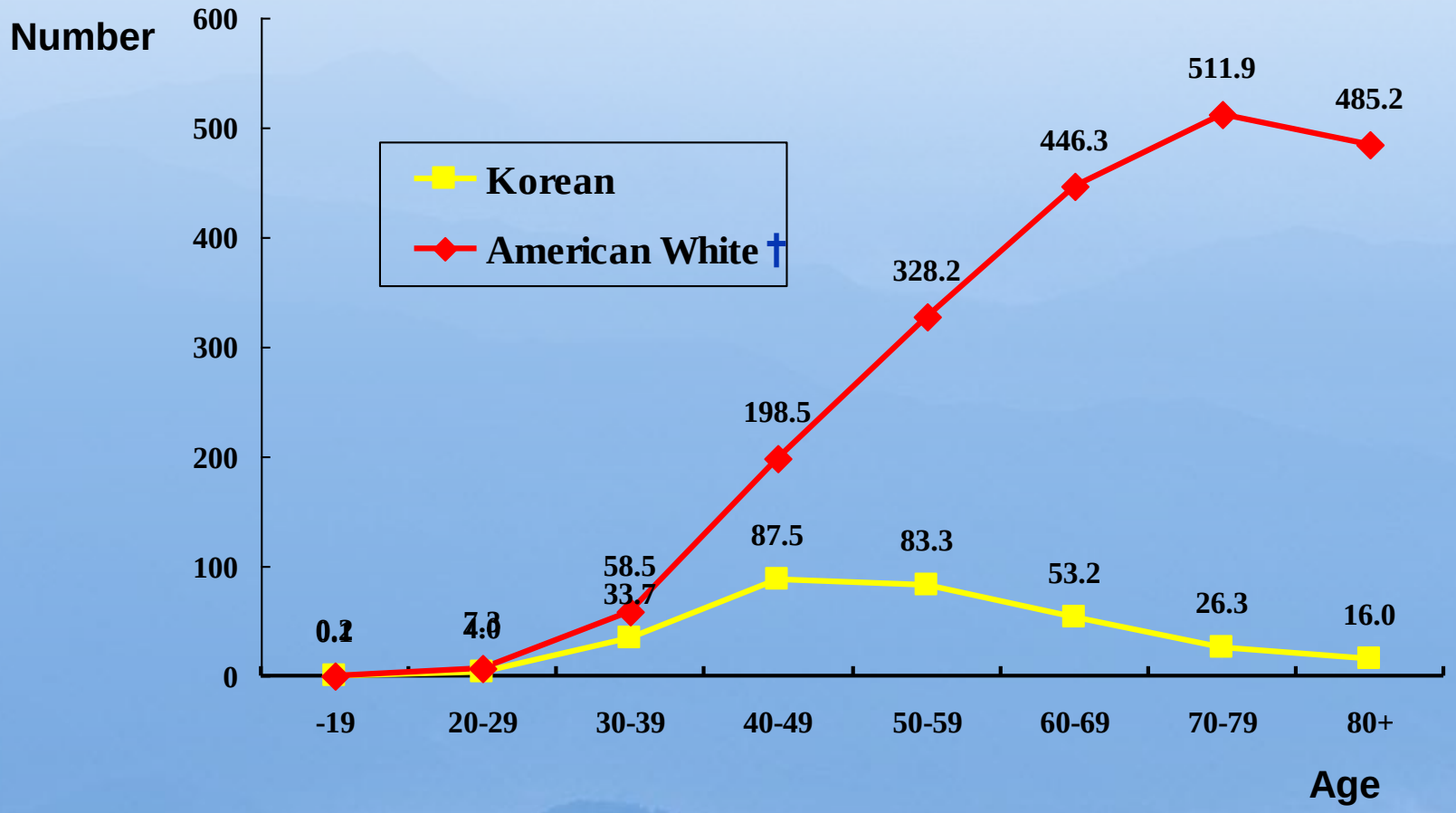
Note) Age-standardized incidence rate uses "mid-year population in 2000"as standard population.
Colon and rectum C18-C21 (International Classification of Diseases , ICO-10)

Age-specific Cancer Incidence Rates : Female [2008]



Source) Ministry of Health & Welfare, The Korea Central Cancer Registry, 2010

Age-specific Crude Incidence (2004)



** patients number per 100,000 women*

† SEER 1992-2002

Characteristics of Korean Breast Cancer

- Incidence of breast cancer: continuously and rapidly increase
- Lower incidence than western countries
- Increase in the ratio of asymptomatic, screening detected breast cancer
- Increase in the ratio of early cancer of stage 0 and 1, DCIS
- High proportion of young age premenopausal patients
- Good survival rate in most stages

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National Cancer Screening Program (NCSP) in Korea

- NCSP began in 1999
- For five major cancers (stomach, breast, uterine cervix, liver, colorectal cancers)
- The protocol of the NCSP was constructed around evidence-based literature and the current national screening policy.
- The Support & Evaluation Board of the National Cancer Screening Program in the National Cancer Center as well as associated academic societies.

The NCSP Guideline

Cancer	Target Population	Frequency	Test or Procedure
Stomach	40 & over (adults)	every 2 years	Endoscope or UGI
Breast	40 & over (women)	every 2 years	Mammography ± CBE
Cervix	30 & over (women)	every 2 years	Pap smear
Liver	40 & over high risk group*	every 6 months	Sonography & AFP
Colorectal	50 & over (adults)	every 1 year	FOBT → Colonoscopy or Barium enema

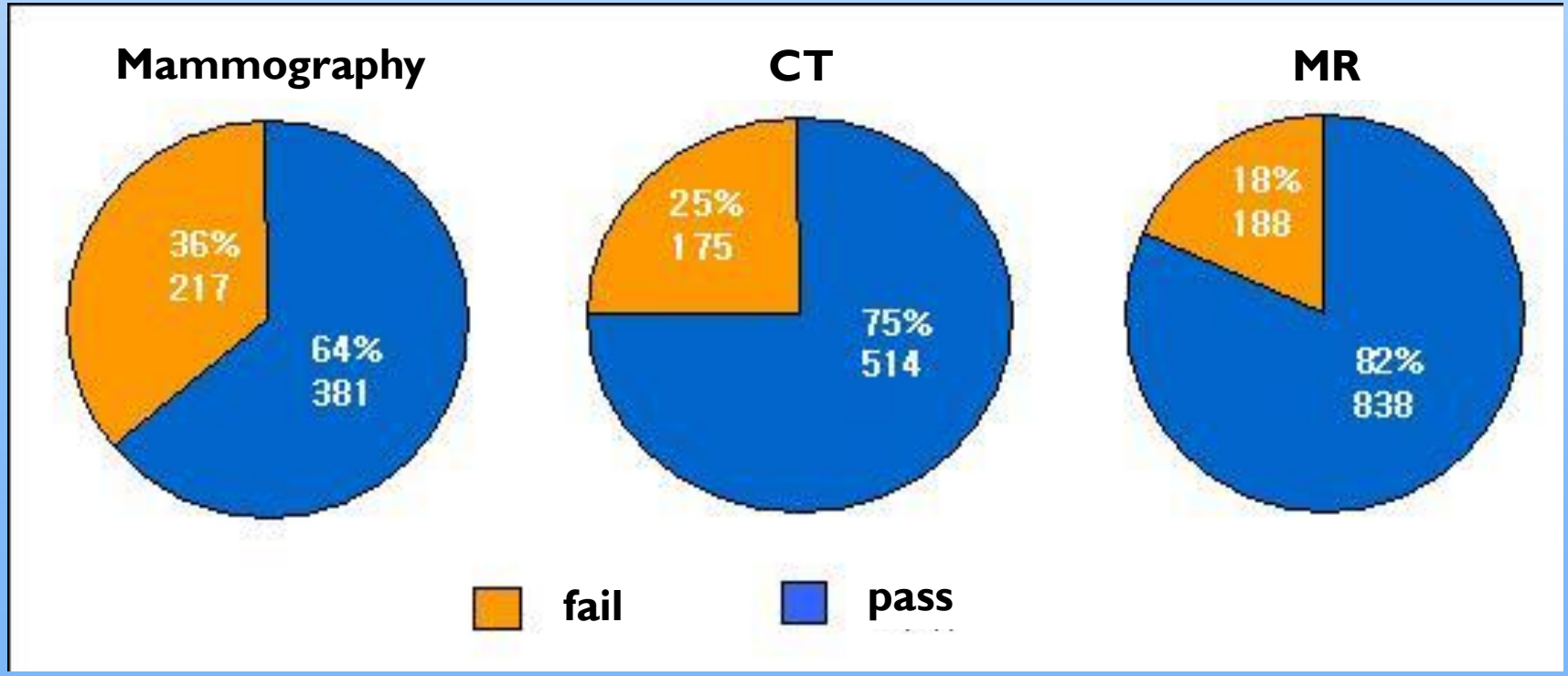
* 40 & over with HBsAg positive or anti-HCV positive or liver cirrhosis

Quality Assurance for Mammography

- Korean Radiological Society (KRS) & Korean Society of Breast Imaging (KSBI)
  - Voluntary guidelines and standards of quality management (1999 ~ 2001)

Nationwide Survey for Quality of Radiological Imaging (2001)

Failure Rate



New Legislation

- In January 14, 2003, the National assembly of Korea approved the Acts including quality management for specific medical equipments (Mammography, CT and MRI).

Key Features of the MQSA

- All mammography unit in Korea must be accredited and certified every year.
- Inspection
  - Every 1 year: Review of records for personnel, equipments and QC, and inspection of phantom image
  - Every 3 year: Every 1 year inspection + On-site survey and inspection of clinical image
  - Every new equipment must be also certified prior to start operation.

Key Features of the MQSA

- Accreditation: endorsed to Korean Institute for Accreditation of Medical Image (KIAMI)
- Certification: Ministry of Health and Welfare (MHW).
- Mammography that does not meet the quality standards is banned from using by the government.

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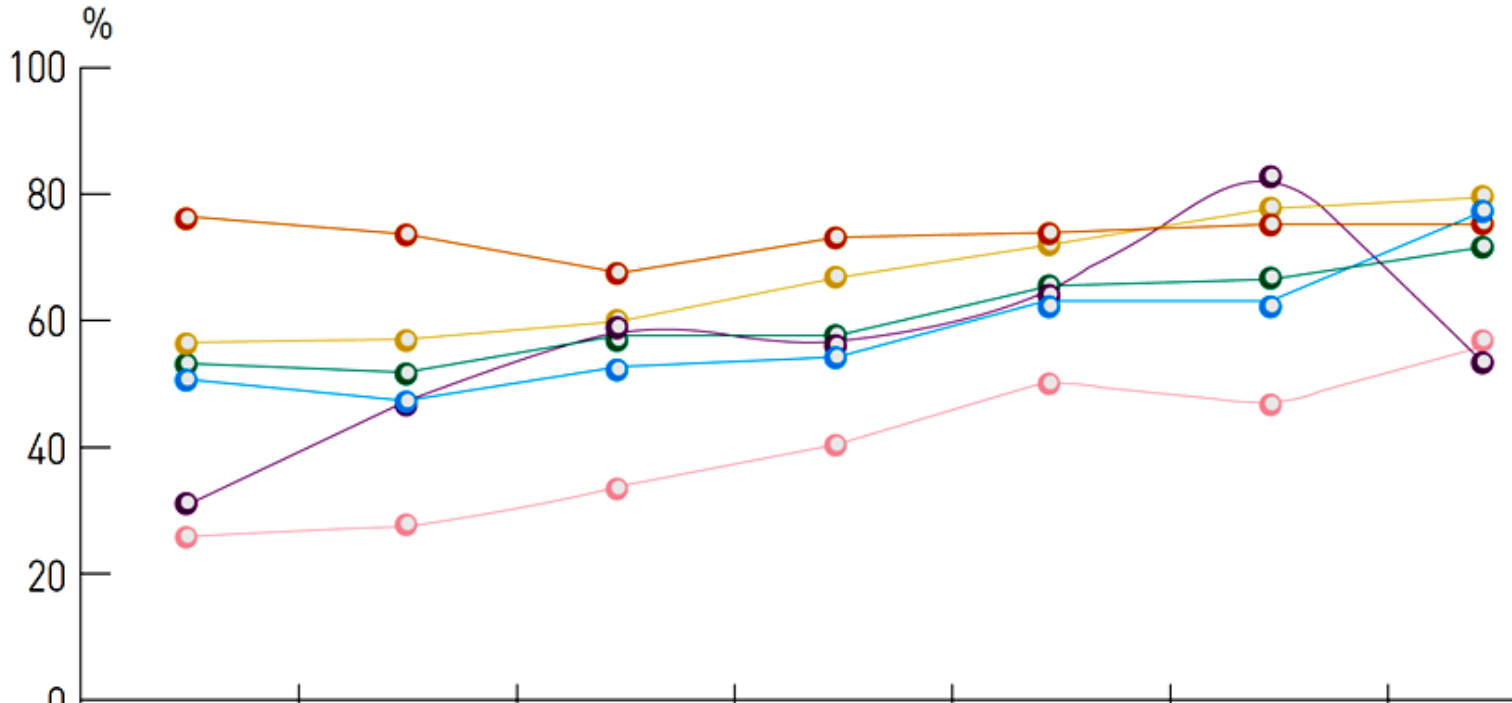
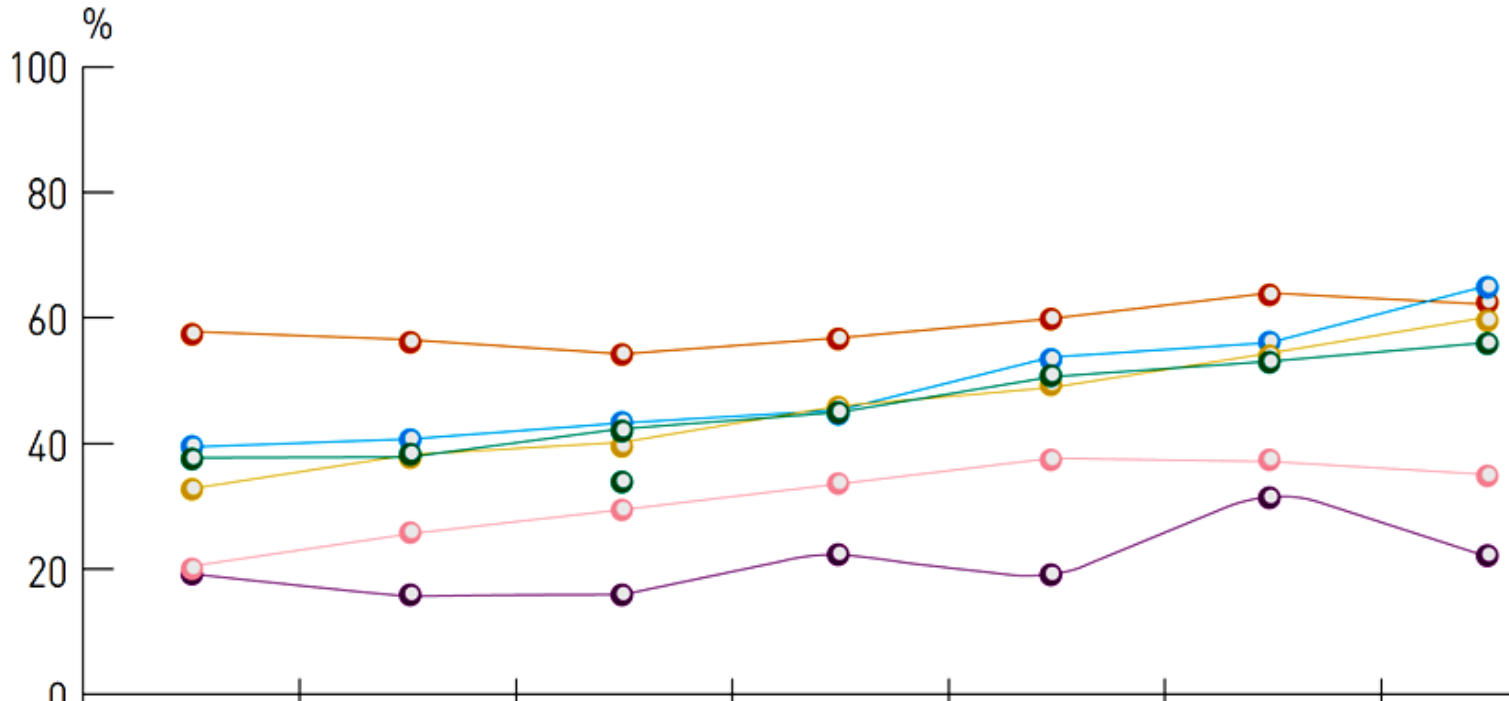
Lifetime Cancer Screening Rates (2004-2010)



	2004	2005	2006	2007	2008	2009	2010
Mean	51.4	25.4	55.7	58.9	65.7	66.9	72.1
Stomach	52.0	48.5	53.5	55.3	65.0	65.1	76.7
Liver	31.8	47.7	58.3	57.6	64.8	81.3	54.2
Colon & rectum	25.2	27.9	34.0	40.7	50.4	48.1	57.1
Breast	55.9	57.4	60.2	66.4	72.7	78.1	79.5
Cervix uteri	76.8	74.0	68.0	73.6	74.4	76.1	75.0

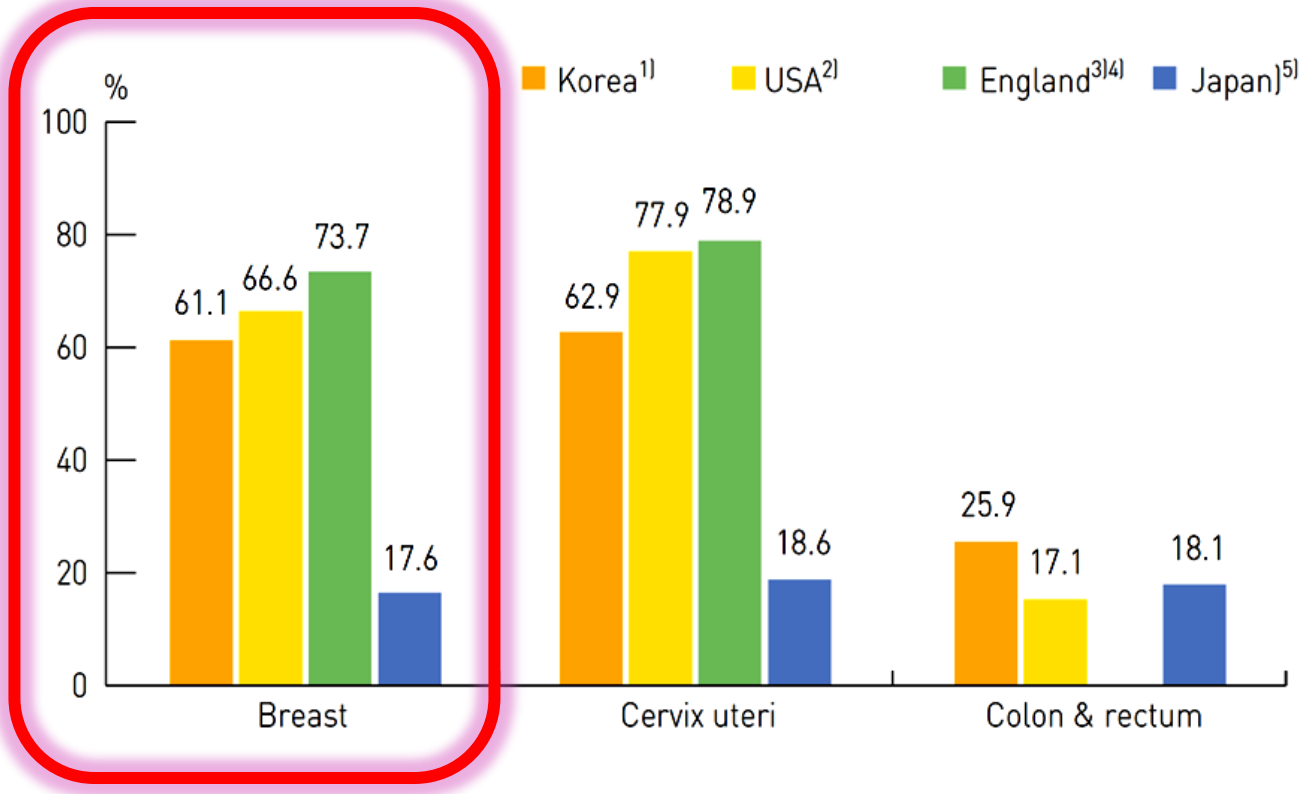
Cancer Screening Rates with Recommendations (2004~2010)



	2004	2005	2006	2007	2008	2009	2010
Mean	38.8	40.3	42.3	45.6	50.7	53.3	56.6
Stomach	39.2	39.4	43.3	45.6	53.5	56.9	65.1
Liver	20.0	16.3	16.5	22.7	19.7	31.3	22.9
Colon & rectum	19.9	25.4	29.4	34.1	37.9	34.7	35.5
Breast	33.2	38.4	40.6	45.8	49.3	55.2	61.1
Cervix uteri	58.3	57.0	54.9	57.0	59.9	63.9	62.9

Source) Korean National Cancer Screening Survey, 2004-2010

Cancer Screening Rates: International Comparison



		Korea [1]	USA [2]	England [3][4]	Japan [5]
Breast	Cancer Screening Rates	61.1%	66.6%	73.7%	17.6%
	Target Population	40 & over	40 & over	45-74	40 & over
	Interval	every 2 years	every 2 years	every 3 years	every 2 years
	Test or Procedure	Mammography	Mammography	Mammography	Mammography & CBE

Source) 1) Korean National Cancer Screening Survey, 2004-2010
2) National Cancer Institute. Cancer Trends Progress Report, 2010
3) NHS Cancer Screening Programmes. NHS Breast Screening ProgrammeAnnual Review, 2009
4) NHS Cancer Screening Programmes. NHS Cervical Screening ProgrammeAnnual Review, 2009
5) Health Statistics in Japan, 2007

Comparison of Medical Audit Data of Screening Mammography with Published Data in Korea and the Ideal Goal of ACR in USA

Audit Data	Goal (ACR)	Kim et al (SMC)	Kim et al (YUMC)	Choi et al (AMC)	Lee et al
Total exam		32,289	15,308	43,329	118,183
PPV1	5-10%	2.5%	0.8%	2.3%	0.9%
PPV2	25-40%	20%	18%	27.7%	24%
Cancers found/1,000cases	2-10	2.0	1.2	1.2	0.5
Recall rate	<10%	6.2%	13%	5.1%	6.7%
Sensitivity	>85%	85.0%	89.5%	91.5%	85%
Specificity	>90%	99%	>99%	95.0%	95.0%

In the near future, results of 10 year performance and outcome measurements of NCSP in Korea will be reported.

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Breast Cancer Screening

- Screening Mammography: **Pros**
  - Critically important examination for early detection of breast cancer
  - Reduction in mortality: ~ 25%
  - In screening mammography: 22~45% of all detected breast cancer
  - The only examination specially approved by the U.S. FDA to screen for breast cancer in asymptomatic women with unknown risk levels.

Breast Cancer Screening

- Screening Mammography: Cons
  - False negative results
    - 4 – 34 %
    - Dense, Younger women, HRT
  - False positive results, recall, biopsy
  - Radiation hazards
    - The developing breast is most susceptible to radiation hazard

Dense Breast

- Dense breast tissue itself is a risk factor for breast cancer.
- The risk is 4~6 fold higher in women who have extremely dense breasts than in matched controls who have fatty breasts
- Mammography has reduced sensitivity in dense breast tissue, with sensitivity as low as 30% to 48% in extremely dense breast.
- There is a high rate of interval cancers.

Breast Density

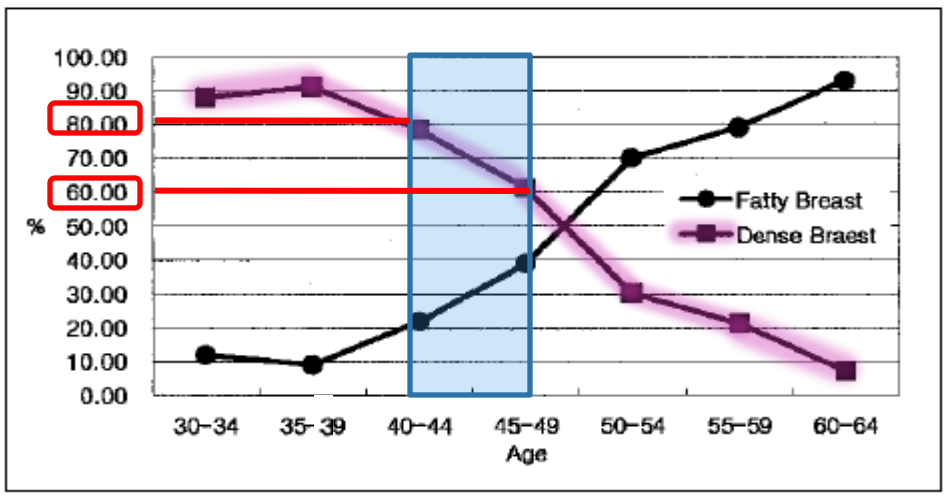


Fig. 3. Parenchymal Density on Mammograms in Korean Women 30 - 64 Years (Categorized as Fatty and Dense Breast). The frequency of dense breast becomes abruptly decreased in 40 - 54 year-old Korean women.

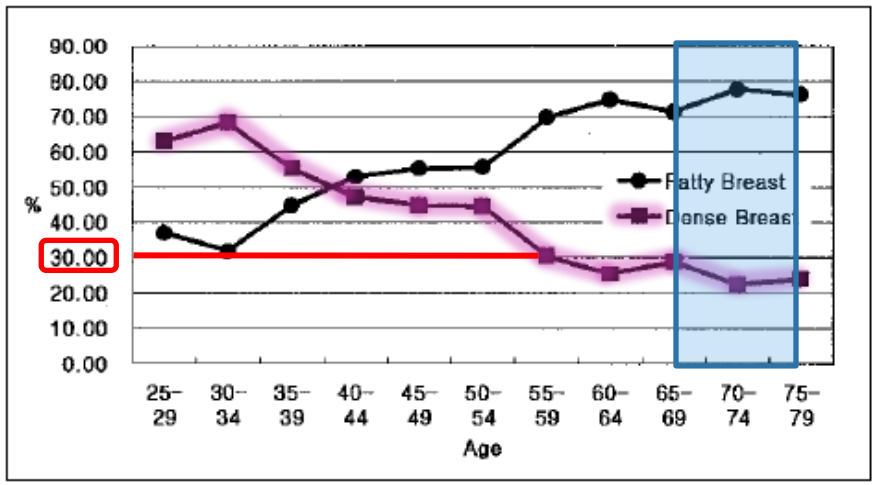


Fig. 4. Parenchymal Density on Mammograms in Western Women 25 - 79 Years Old (Categorized as Fatty and Dense Breast). The frequency of dense breast becomes gradually decreased without abrupt change in 40 - 54 year-old western women (Stomper et al. AJR 1996;167:1261-1265).

Kim SH et al. A n a l ysis and Comparison of Breast Density according to Age on Mammog ram between Korean and Western Women. J Korean Radiol Soc 2000;42:1009-1014

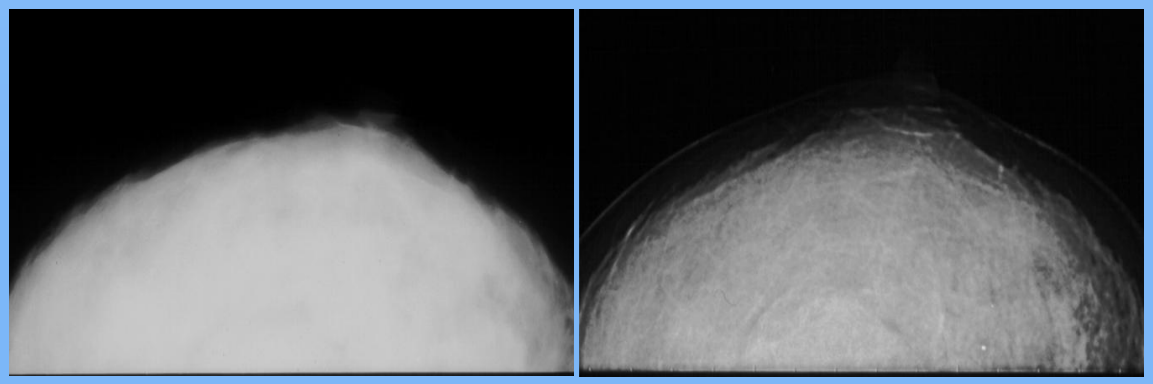
Other or Adjunctive Screening Modalities

- Digital Mammography
- Ultrasound (Hand-held vs. Automated)
- MRI
- Digital Breast Tomosynthesis
- Etc.

Digital Mammography

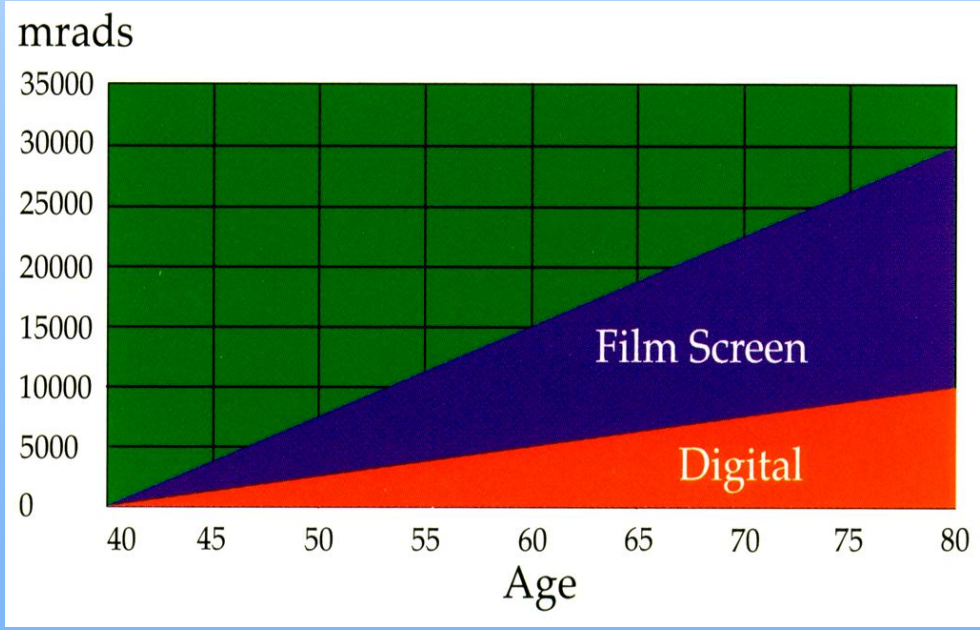
- The multicenter Digital Mammographic Imaging Screening Trial (DIMIST) :

  Improved performance of digital mammography in women who had dense breasts, with 70% sensitivity compared with 55% sensitivity for film-screen mammography



Digital Mammography

- Reduced Radiation Dose



Cumulative Dose for a 6.5 cm Breast

Screening Breast US

- Pros
  - Better sensitivity
  - Relatively inexpensive (especially compared to MRI)
  - No radiation
  - Well-tolerated, noninvasive exam
  - More effective in women with a high risk of breast cancer, especially young women

Screening Breast US

- Cons
  - Highly operator-dependent
  - High false-positive rate compared to MMG
  - Clinical significance of additional cancers found with ultrasound is unknown.

Results with screening breast ultrasound

Author	No.	No. Bx. (%)	No. Cancers (%)	Prevalence (%)
Gordon & Goldberg (1995)	12,706	279 (2.2)	44 (16)	44/12,706 (0.35)
Buchberger et al (2000)	8,103	362 (4.5)	32 (8.8)	32/8,103 (0.39)
Kaplan et al (2001)	1,862	102 (5.5)	6 (6.6)	6/1,862 (0.3)
Kolb et al (2002)	13,547	358 (2.6)	37 (10)	37/13,547 (0.27)
Crystal et al (2003)	1,517	38 (2.5)	7 (18)	7/1,517 (0.46)
Leconte et al (2003)	4,236	Not stated	16	16/4,236 (0.38)
Corsetti et al (2006) with update by S. Ciatto	7,615	Not stated	36	36/7,615 (0.47)
Total	**49,586**	**1,139/37,735 (3.0)**	**178**	**178/49,586 (0.36)**

Berg WA. Radiol Clin N Am 2007;24:895-906

Screening Breast US

- 178 cancers seen only on US
  - 94%: Invasive cancer
  - 6%: DCIS
- Invasive cancer
  - 70%: 1cm or smaller in size
- Stage
  - 86%: Node Negative
- Breast density
  - Fatty breast tissue were exclude
  - > 90%: Dense (either parenchymal pattern III or IV)

Berg WA. Radiol Clin N Am 2007;24:895-906

Screening Breast US

- American College of Radiology Imaging Network study (ACRIN 6666)
  - Evaluation of ultrasound screening in women with elevated risk of breast cancer
  - Adding a single screening US to MMG yield an additional 4.2 (1.1 to 7.2) cancers per 1000 high-risk women.
  - Diagnostic accuracy (AUC): 0.78 (M), 0.91 (M+US)
  - Supplemental cancers: 92% invasive cancer, median size 10mm, 89% negative node,
  - Substantially increases the number of false positives.

Screening Breast US in Korea

Investigator / Yr	No.	No. Bx. (%)	No. malignant (%)	Prevalence (%)
Overall of 7 studies (1995-2006)	49,586	1,139 (3.0)	126/1,139 (11.1)	178/49,586 (0.36)
Shin et al (2005)	576	73 (12.7)	2/73 (2.7)	2/576 (0.35)
Kwak et al (2005)	3998	433 (10.8)	2/433 (0.5)	2/3998 (0.05)

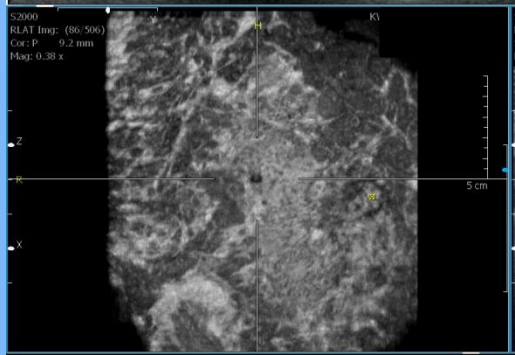
Screening Breast US

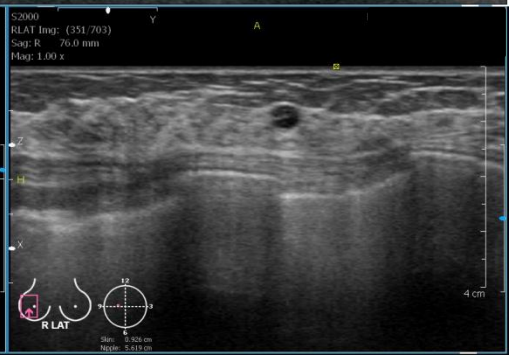
- Ultrasound remains unproven as a screening tool.
- Potential role in screening: limited to women with dense breasts on mammography
- In order to prove a clear outcome benefit for screening ultrasound, large multicenter randomized clinical trial is needed in Korea.
- Until a clear outcome benefit is established for routine ultrasound breast cancer screening, it is unlikely to be widely accepted.

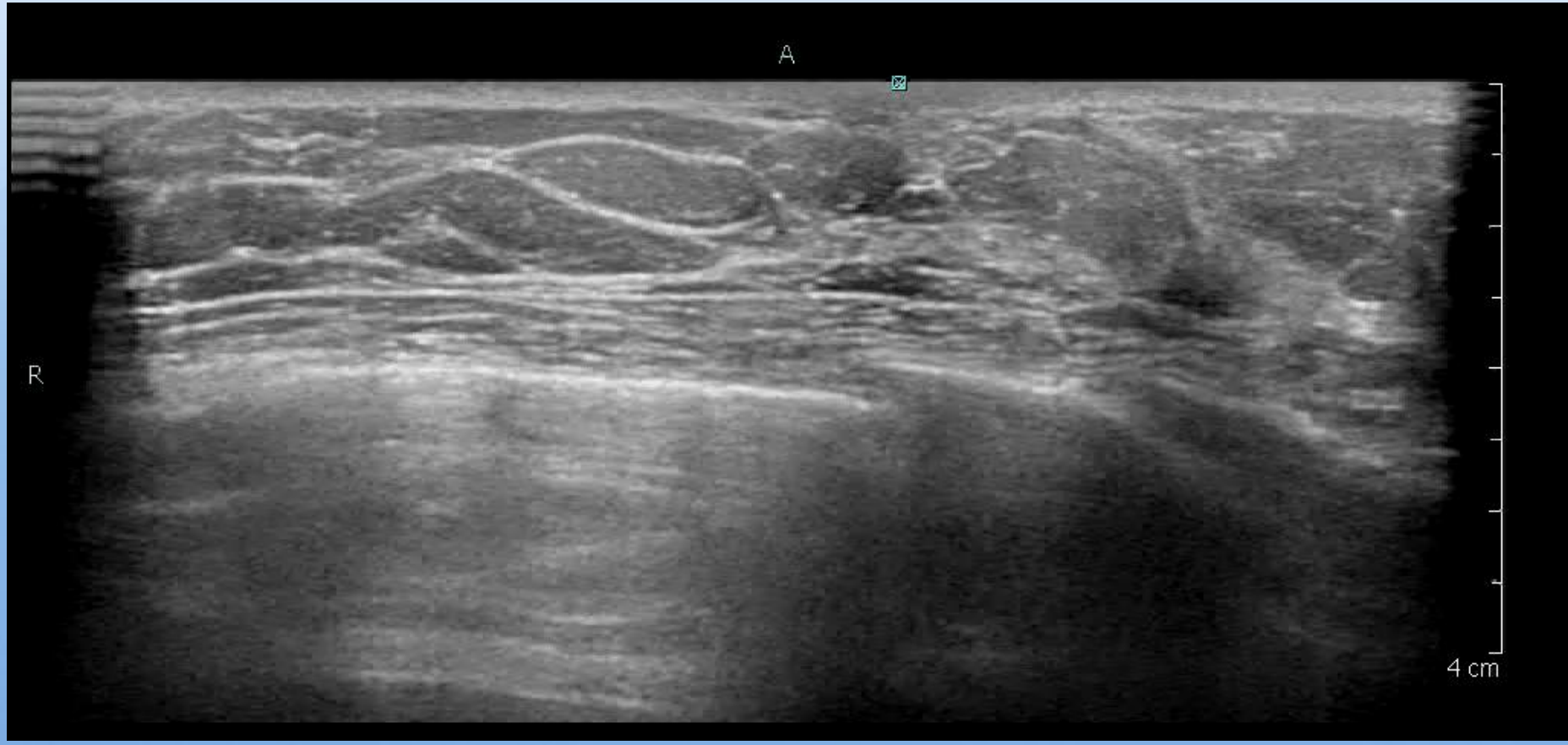
Automated Whole Breast US

Operator dependency

Reproducibility






A
R
4 cm

Automated Whole Breast US

- Potential for complete documentation
- More readily reproducible
- 3D capability through multi-planar reconstruction
- Delayed interpretation outside of real time
- Optimizing the radiologist's reading environment

Automated Whole Breast US

- Breast cancer detection doubled from 23 to 46 in 6,425 studies using AWBU with mammography, resulting in an increase in diagnostic yield from 3.6 per 1,000 with mammography alone to 7.2 per 1,000 by adding AWBU.
- PPV for biopsy based on mammography findings was 39.0% and for AWBU 38.4%.
- The number of detected invasive cancers 10 mm or less in size tripled from 7 to 21 when AWBU findings were added to mammography.
- AWBS may improve the practical implementation of screening US.

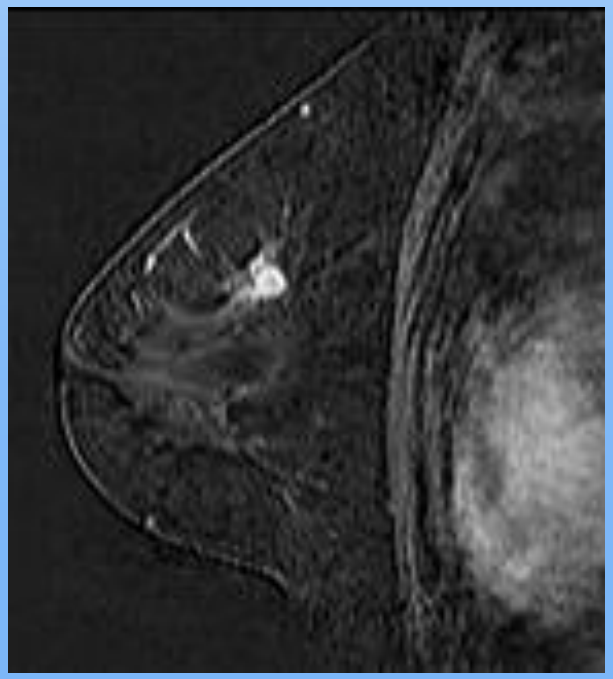
Kelly KM, et al. Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. Eur Radiol (2010) 20: 734–742

Screening MRI

- Advantages
  - High Sensitivity for malignancy: 80-100%
    - Invasive 90-95%
    - DCIS 70-80%
  - Sensitivity is not affected by breast density
  - All breast tissue is visualized
  - No radiation hazard
  - No operator dependent

Screening MRI

- Recent clinical trials:
  - Surveillance of women with high risk
  - Significantly improve the detection of occult breast cancer

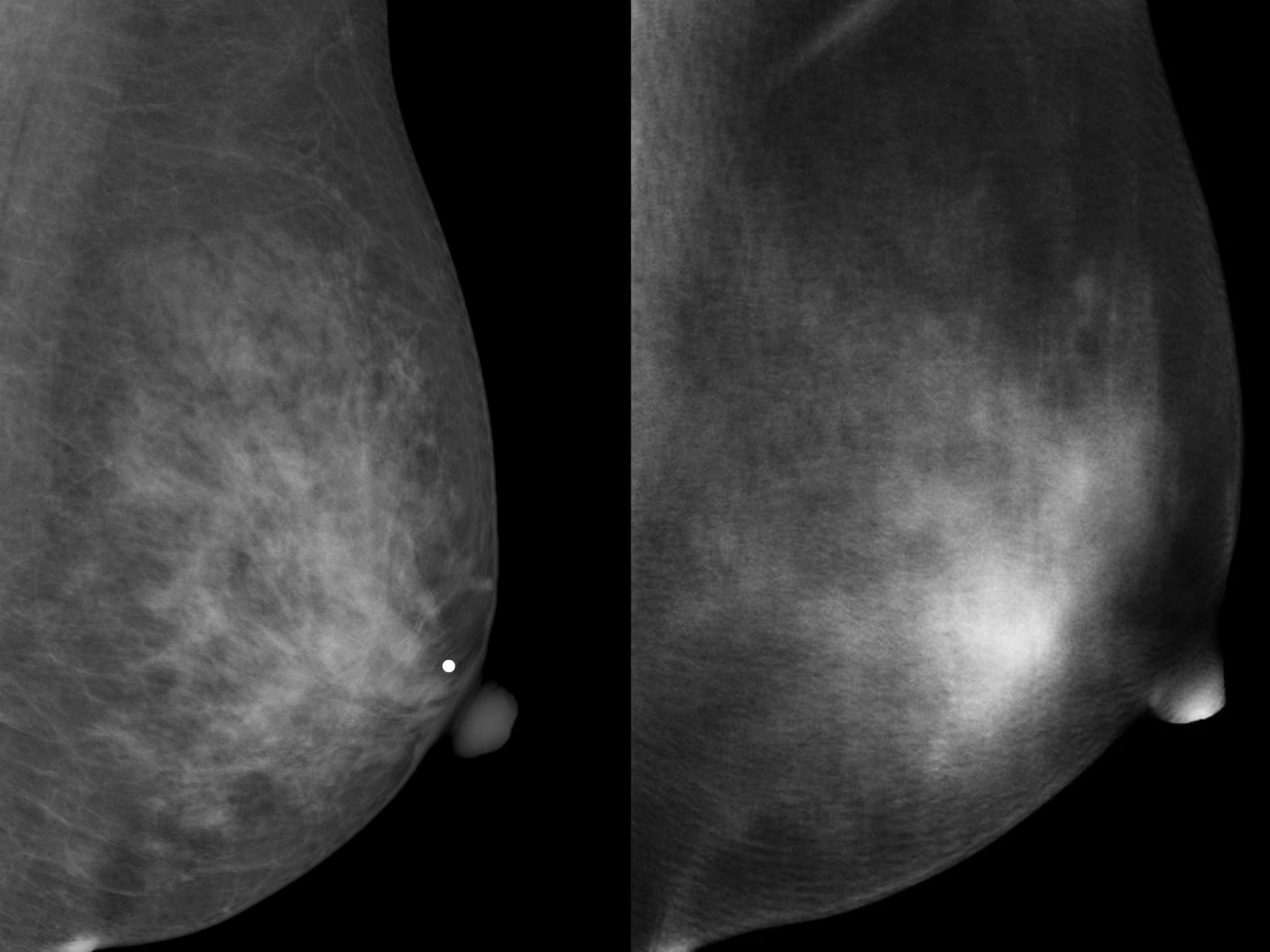


Screening MRI

- 2007 March, American Cancer Society
  - New screening MRI guidelines
  - Based on available evidence
  - Screening Breast MRI in addition to mammography for women at high risk for breast cancer
    - *BRCA* mutation
    - First-degree relative of *BRCA* carrier, but untested
    - Lifetime risk ~20–25% or greater, as defined by BRCAPRO or other models that are largely dependent on family history
    - Radiation therapy to chest between age 10 and 30 years

Digital Breast Tomosynthesis

- Digital Breast Tomosynthesis (DBT) is a new tool that can provide mammographic images as slices through the breast.
- Reducing or eliminating tissue overlap



Digital Breast Tomosynthesis

- Advantages
  - Lower recall rate & additional views
  - Better delineation of anatomy, mass & architectural distortion
  - Increased conspicuity due to elimination of overlapping tissue
  - Higher cancer detection rates
  - Improved specificity
  - No change in sensitivity
- Potential to be used as a screening, especially dense breasts

Summary

- Characteristics of Korean breast cancer are continuously and rapidly increasing incidence and high proportion of young (premenopausal) age cancer
- The National cancer screening program for breast cancer began in 1999.
- MQSA was legislated in 2003.
- The breast cancer screening rate has been increased.

Summary

- Korean women in their 40s showed a higher frequency of dense mammograms (80 - 60%).
- The mortality rate of breast cancer has not decreased yet.
- Published Data in individual institution revealed low PPV_1 and low prevalence.
- In the near future, results of 10 year performance and outcome measurements of NCSP in Korea will be reported.

Summary

- Due to the limitation of mammography, particularly in women with dense breast or high risk, other or adjunctive screening modalities should be considered.
- Further studies are needed to investigate the role of mammography and other modalities as a screening tool in Korea.

Thank You for Your Attention !

Brief Hx. of the NCSP in Korea

1999	The National Cancer Screening Programme launched for stomach, breast, and cervical cancer free-of-charge. Target population was Medical Aids.
2002	Target population expanded including the lower 20% of National Health Insurance beneficiaries.
2003	Liver cancer was additionally serviced and the target population expanded to the lower 30% of National Health Insurance beneficiaries.
2003	Cancer Control Act, a legal framework for controlling cancer in Korea, was legislated.
2004	Colon cancer screening was additionally serviced.
2005	Target population expanded to the lower 50% of National Health Insurance beneficiaries.