

Innovation and Challenge



Seigo Nakamura, M.D., Ph.D.

**Professor of Surgery
Director of Breast Center
Showa University Hospital
Auditor of Japanese
Breast Cancer Society**



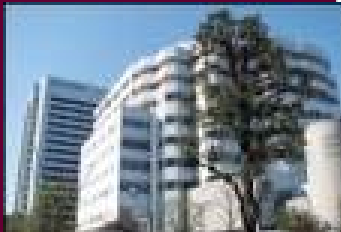
 **SHOWA UNIVERSITY HOSPITAL**
BREAST CENTER

Seigo Nakamura

Personal History



Born in Asakusa, 1956



A new breast center at Showa university Hospital since 2010

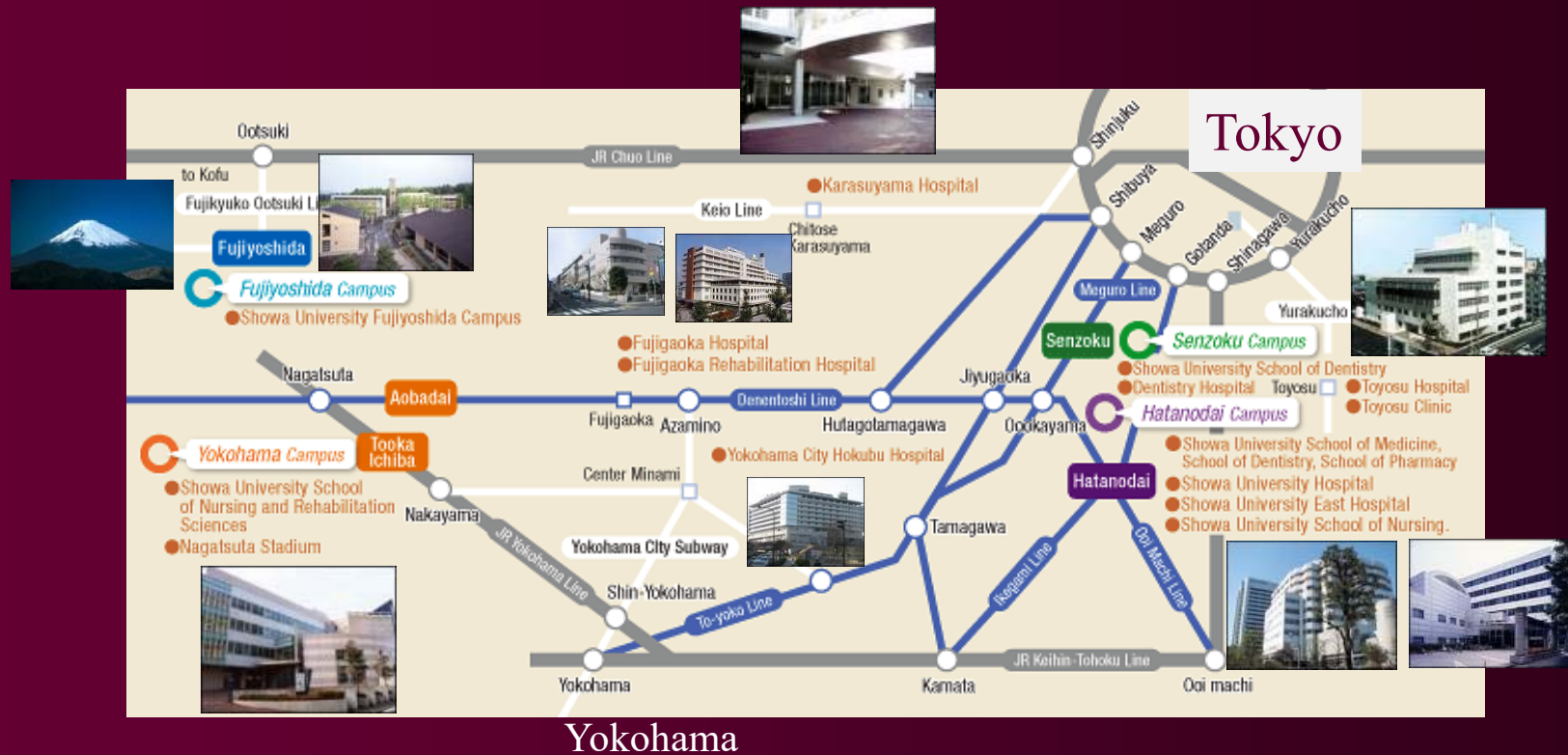


Graduated from Chiba university in 1982



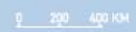
Finished surgical residency and established breast center in 2005

In 1928, Showa University founded the University Hospital; it has provided high quality medical education for a long time. Subsequently, several affiliated hospitals were established with various functions to meet the needs of the local community. Following a unique conception, these hospitals aim towards a true medical education involving neighboring fields such as pharmaceuticals, dentistry, and nursing. The role of Showa University affiliated hospitals has steadily increased in importance in an era of transition in Japan.





Showa university
Koto Toyosu Hospital



A new university hospital has opened at Tokyo Bay side area in 2014





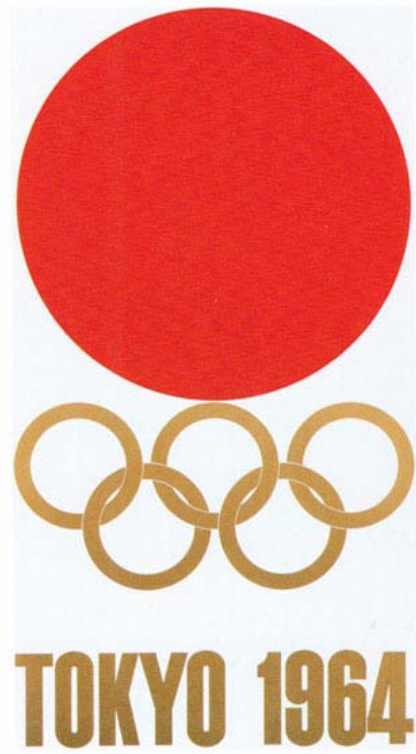
Japanese river otter
Extinct animal
Never seen for more than 30
years



THE UNIVERSITY OF TEXAS

MD Anderson
~~Cancer Center~~

Making Cancer History®



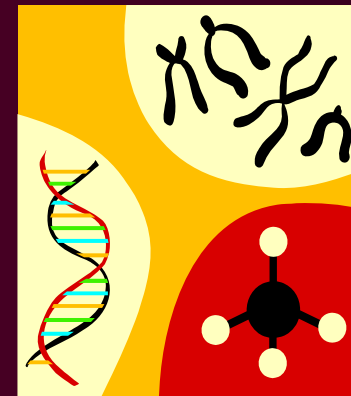
Paradigm shift in Breast Cancer treatment



Halstead
1900-



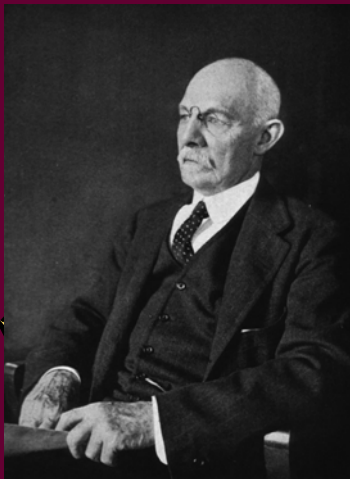
Fisher
1980-



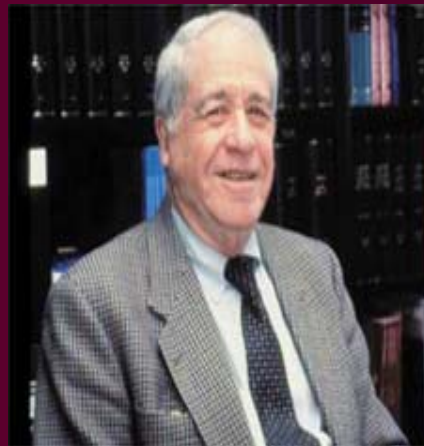
Molecular approach
2000-

Mastectomy+Ax ⇒ BCS ⇒ BCS+SLNB ⇒ Non surgical approach

Paradigm shift in Breast Cancer treatment



Halsted
1900-



Fisher
1980-



Molecular approach
2000-

Mastectomy+Ax ⇒ BCS ⇒ BCS+SLNB ⇒ Non surgical approach

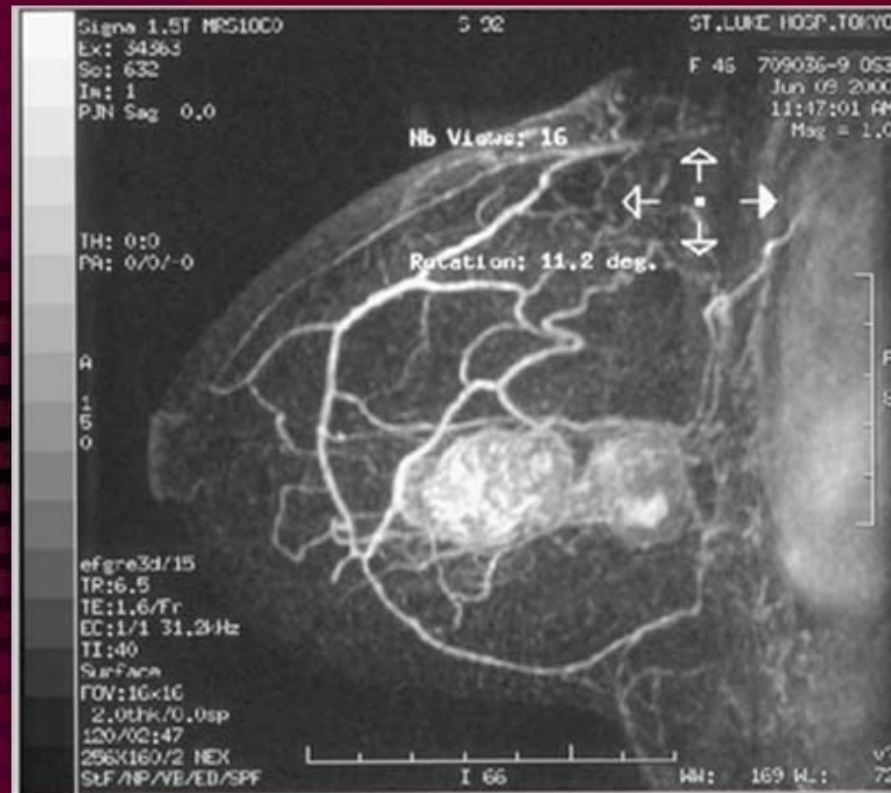
Molecular diagnosis

Molecular imaging

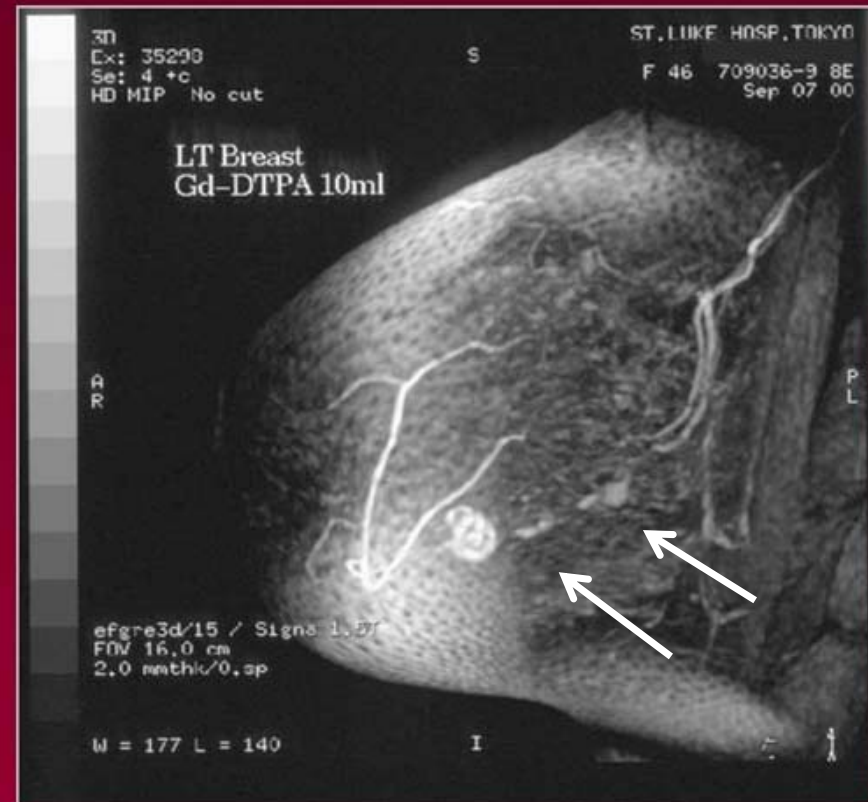
Molecular based surgery

**To assure
complete resection
with minimal margin**

Dendritic type. Residual in situ component (+)



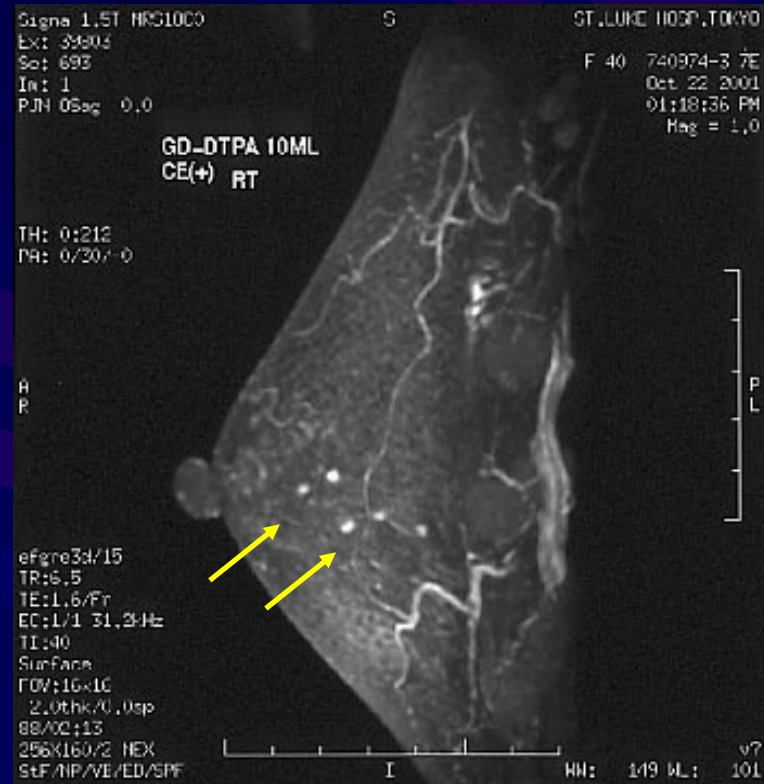
Pre chemo Tx



Post chemo Tx



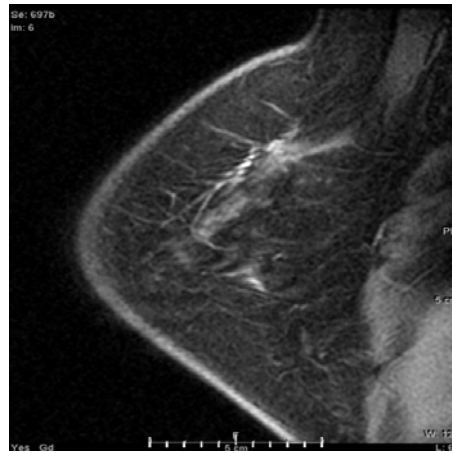
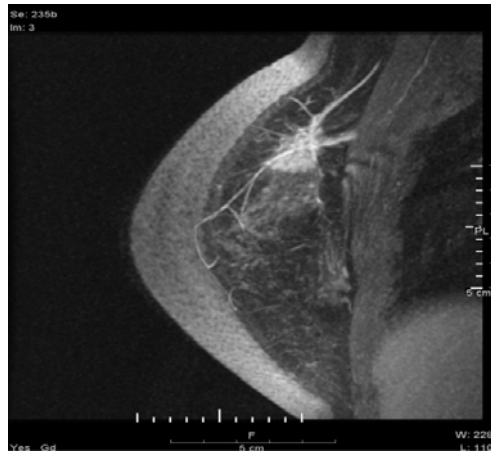
Before AT



After AT



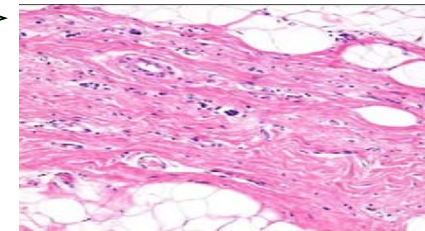
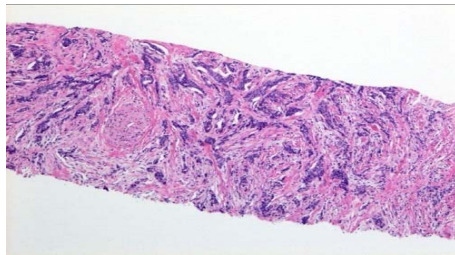
Near pCR



Pre

FEC100

DOC 75



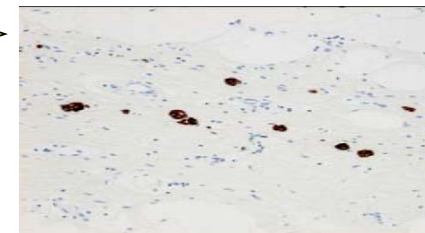
H&E staining, original magnification $\times 100$



H&E staining, original magnification $\times 40$



keratin staining, original magnification $\times 100$



Role of breast imaging for primary chemotherapy

MMG



US



US guided biopsy



MRI

Pathological exam.



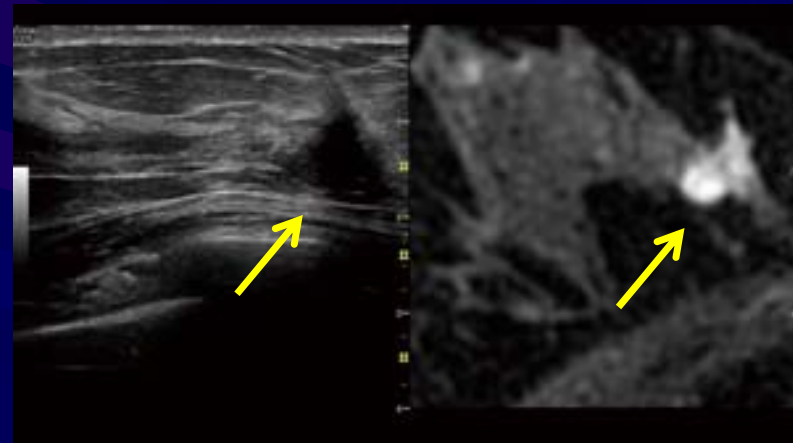
Select surgical procedure
US guided mapping

MR guided Mammotome



Volume Navigation(LOGIQ E9)

A tool that combines real-time ultrasound images with previously acquired CT, MR, or PET images. (**GPS-like technology**)

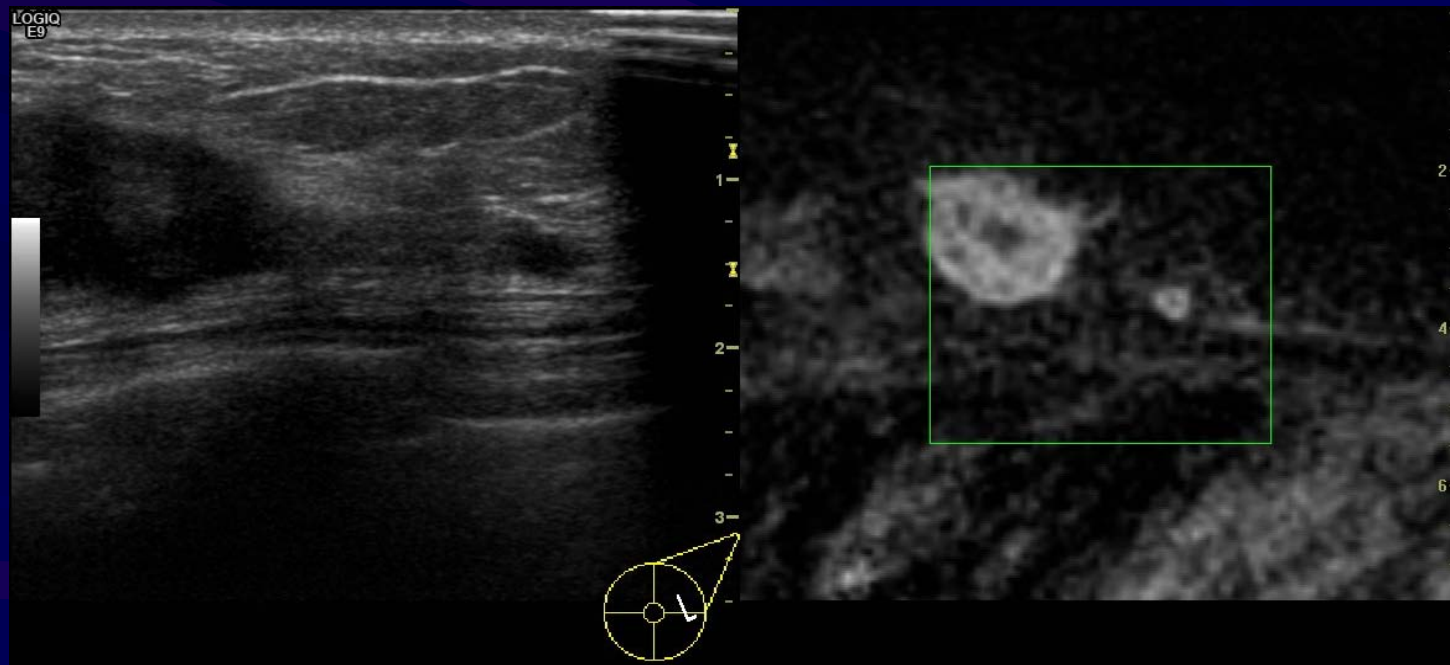


Urtrasound

MRI

Volume Navigation

Small daughter nodule detected by high resolution MRI can be easily identified by US under Volume Navigation

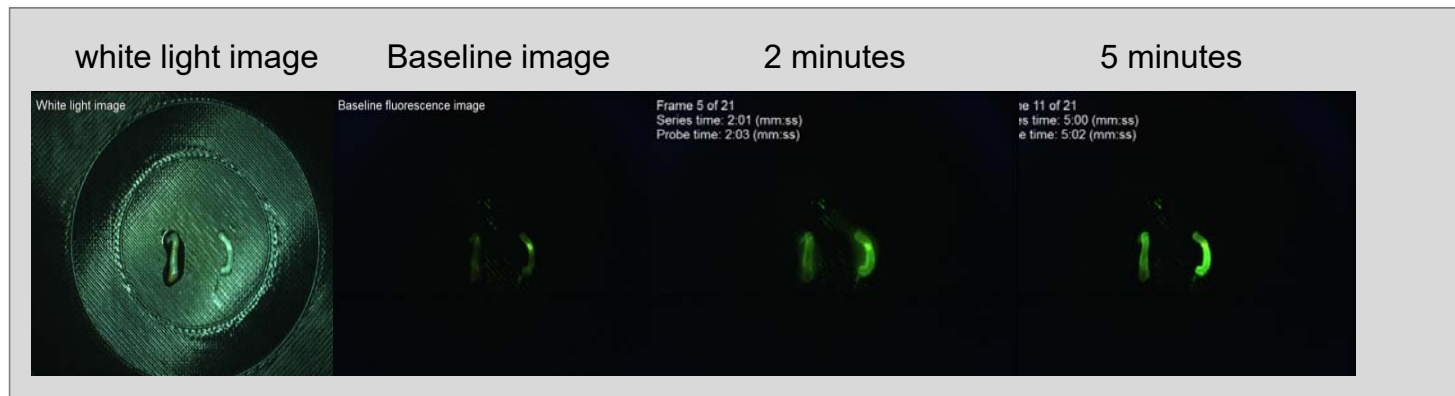




Cancer Detection in CNB Specimens using Realtime Cancer Imaging with Fluorescence

Tomoko Takamaru¹⁾²⁾, Sadako Akashi-Tanaka²⁾, Murasaki Ikeda²⁾,
Rikako Hashimoto²⁾, Reiko Yoshida²⁾, Takashi Kuwayama²⁾,
Katsutoshi Enokido¹⁾, Miwa Yoshida¹⁾, Terumasa Sawada²⁾, Yuko Hirota³⁾,
Yasuteru Urano⁴⁾ and Seigo Nakamura¹⁾

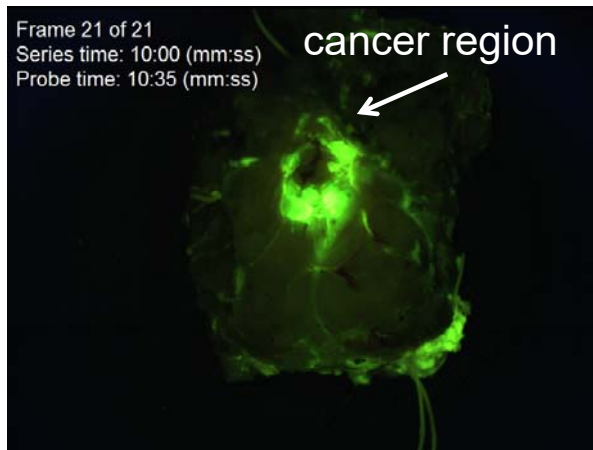
- 1) Breast Surgery, Showa University Koto Toyosu Hospital
- 2) Breast Surgical Oncology, Showa University Hospital
- 3) Pathology, Showa University Koto Toyosu Hospital
- 4) Laboratory of Chemical Biology and Molecular Imaging, Graduate School of Medicine,
The University of Tokyo



Fluorescence Images were automatically obtained every 30 seconds for 10 minutes after adding gGlu-HMRG(γ -glutamyl hydroxymethyl rhodamine green) on the specimens.

This is a representative time-course fluorescent images of CNB upon treatment with gGlu-HMRG.

Cancer samples : Invasive breast carcinoma (schirrous carcinoma)



Breast-conserving surgery specimen:

MR-guided Focused Ultrasound Surgery of ductal carcinoma in situ: Therapeutic effect and safety

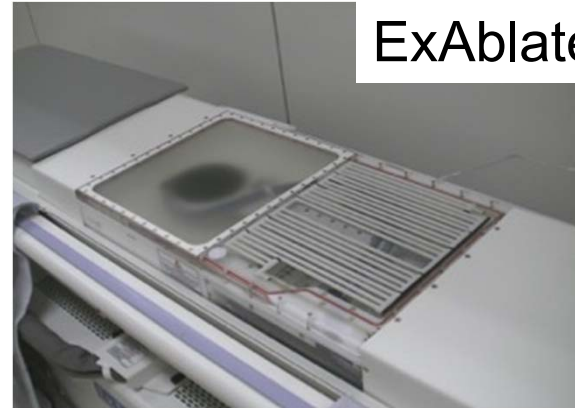
Dep. Breast surgical oncology, Showa university school of Medicine
Cancer precision medicine center, Cancer Institute

Akiko Matsutani, Yoshimi Ide, Takashi Kuwayama, Sadako Akashi,
Akiyoshi Sawada, Hitoshi Zembutsu, Sadao Amano,
Hutoshi Akiyama, Seigo Nakamura

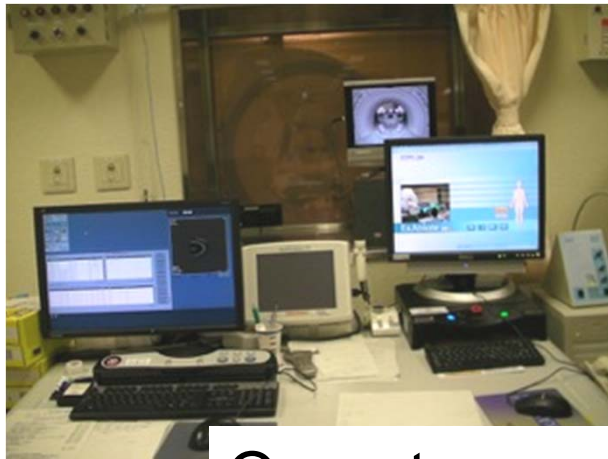
ExAblate system



3T-MRI (GE)



ExAblate[®] 2000 (InSightec)

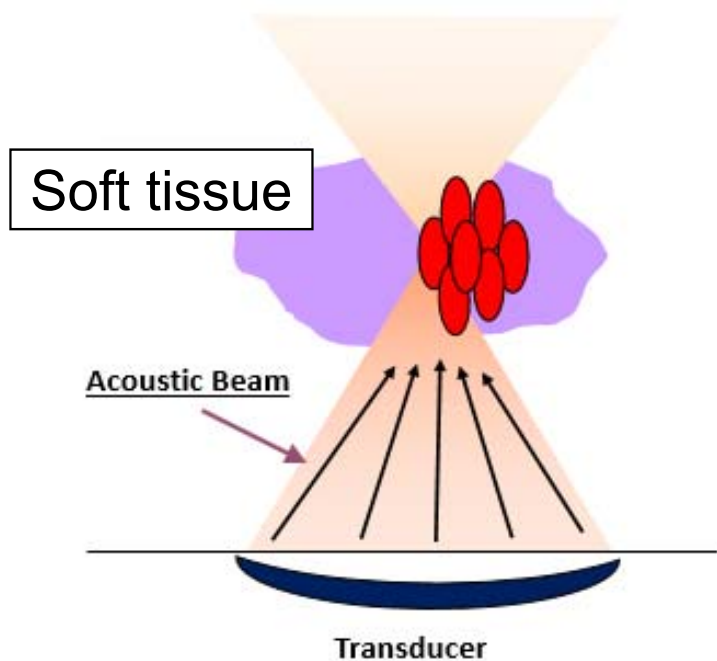


Operator console



Equipment cabinet

HIFU: High-Intensity Focused Ultrasound, FUS: Focused Ultrasound Surgery



US	For diagnosis	For treatment
Frequency	3-20 MHz	0.5-2 MHz
Output	< 5mW/ cm ²	> 100 W/ cm ²

Heat caused by acoustic beam generates denatured protein of the target lesion.
Heat effect to surrounding tissues is limited.

Using new instruments different from previous research

If we verify no residual tumor using VAB, this leads to active surveillance trial.

DCIS (n=10)

MRgFUS

VAB+operation

Radiation therapy

f/u after surgery

Within 2 weeks

Treatment is performed according to the guidelines

VAf

To verify the amount of cfDNA in plasma

Before FUS

Afer FUS

Study design₆



**Accurate assessment of pCR
after neoadjuvant chemotherapy
→ Omission of breast surgery**

Naoki Hayashi, St.Luke's International Hospital

step 1

- Retrospective study to assess the accuracy of cCR by conventional radiological findings

Done!

step 2

- Multicenter prospective trial to assess the accuracy of cCR by vacuum assisted breast biopsy in addition to radiological findings

step 3

- Multicenter prospective trial to assess the prognosis of patients with cCR by VAB and radiological findings omitting breast surgery



Mammotome One

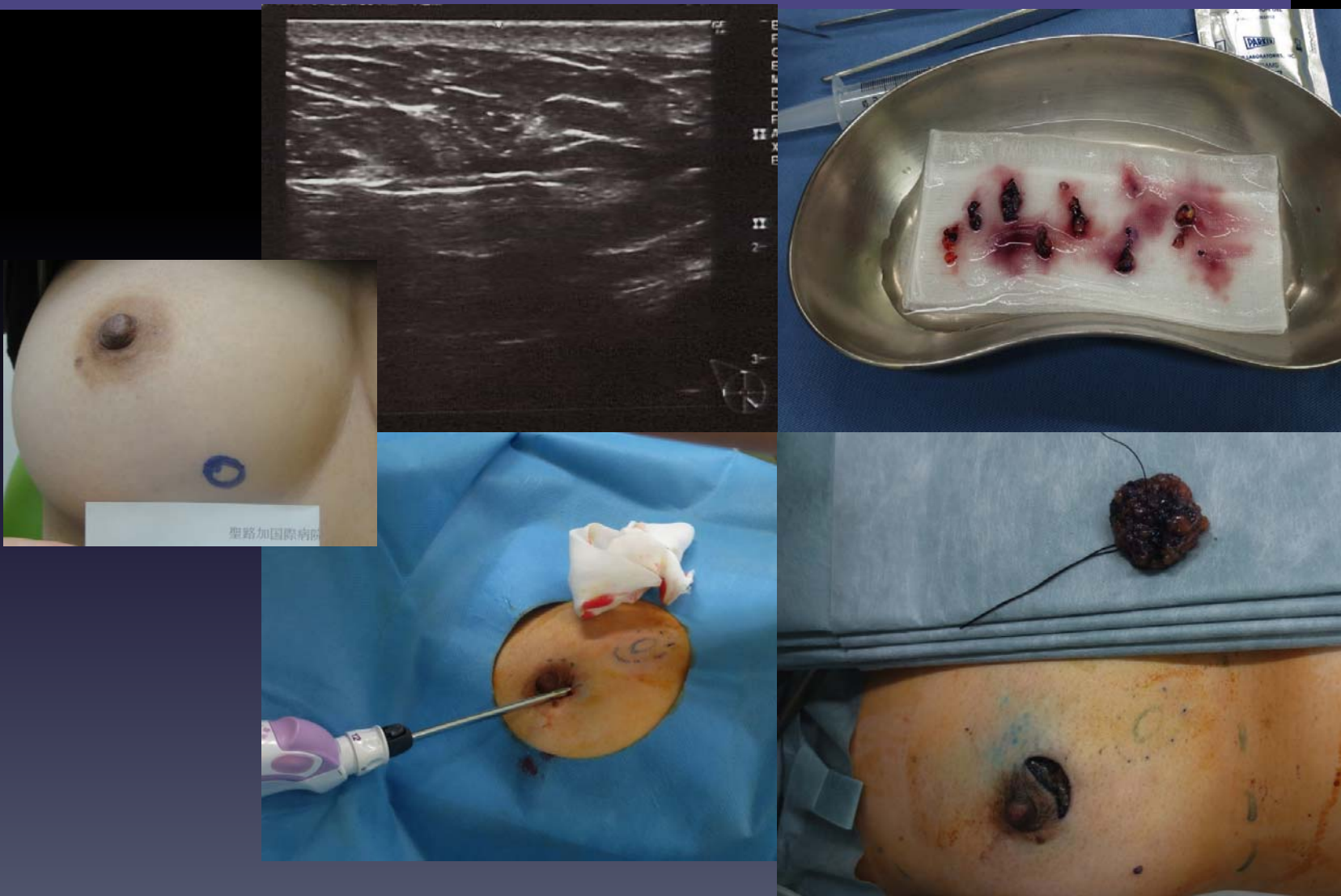
Primary endpoint

- ① PPV of cCR by radiological assessment
- ② PPV of cCR by VAB in addition to radiological assessment

Secondary endpoint

- ① PPV for the presence of residual in situ component by VAB

MMT before surgical excision



Diagnostic performance of dedicated breast PET scanner with a ring detector

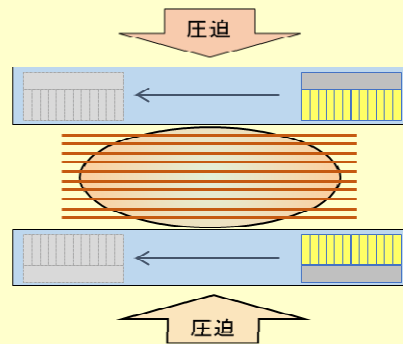
R. Hashimoto¹, S. Akashi-Tanaka¹, M. Ikeda¹, C.
Watanabe¹, H. Masuda¹, K. Taruno¹, T. Takamaru¹, Y. Ide¹,
T. Kuwayama¹, S. Nakamura¹ et.al

Department of Breast Surgical Oncology, Showa University
Hospital¹

対向型乳房専用PET装置

PEM: Positron Emission Mammography

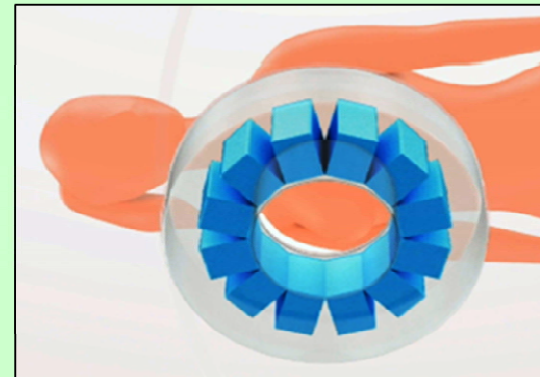
X線マンモグラフィのように乳房を圧迫し、移動型検出器により複数平面断層を得る



リング型乳房専用PET装置

dbPET: dedicated breast PET

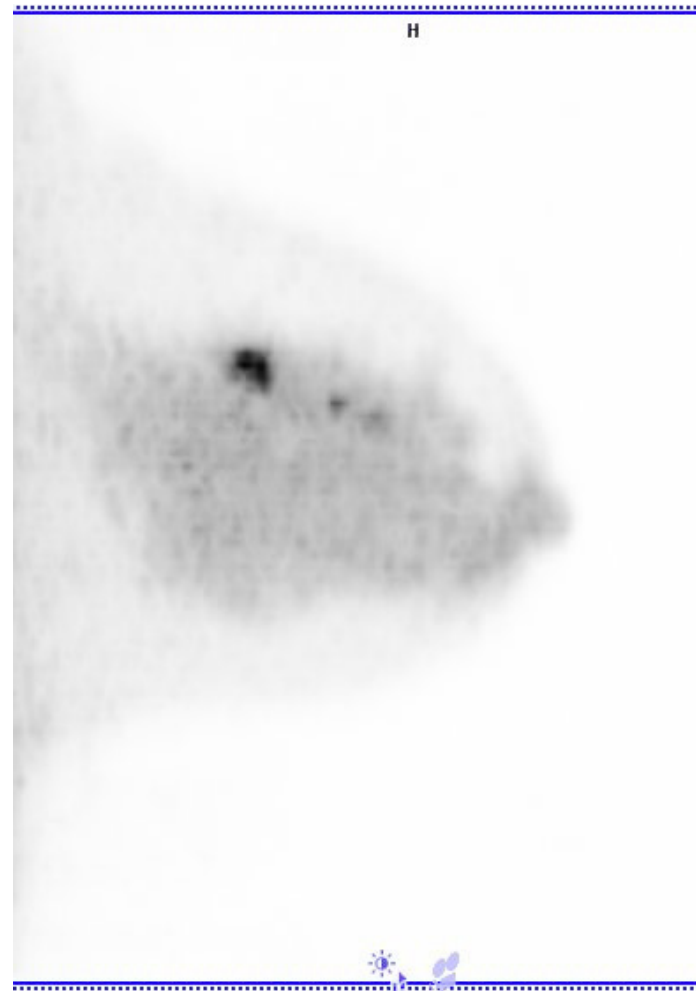
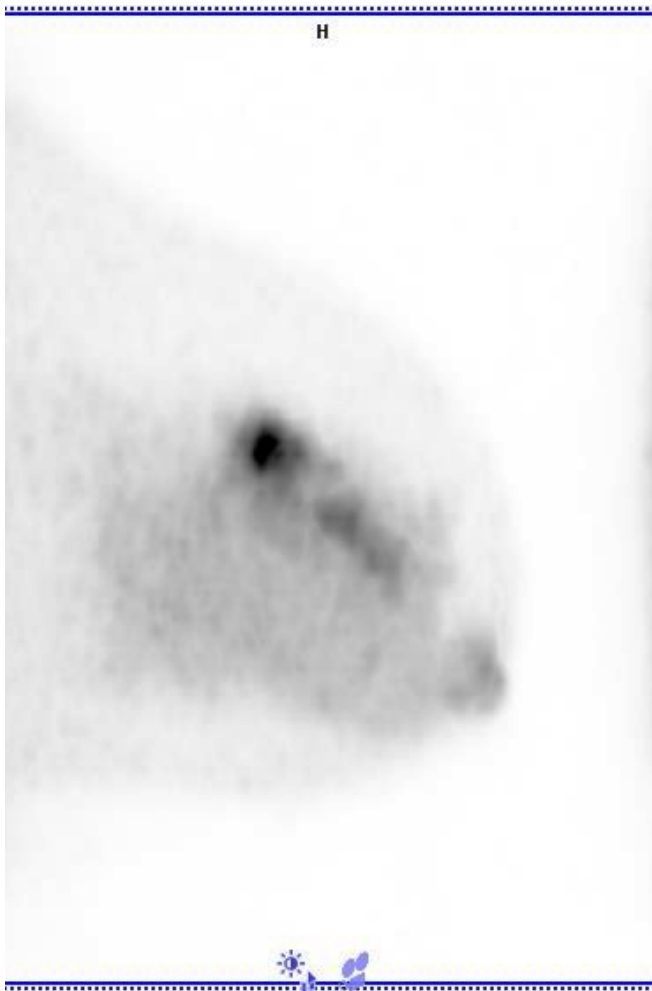
全身用PET装置と同じように、円周上に検出器を配して、乳房の断層画像を得る



参考文献: MacDonald et al. JNM 2009 Vol.50 P.1666-1675

All patients underwent a wb-PETMRI using Biograph mMR[®](Siemens Healthcare) approximately 80 minutes after fluorine-18 fluorodeoxyglucose ((¹⁸F)-FDG;3.0MBq/kg) injection, followed by dbPET using Dedicated Breast PET System Elmammo[®] (Shimadzu, Kyoto, Japan) which required 5 minutes per breast.





SUV7.99→2.69

Oncotype DX[®] 21-Gene Recurrence Score (RS) Assay

16 Cancer and 5 Reference Genes From 3 Studies

PROLIFERATION

Ki-67
STK15
Survivin
Cyclin B1
MYBL2

ESTROGEN

ER
PR
Bcl2
SCUBE2

$$RS = + 0.47 \times \text{HER2 Group Score} \\ - 0.34 \times \text{ER Group Score} \\ + 1.04 \times \text{Proliferation Group Score} \\ + 0.10 \times \text{Invasion Group Score} \\ + 0.05 \times \text{CD68} \\ - 0.08 \times \text{GSTM1} \\ - 0.07 \times \text{BAG1}$$

INVASION

Stromelysin 3
Cathepsin L2

GSTM1

BAG1

CD68

REFERENCE

Beta-actin
GAPDH
RPLPO
GUS
TFRC

HER2

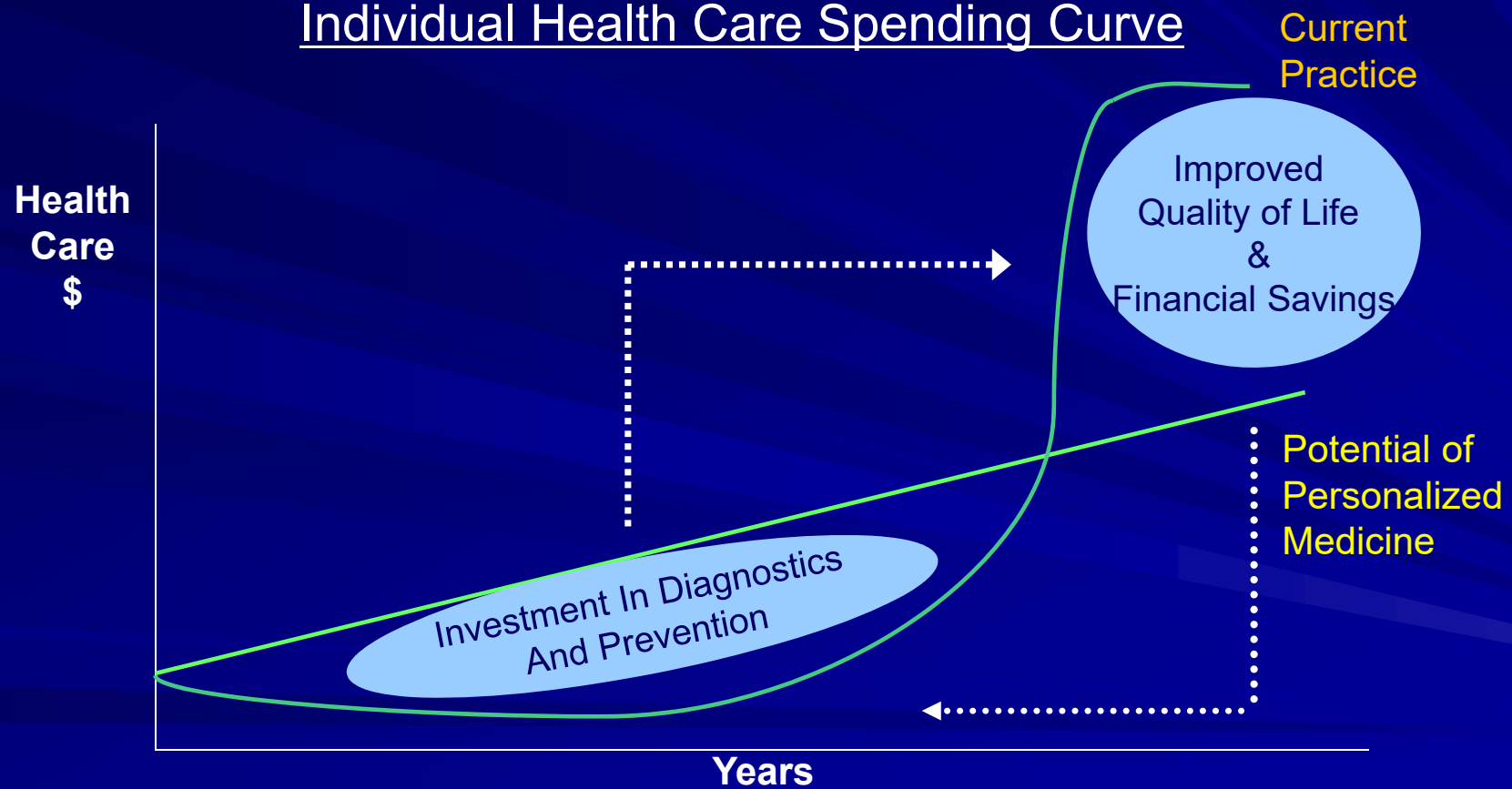
GRB7
HER2

Category	RS (0 -100)
Low risk	RS <18
Int risk	RS 18 - 30
High risk	RS ≥ 31

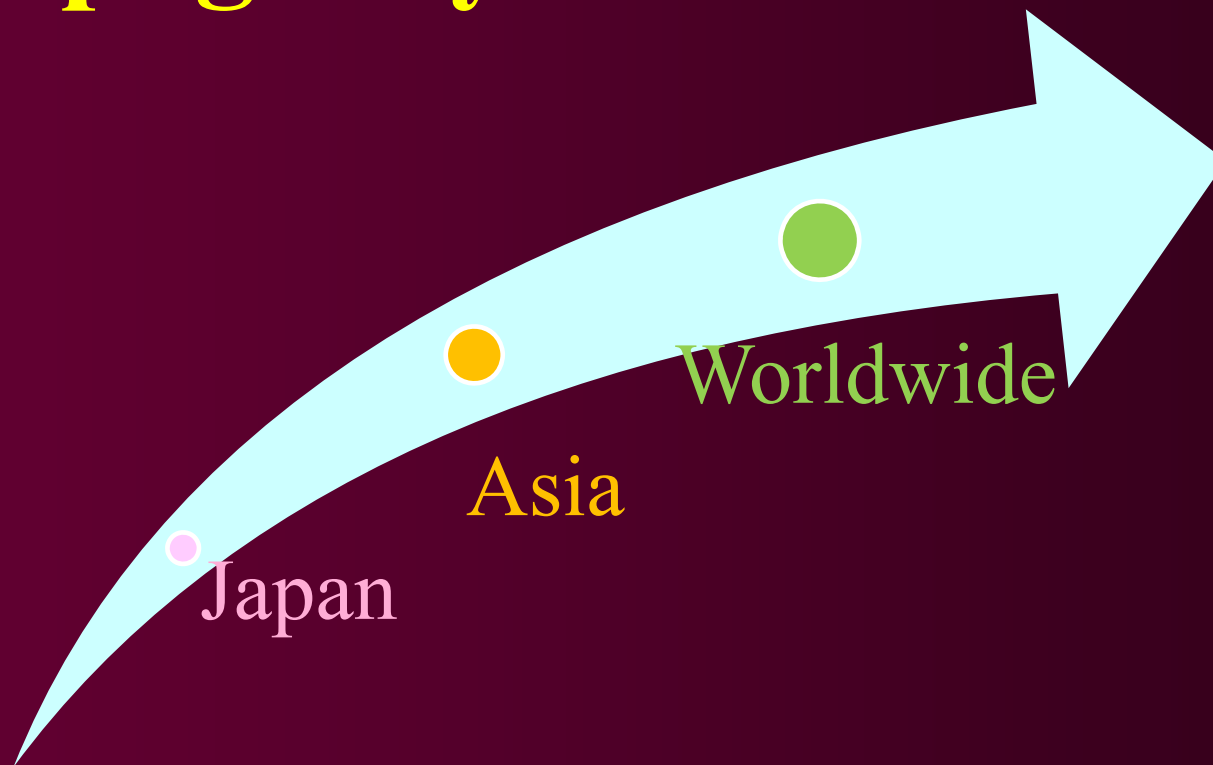
Paik et al. *N Engl J Med.* 2004;351:2817-2826.

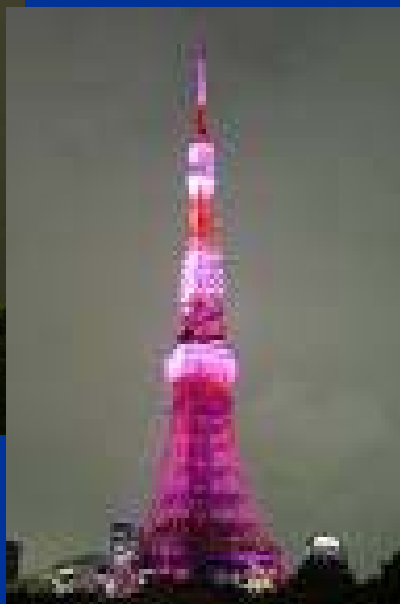
Future Health Care Spending

Individual Health Care Spending Curve



Escape from Galápagos syndrome

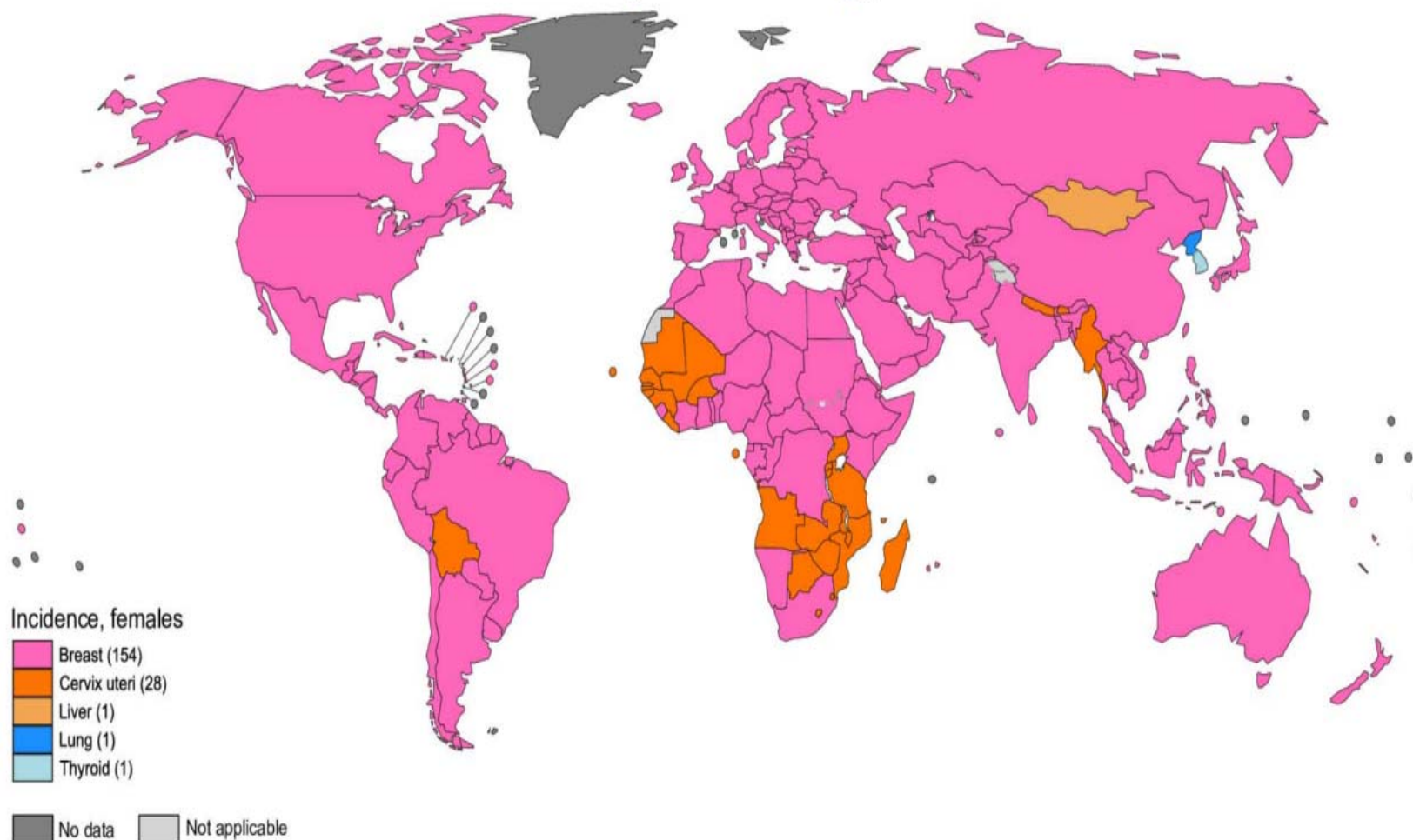




Innovation & Challenge



Most common cancer by country, females 2018



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: Globocan 2018
Map production: IARC
World Health Organization



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Asian BRCA Consortium

China: Zhen Hu

India: Rajiv Sarin, Sunita Saxena

Hong Kong: Ava Kwong

Indonesia: Teguh Aryandono

Japan: Seigo Nakamura

Korea: Kim Sung-Won, KOHBRA

Malaysia: Soo Teo

Philippines: Rodney Dofitas

Singapore: Philip Iau

Thailand: Pimpicha Patmasiriwat

Taiwan: CS Huang

Vietnam: Olphira Ginsburg, LeMong Quang



Re: Angelina Jolie's double mastectomy and the question of who owns our genes

2 June 2013

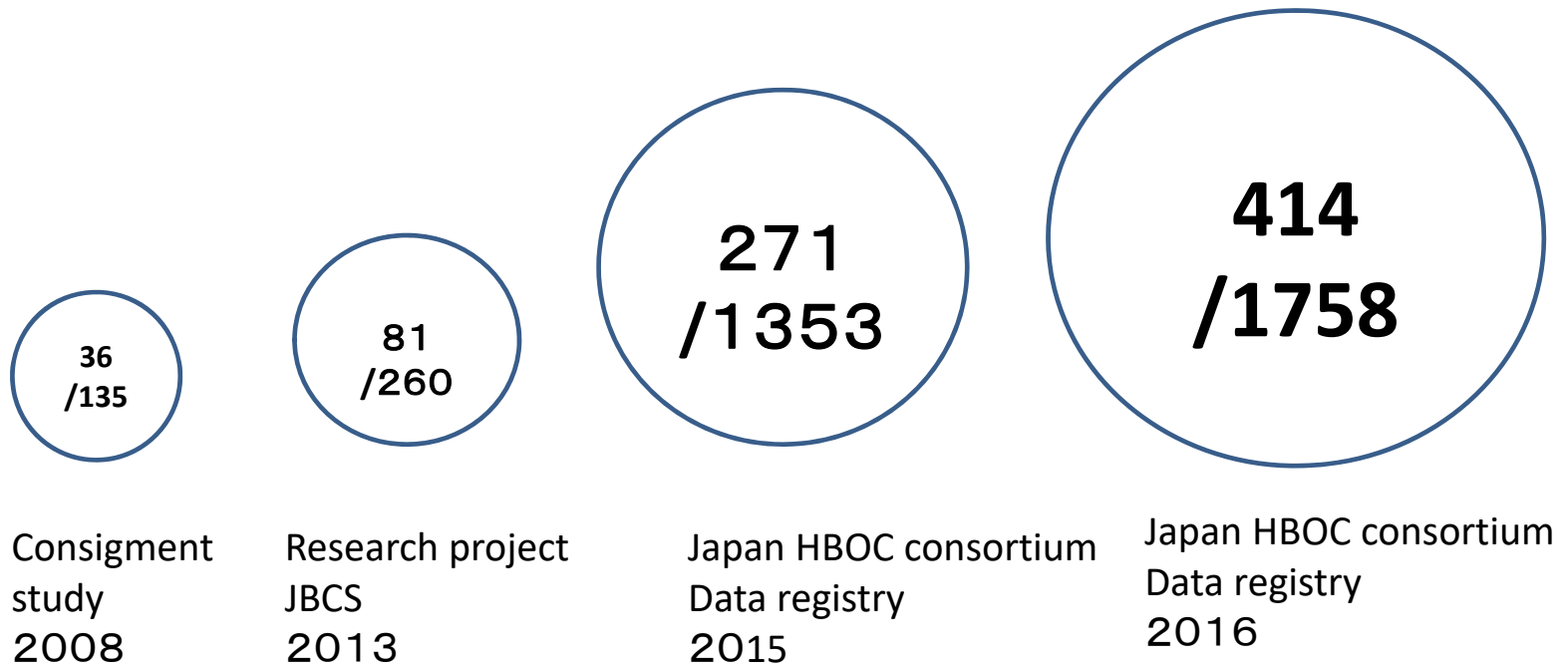
It is estimated that **at least 60% of the world's 7 billion people are Asians, but yet less than 5% of the known BRCA carriers** that have been identified are Asians [1]. In order to share knowledge of and improve the quality of hereditary breast and ovarian cancer patients in Asia, we have established the Asian BRCA consortium in October 2011. The consortium has members in 12 Asian countries and welcomes new members with a shared vision of collaborating for research in Asia. **We urgently need to advocate for change in the legal protection against genetic discrimination**, and to advocate that **governments should at least pay for testing fees, surveillance and risk reducing strategies** so that we are able to offer the best strategies for BRCA carriers regardless of where they live.

Authors: ABRCA Consortium

1. Teo Soo Hwang (Malaysia)
2. Kim Sung-Won (Korea)
3. Ava Kwong (Hong Kong)
4. Philip Iau (Singapore)
5. Rajiv Sarin (India)
6. Seigo Nakamura (Japan)
7. Shao Zhimin (China)
8. Teguh Aryandono (Indonesia)
9. Pimpicha Patmasiriwat (Thailand)
10. Le Huang (Vietnam)
11. Ophira Ginsburg (Bangladesh)
12. Rodney Dofitas (Philippines)

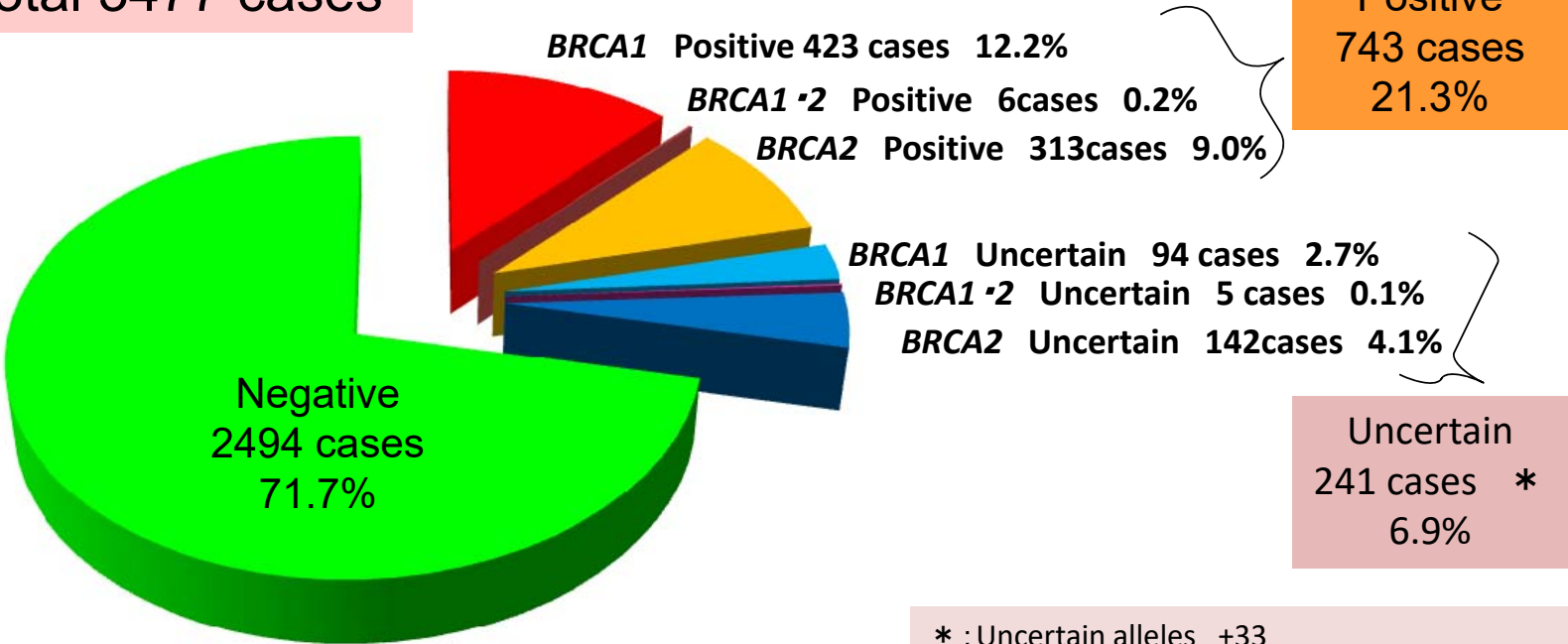
Transition of HBOC registry

(career/examination)



Data Collection Study in Japan (2018)

Total 3477 cases



Positive
743 cases
21.3%

Uncertain
241 cases *
6.9%

Variant Allele



	Positive	Uncertain
<i>BRCA1</i>	429	112
<i>BRCA2</i>	319	167


* : Uncertain alleles +33
 BRCA1:Positive + BRCA1:Uncertain • 3cases
 BRCA1:Positive + BRCA2:Uncertain • 16cases
 BRCA2:Positive + BRCA1:Uncertain • 7cases
 BRCA2:Positive + BRCA2:Uncertain • 2cases
 BRCA1:Duble Uncertain • 2cases
 BRCA2:Duble Uncertain • 2cases
 BRCA1-2:Uncertain + BRCA1:Uncertain • 1case



Article | [OPEN](#) | Published: 04 October 2018

Germline pathogenic variants of 11 breast cancer genes in 7,051 Japanese patients and 11,241 controls

Yukihide Momozawa , Yusuke Iwasaki, Michael T. Parsons, Yoichiro Kamatani, Atsushi Takahashi, Chieko Tamura, Toyomasa Katagiri, Teruhiko Yoshida, Seigo Nakamura, Kokichi Sugano, Yoshio Miki, Makoto Hirata, Koichi Matsuda, Amanda B. Spurdle & Michiaki Kubo 

Nature Communications **9**, Article number: 4083 (2018) | [Download Citation](#) 



Global conference

on

Breast Health

At Kamijo Memorial Hall
On 23rd ,July 2020

20th anniversary







TEAMWORK

**Coming Together Is Beginning. Keeping Together
Is Progress. Working Together Is Success.**
~ Henry Ford ~

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