Gerald R. Kolb

- Recovering attorney
- 23 year career in healthcare
- 20+ years devoted to breast care
- Hospital CEO, consultant, executive, and entrepreneur
- Prolific speaker and writer
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Conflicts

- Consultant/owner the Breast Group
- Consultant to Volpara Solutions, Ltd.
- Uncompromising evangelist for excellence!

Goals

- In this session we will . . .
  - Review the evolution of breast screening from one-size-fits all to multi-modality personalized care
  - Discuss legislation/regulation changes, including the impending application of the USPSTF guidelines on operations
  - Discuss and develop practical alternatives that preserve early detection while limiting economic contraction due to guideline changes

Caveat

- Many people in healthcare look upon “business” with a note of disdain. We live and work, however, in a world where success is a bilateral concept, requiring:
  - *Clinical* performance
  - *Economic* performance
- Without *both*, a healthcare enterprise *cannot* succeed

Screen·ing (skrēn'ing)

Examination of a group of usually asymptomatic people to detect those with a high probability of having a given disease . . .

1. Access to large percentage of target population
2. Ability to detect/diagnose at a time when outcomes can be positively affected
3. Benign testing
4. Low cost

A Brief History of Breast Screening

- 1913–63. Mammography becomes reproducible
- 1963–66. HIP study (Strax, et al) first RCT establishes mortality reduction with screening mammography.
- 1965. CGR produces first dedicated mammography unit
- 1970's. Diagnostic techniques developed and improvements in technology allow increased "screening"
- 1976. Wolfe publishes discussion of parenchymal density patterns on mammography

Screening History, Cont.

- 1985. Tabar reports initial results from Two-County Trial
- 1990's. Based on trial results recommendations move to 2-view studies provided annually for women age 50 and over — moving to 40 and over by the end of the decade.
- 1995. First ultrasound paper addressing mammo occult cancers (Gordon, et al)

Screening History, cont.

- 1998–Present. Long line of studies validating utility of using ultrasound as supplemental screening for women with dense breast tissue
- 2000. GE receives FDA approval for FFDM
- 2005. DMIST (Pisano, et al) validates FFDM

Screening History, cont.

- 2007. ACS recommends breast MRI for high risk women
- 2008. ACRIN 6666 (Berg, et al) validates ultrasound as supplemental screening for women with dense breast tissue.
- 2009. Connecticut passes breast density notification law.

Screening History, cont.

- 2011. First FDA approval for DBT (Hologic)
- 2013. Synthetic 2D view (C-view) approved for DBT (Hologic)
- 2014. GE receives FDA approval for DBT (SenoClaire)
- 2015. FDA approves Siemens Mammomat Inspiration DBT
- 2015. CMS establishes reimbursement codes for DBT (add-on CPT® - 77061) and for screening (whole breast) ultrasound (CPT® - 76641)
- 2017. CMS removes separate CAD reimbursement, rolling it into mammography codes.

Paradigm Shift

- Early screening involved diagnostic examination of images, looking for problems
  - If suspicious area was seen, loc wire would be placed and patient would receive surgical biopsy
  - Positive biopsy rate (PPV_3) < 5%
- 1990's screening and diagnostic split
  - Screening *only* for asymptomatic women
  - ***Expect normal***, recall non-normal for additional imaging
  - Reduce biopsy rate and increase positive biopsies
  - PPV_3 25-40%

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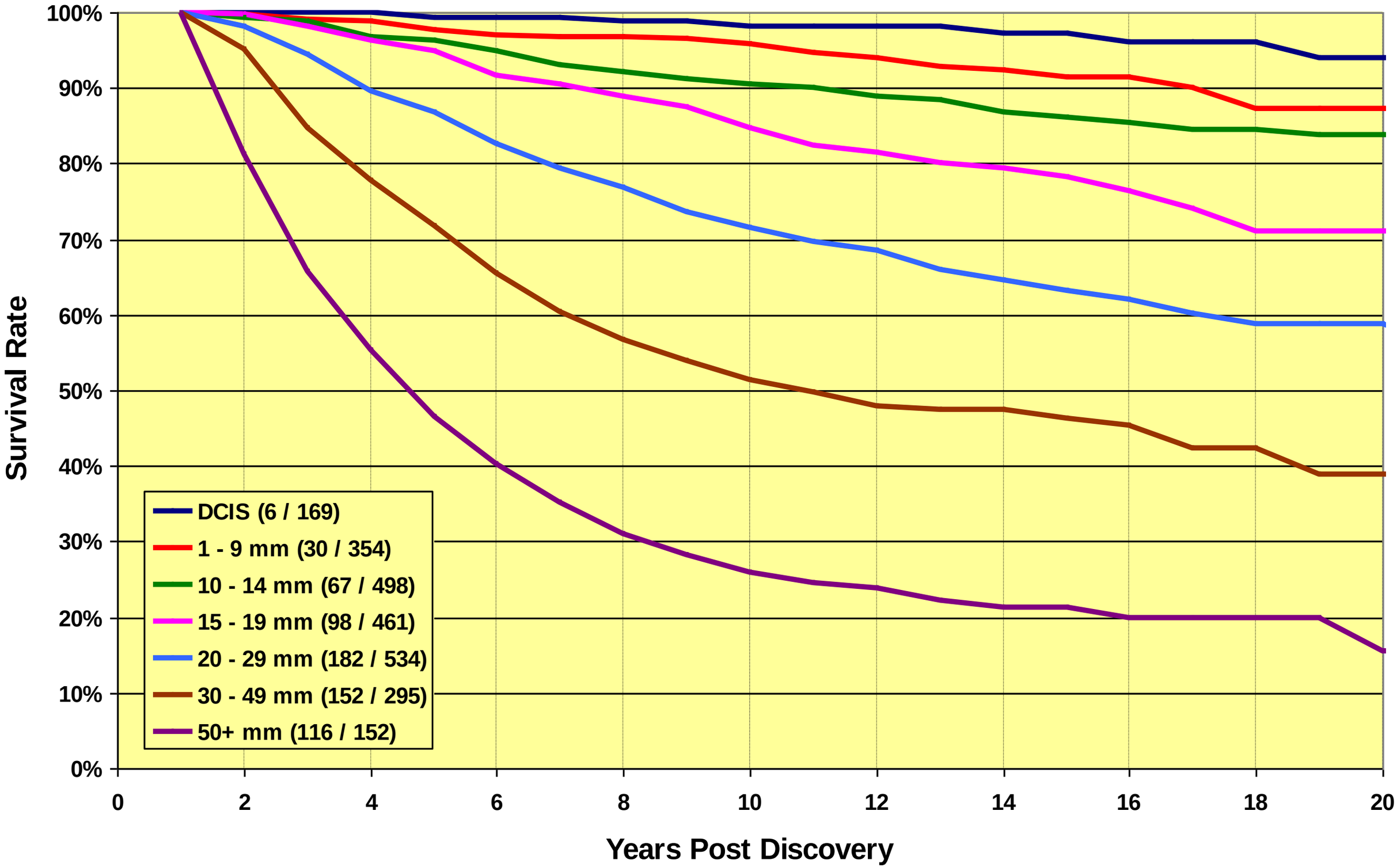
Remember This!!

Why Individualize Screening?

- Mammography misses cancers
  - 30% overall per ASSURE study (EU)
  - Increase CA yields 30-100% in ultrasound studies with dense patients having “normal” mammography findings.
- 3D mammography reduces recall and improves CDR
  - But continues to miss 50-65% of the occult cancers in women with dense breasts
- Missed cancers will be diagnosed later, commonly appearing as interval cancers



20-Year Survival – Death from all causes

(DCIS is Baseline Death Rate)

Duffy SW, Tabar L, Vitak B, et al. Tumor size and breast cancer detection: what might be the effect of a less sensitive screening tool than mammography. *Breast J*, 2006;12 Suppl 1:S91-5.

Why Individualize Screening?

- The goal of screening is to positively impact outcomes
  - Mortality — obviously smaller tumors have a better short and long-term prognosis
  - Morbidity — often ignored, but debilitation increases dramatically at stage II (2cm) because chemotherapy is standard of care at this tumor size
  - Cost — therapy cost increases exponentially at stage II because of the use of expensive drugs
    - Herceptin = $85,000/year for 2 years
    - Neulasta = $40,000 for 5 weeks
    - New drug development is primarily life extension rather than curative

What *is* Individualized Screening?

- We suggest that individualized screening is multi modality screening individually applied to women based on relative risk
  - Highest risk (20-25%) — breast MRI per ACS recommendation
  - Increased risk — mammography plus supplemental ultrasound
  - Normal risk — mammography

Europe moves toward individualization

Presented by Gerald Kolb

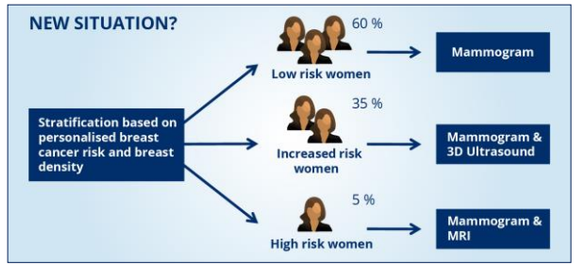
Adapting Breast Cancer Screening Strategy Using Personalised Risk Estimation

Personalised Breast Cancer Screening

ASSURE - Adapting Breast Cancer Screening Strategy Using Personalised Risk Estimation - consists of 10 project partners from 7 countries with leading expertise in the field of breast imaging, with the Radboud University Nijmegen Medical Centre as the coordinating partner.
The project started in December 2012 and is supported by the European Commission under the 7th Framework Programme for Health Research.

Approximately 1 in 8 women develop breast cancer during their lifetime. Screening programs have been introduced, decreasing the mortality rate and allowing for less radical treatment options for early detected cancers. Unfortunately not all cancers are detected in screening. Approximately 30% of breast cancers are detected between screening rounds. This constitutes a need for improved cancer screening.

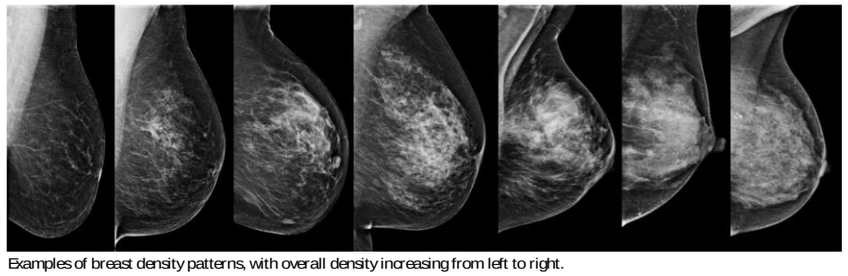
The ASSURE project promotes going from a one-size-fits-all approach to a personalised screening protocol. Nowadays all women undergo the same screening protocol, independent of the density of their breast tissue and the risk to develop breast cancer. Almost all women make use of the same diagnostic modality, X-ray mammography.



Unfortunately the sensitivity of mammographic screening is seriously impaired in women with dense breasts. Fibroglandular and stromal tissue look equally bright as tumours on mammographic images. This causes tumours to remain masked for radiologists and thus breast cancer to remain undetected.

One task of the project is to estimate personal risk depending on breast density, age, gene mutations, family and/or personal history, etc., and based on this risk, propose an optimal, cost effective, personalized screening strategy.

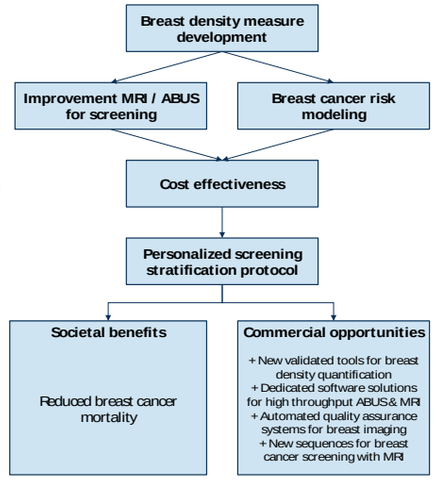
Another task is to improve the use of MRI and Automatic Breast UltraSound (ABUS) as additional breast cancer screening modalities, by optimizing protocols, enhance reading workflow, and by offering better diagnostic performance through new and improved software solutions.



Examples of breast density patterns, with overall density increasing from left to right.

Expected Results & Impact

Effective breast cancer screening substantially reduces mortality and maintains the quality of life of women. Additionally, less disfiguring treatments are required. A new stratification protocol and new screening tools will result from this project. The screening process will be optimised in response to the increased awareness regarding the low sensitivity of current breast cancer screening in women with dense breasts. Our estimations show that a reduction of interval cancers of at least 30% is achievable, assuming the efforts in this project lead to a sensitivity for dense breast comparable to that of non-dense breasts. Furthermore, the risk stratification enabled by this project will benefit a very low risk group (10-15% of women) as their screening interval may be further optimized (and increased) to limit the adverse effects due to the radiation inherent with X-ray mammography screening, and reduce the risk of false positives and over-diagnosis.
The ASSURE project will be an excellent opportunity for the participating SMEs (small and medium-sized enterprises), which each is a recognized innovator in its market segment, to join forces with leading research institutions and national screening experts. This joint effort will allow the ASSURE consortium to excel at demonstrating their combined technologies and future products have the potential to substantially improve breast cancer screening in Europe.



Exploitable results from this project are expected to include (1) new and validated measures for breast density (Mātakina and Biomediq), (2) a quality assurance system for breast cancer screening with ABUS and MRI (Mediri), (3) new sequences for breast cancer screening with MRI (Mediri) and (4) dedicated screening software for high-throughput ABUS and MRI reading (MeVis Medical Solutions).

Partners

Radboud University Nijmegen Medical Centre
Dept. of Radiology
Nijmegen, The Netherlands
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But How to Individualize?

- Individualization is based on risk
  - Historic risk (e.g., Tyrer-Cusick, etc.)
  - Personal risk (density)
- The challenges:
  - Eliminating operator variability for BI-RADS density assessment (Melnikow/Alonzo-Proulx)
  - Where does 3D mammography fit in this continuum? (Rafferty/Tagliafico)
  - How can multimodality screening “fit” within a screening visit?
    - Little patient tolerance for multiple screening visits
    - Connecticut experience is that recall cuts compliance to @30% (Weigert)

Tomosynthesis

- DBT or 3D mammography represents the evolution of 2D digital mammography
  - Improves recall rate
  - Improves cancer detection rate
    - However it remains limited by X-ray physics
- Implies
  - DBT *should* replace 2D
    - Difficult to switch between 2D and 3D interpretation
    - “Who” gets 3D in a mixed system is very problematic
  - But, DBT does *not* replace the need for a multi modality approach to screening

Supplemental Imaging

- Experience at Yale has shown that DBT finds about 1/3 of the occult cancers in dense tissue patients (BI-RADS C-D), with 2/3 being detected by ultrasound (Philpotts, et al)
  - Four years of experience
- We view automated US (AUS) as the only *viable* supplemental imaging to 2D or 3D mammography for medium risk women
  - MRI, molecular imaging and contrast enhanced mammo all require the injection of contrast or isotopes
  - MRI requires precertification and qualifies only for high risk (20-25%+) women
  - AUS is the only technology that can easily accommodate the timing and volumes expected in multi-modality screening

Business Reality

- *How* to add a *second* screening procedure for up to 47% of patients?
  - Must be convenient
    - Today's patients are busy
    - 30% compliance if they need to come back (Weigert)
  - Must provide density education
    - Eliminate an onerous task for the PCP
    - Control the message to the patient
  - European experience of integration into high volume screening programs have been successful

The *True* Screening Exam

- Asymptomatic patient
  - Expect normal (remember this?)
  - Abnormal will stand out
  - The same approach as with a screening mammo
- Increases recalls, but dramatically reduces screening time
  - Part of the learning curve with DBT
  - Very difficult to do with hand held US
  - Well suited for AUS
    - Allows bifurcation of exam into *acquisition* and *interpretation*

Determining Density

- BI-RADS 5th edition requires a determination of volumetric density.
  - a – The breasts are almost entirely fatty
  - b – There are scattered areas of fibroglandular density
  - c – The breasts are heterogeneously dense, which may obscure small masses
  - d – The breasts are extremely dense, which lowers the sensitivity of mammography

More Density

- Breast density is a *contemporaneous* finding
  - Density changes over time
  - Density language is in the present tense (“your mammogram indicates …”)
  - May be determined *objectively* using density software (AlonzoProulx)
    - Requires a protocol if objective finding is to be used to vector patients to screening US
  - Should *not* be taken from prior reports
    - Although immediate prior year *may* be used for <u>schedule planning</u>

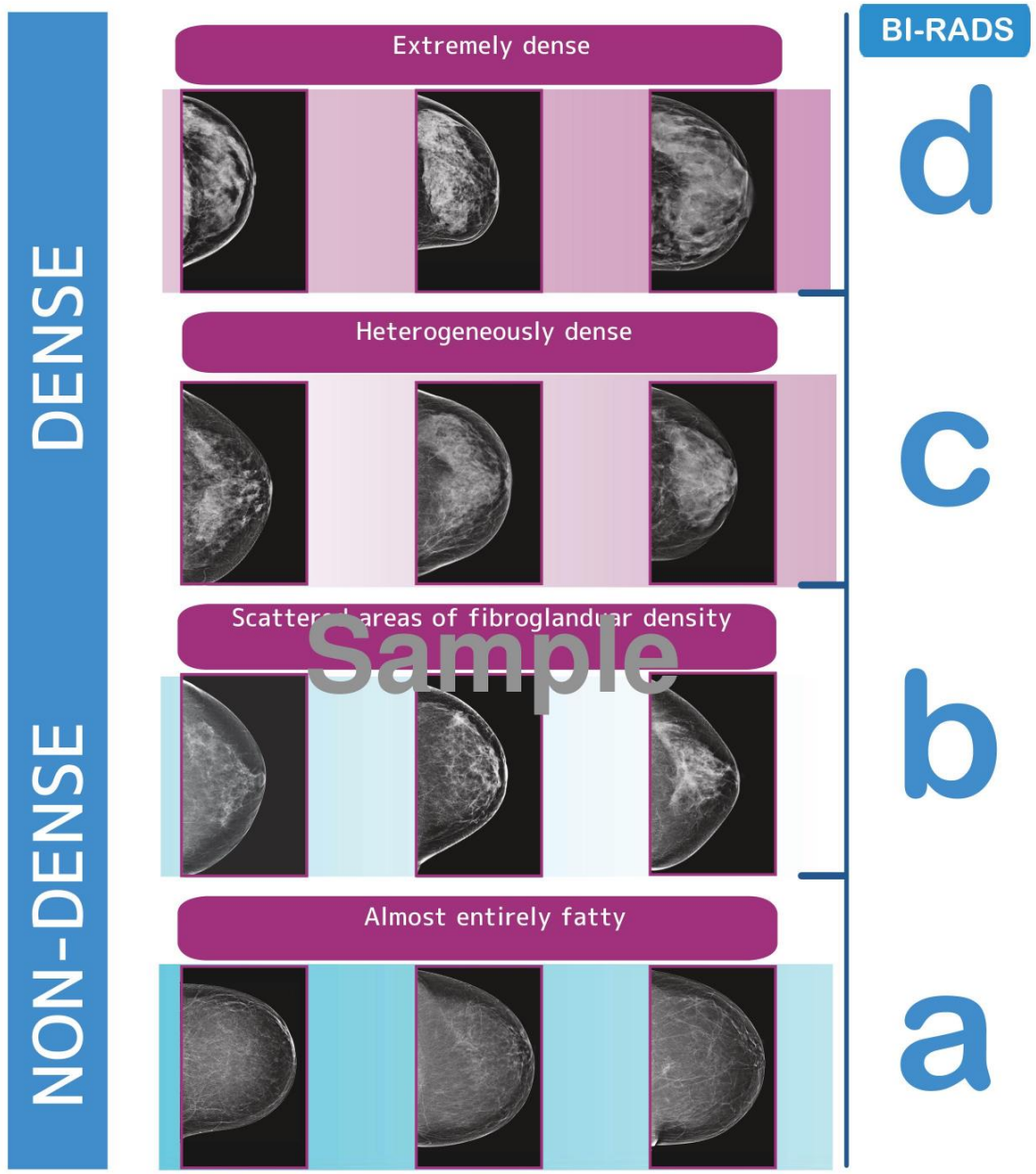
The Screening Process

- Begin with screening mammogram
- Analyze patient density using density software
- Technologist educates patient about density using visual aids
  - If high density (c-d), offer patient screening US
  - If low density, inform and remind her to return for her mammogram in one-year

Educating Patients

- Brochure sent to patients along with reminder letter
  - Brief explanation of density and how it may reduce the sensitivity of the mammogram
  - Explanation of screening US
- Same brochure is given to each patient at registration
- Explanation of density by technologist
  - After 4th view
  - Use script and visual aids
  - Culminates with presenting the patient's objective density

Volumetric Breast Density Scale



volpara® density™
Automated breast density™

volparasolutions.com

THE BREAST GROUP

volpara

Patient Name	HSR_BIRADS3b
Patient ID	HSR_BIRADS3b
Patient DOB	01/01/2000
Accession #	
Study Date	01/01/2000

C

VDG®

15.5 –

– 11.6

7.5 –

4.5 –

	Right	Left
Volume of Fibroglandular Tissue (cm^3)	34.0	34.5
Volume of Breast (cm^3)	285.7	305.3
Volumetric Breast Density (%)	11.9	11.3

1.7 mGy	14.4 kPa	11.6%
v1.0	v1.0	v1.5.12

Why the Technologist?

- Most patients never have contact with the radiologist who reads their mammogram
  - The technologist is the most trusted individual in the delivery process!
  - Process takes about 90-seconds

Educating Physicians

- Important that referring physicians be informed of the implications of density and what you are doing
  - PCPs generally welcome radiology taking the lead with their patients on matters concerning breast imaging
  - Screening US is a Designated Health Service (DHS) and a referral is required for Medicare
  - It is important for them to understand the benefits of early detection
  - We recommend a personal letter and a density memo be sent to each referring physician
  - Personal contact with top ten referrers

Facilitating Process

- Consider using a conditional contingent order
  - *Individual* – not a standing order
  - Requires a contingency, e.g., finding of density
  - Meets the referral requirement

Appendix H

The Conditional Contingent Order

Date: _____

Patient Name: _____

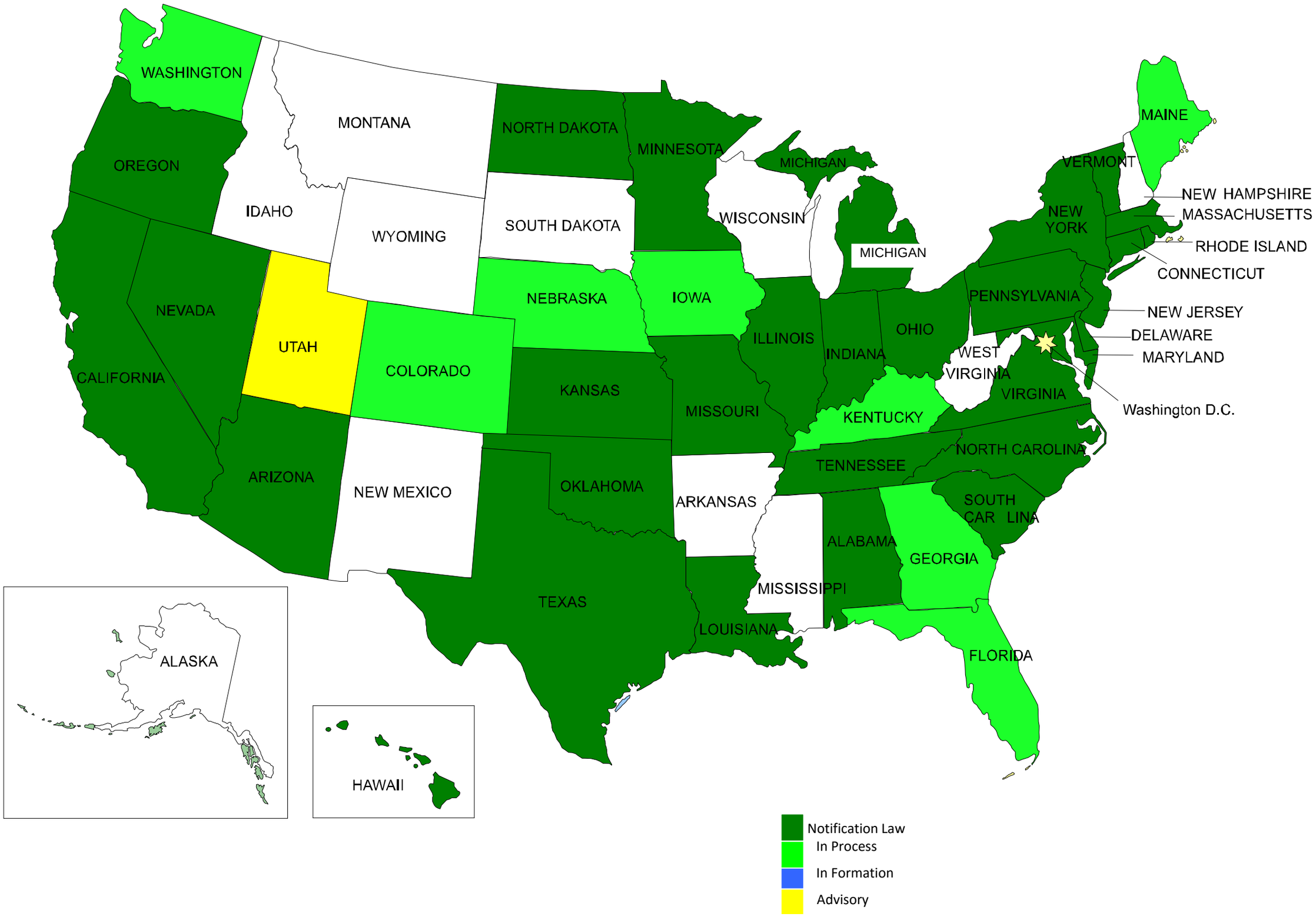
Screening Mammogram _____

____ If mammogram discloses high breast density please add screening ultrasound.

____ Other _____

_____
Physician

Please check all that apply.



Note 1: CT, NJ and IL have payment mandates

USPSTF Guidelines

- Originally released in 2009
- Updated and ratified in 2016
  - Individual decision to begin screening before age 50 [C]
  - Biennial screening mammography age 50–74 [B]
  - Recommends against breast self examination [D]
  - Insufficient [I] evidence to assess benefits or harms of:
    - Mammography in women age 75+
    - Clinical breast exam
    - Digital mammography or MRI instead of film screen

USPSTF Radiology Rejection

- Immediate rejection by radiology
  - Failed to account for the fact that over half of the life years lost occur in women under the age of 50
  - Attack on statistical basis
  - Attack on the CISNET model (use of statistics)
  - Failure to address the risk factors that would lead individuals 40-49 to benefit from mammography
- Legislative delay for Federal implementation
  - Now delayed until January 1, 2017

USPSTF Results

- Mammography biennial screening rates are declining
  - Notwithstanding Federal implementation delays:
    - *Significant declines in young, white, well-educated, insured women*
    - Regional decline in compliance is higher in West and higher for 40-49 age group
    - Despite noting that guidelines are influential, PCPs do not consistently follow the recommendations.
    - In a 5.5M cohort of insured women, the compliance decline ranged from 6-17% among white, Hispanic and Asian women, but was negligible for black women.

USPSTF Conclusions

- Congress may defer USPSTF Guidelines — but don’t count on it!
- Impact will largely be in the 40-49 age group
  - Stakes are highest for this group — half of life years lost
  - Need to market to this group and to their PCPs
- Biennial rates pre and post 2009 are not that different
  - 30-35% of women are NOT compliant
  - Compliance change greatest in young, insured, high SES women!

USPSTF Recommendations

- Create personalized multi-modality program
- Market benefits of personalized program to all women
  - Imaging surveillance is still the ***only*** way to achieve early detection
  - Early detection provides the best prognosis for recovery
- Do not ignore the 30-35% of women who are currently unserved — this group is significantly larger than the projected attrition due to USPSTF

Remember

Rules will change, new challenges will arise, and different technologies will come into use, but our mission remains the same —— to reduce the impact of breast cancer on the population we serve — through early detection achieved by providing excellence in clinical care, respecting our patients and colleagues, and serving our communities.

Keep your focus on solutions,
not on the problems.

Thank you!