Recent Papers That Will Help Or May Change Your Practice

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Murray Rebner

- I disclose the following financial relationships with relevant commercial interests:
- Previously- General Electric Medical Systems, Siemens Medical Systems, Hologic, Agfa- paid consultant.
- None currently

Goals And Objectives

- Review 5 recent papers which will impact practice
- Demonstrate how literature can affect use of different breast imaging modalities

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Paper 1

- Pan-Canadian Study of Mammography Screening and Mortality from Breast Cancer
- Andrew Coldman et al
- JNCI J Natl Cancer Inst (2014) 106 (11): dju261 doi:10.1093/jnci/dju261

Paper 1

Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial

(Published 11 February 2014)

BMJ 2014;348:g366

Anthony B Miller, professor emeritus1, Claus Wall, data manager1, Cornelia J Baines, professor emerita1, Ping Sun, statistician2, Teresa To, senior scientist3, Steven A Narod, professor

Design

- **Interventions:** Women aged 40-49 in the mammography arm and all women aged 50-59 in both arms received annual physical breast examinations. Women aged 40-49 in the control arm received a single examination followed by usual care in the community.
- **Main outcome measure:** Deaths from breast cancer.

Results

- The cumulative mortality from breast cancer was similar between women in the mammography arm and in the control arm (hazard ratio 0.99, 95% confidence interval 0.88 to 1.12).
- After 15 years of follow-up a residual excess of 106 cancers was observed in the mammography arm, attributable to over-diagnosis.

Conclusion

- Annual mammography in women 40-59 does not reduce mortality from breast cancer beyond that of physical examination or usual care when adjuvant therapy for breast cancer is freely available.
- Overall, 22% (106/484) of screen detected invasive breast cancers were over-diagnosed, representing one overdiagnosed breast cancer for every 424 women who received mammography screening in the trial.

Study Design Problems

- Breast PE BEFORE randomization by nurses
- Quality of mammography poor-equipment and tech performance
- No tech/rad training
- Consulting radiologists resigned; physicist critical of mammography quality
- Surgeon decided if mammography detected lesions got biopsied

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Garbage In; Garbage Out!

Paper 1

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Background

- Mammography screening randomized controlled trials show reduced breast cancer mortality in women 40 to 74 years.
- Estimates from observational studies post screening implementation in different countries show varied findings.
- Findings from seven Canadian breast screening programs analyzed.

Methods

- Study proposed by Canadian Breast Cancer Screening Initiative (CBCSI)
- Supported by Public Health Agency of Canada (PHAC)
- 12 breast cancer screening programs invited- 3 unable to provide data, 2 declined , 7 participated

Methods

- 7 provincial participants= BC, MN, ON, QC , NB, NS and NL.
- All programs used 2 view (mostly analog) mammography.
- Single radiologist interpretation.
- Entry based on self-referral; some received personal invitation letters and periodic reminder letters

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Methods

- All programs had study approved by local IRB
- All breast care managed by primary care physicians.
- Reports received by primary care providers
- Refer to tertiary centers when necessary.

Study Design

- Compare mortality of women who participated in screening with estimate of mortality if they did not
- Based estimate on experience of women in same area who were not screened.
- Separate cohorts created in each program- women with at least I screen between ages 40-79 and between 1990-2009. In cohort either until death or end of 2009.

Study Design

- Link between screening program database and provincial cancer registry
- Established deaths from breast cancer from each cohort
- Standardized mortality ratios calculated- observed mortality in participant group/province-specific expected mortality
- Estimates of absolute benefit expressed as Numbers Needed to Participate (NNP) to prevent 1 breast cancer death within 10 years of entry

Results

- 2.79 million screened participants.
- 20.2 million life-person years of observation
- Maximum years post entry in provincial programs 12-20

Results

- Average breast cancer mortality 40% (95% CI=33-48%) lower than expected
- Range of decreased mortality across provinces 27-59%
- NNP(10): 40-49= 1247, 50-59=757, 60-69=552, 70-79=498

Discussion

- Results not influenced by trends in treatment or population awareness of breast cancer symptoms- contemporaneous cases in both populations
- Different results in different provinces due to age eligibility, annual screening for high risk population, annual screening of average risk groups etc.

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Caveats

- Not an RCT!
- Lower strength of evidence for population based service screening study
- Multiple differences in methods between various provinces
- Biases controlled as best as possible
- HOWEVER, results still show reduction in breast cancer mortality and benefit from screening .

Benefit to You

- Results still show reduction in breast cancer mortality and benefit from screening .
- Use study to defend your screening guidelines

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Paper 2

Value analysis of digital breast tomosynthesis for breast cancer screening in a commercially-insured US population

Bonafede, MM

ClinicoEconomics and Outcomes Research 2015:7 53–63

Background

- DBT benefits defined in multiple published papers
- Increased cancer detection rate 15-30%
- Decreased recall rate 15-40%
- DBT now approved by FDA
- CMS approved Medicare reimbursement January 1, 2015

Data

- Multicenter trials in Norway, Italy and USA
- Oslo
- STORM
- US trial

Purpose

- Conduct DBT value analysis in US commercial health plans
- Assess potential budget impact associated with DBT clinical benefits

Methods

- Economic model developed to estimate system-wide financial impact of annual DBT screening in hypothetical US managed care plan with one million members.
- FFDM compared to FFDM +DBT to measure clinical and financial impact.
- Value = difference between clinical and financial impact

Methods

- Major DBT economic value -reduce the number of recalled women for additional follow-up imaging and diagnostic testing services, and their costs.
- Other benefit- facilitate earlier diagnosis of cancers at less invasive stages when treatment costs are lower
- Offset additional reimbursement costs; produce net cost savings

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Model Inputs: Methods

- Cancer detection rate identified via administrative claims
- Defined as number of women with two breast cancer claims at least 30 days apart during the 6 months following the index screening event
- Ancillary or laboratory claims alone were not sufficient to establish new cancer cases

Methods Scenarios

- For FFDM- breast cancer stage was distributed according to data from a study of 19,373 women with newly diagnosed stage (1-4) who received their primary cancer care at 8 National Comprehensive Cancer Network centers

Model Scenarios

- FFDM+DBT- model based on data from Skaane study
- Fixed percentage (18.3%) shift in stage-diagnosis (from stage 2–4 to stage 1) was estimated according to node negative/ positive cancers detected in Oslo study
- 18.3% fewer stage 2–4 cancers were detected in the FFDM + DBT scenario, but compensated in the distribution by 21.9% more cancers diagnosed in stage 1.
- Stage 0 was assumed to remain constant based on reported trial results comparing FFDM with FFDM + DBT.27

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Post-diagnosis Cancer Treatment Costs

- Mean total health plan cost of newly diagnosed breast cancer patient in year following diagnosis derived from administrative claims data.
- Value was distributed across stages 1–4 using same stage distribution of breast cancer costs as presented in study of costs for women with newly-diagnosed breast cancer by disease stage, and matched to non-cancer controls.

Costs

- Stage 1 costs 25.7% less than mean overall cost
- Costs for stages 2, 3, and 4= 13.4%, 77.1%, and 281.4% higher than mean overall cost.

Cost

- Cost distribution by stage 1-4 calculated using estimates from the claims database analyses.
- Stage 0 costs estimated using percentage difference between stage 0 and stage 1 costs derived from 4-year longitudinal study in a US HMO.
- The difference (stage 0 18.5% <stage 1) applied to stage 1 estimate above to yield stage 0 cost.

Results

- 1,521,667 women (mean age 50.7 years) met study inclusion criteria (evaluate follow-up service utilization and costs).
- Age distribution:
- age 40–49 years= 40.9%
- age 50–59 years= 39.8%
- age 60–69 years= 17.6%
- age 70–75 years= 1.6%

Results

- From claims database costs of follow-up services in the 6 months following abnormal or inconclusive mammogram estimated at $1,200
- Prevalence rate= 4.65 per 1,000, comparable to other studies
- Mean costs- newly diagnosed breast cancer patients were $58,615 in the year following diagnosis

Results

- 84,549 women aged 40–75 years from one million member health plan
- Annual screening mammography
- Assume 100% compliance for each group

Results

- Assumption- current recall rate=15.35%
- Assumption- FFDM + DBT decrease rate to 10%
- 4,523 women screened with FFDM + DBT avoid use of follow-up services
- Total annual cost savings to the health plan- $2.4 million

Results

- $5.5 million savings from avoiding follow-up services
- $1.2 million from earlier detection of breast cancer
- Incremental cost of $4.2 million by adding DBT to screening.
- $5.5M+ $1.2 M= $6.5M -S4.2M= $2.5M net savings

Impact

- DBT clinical benefit shown
- Challenge remains for reimbursement
- Medicare payments (+$57) obtained
- Few private carriers pay
- Presentations required financial plus clinical data
- More financial data needed
- This paper good start!

Paper 3

- Abbreviated Breast Magnetic Resonance Imaging(MRI): First Post-contrast Subtracted Images and Maximum-Intensity Projection—A Novel Approach to Breast Cancer Screening With MRI
- *Christiane K. Kuhl, et al.*
- *J Clin Oncol 32:2304-2310*

Introduction

- Breast MRI has high sensitivity for breast cancer.
- MRI- second-line imaging method for patients with equivocal findings on mammography or ultrasound.
- Use for pre-op staging of breast cancer controversial
- Find unknown breast primary and R/O silicone implant rupture

Screening

- Breast MRI screening increased over the past decade.
- For high risk population MR downstages breast cancers and reduces interval cancers.
- Indirect evidence (no RCT's) suggests MRI screening helps improves the prognosis of population at elevated risk.

Screening MRI Problems

- Lack of sites offer high-level breast MRI; limits clinical access to screening MRI
- Breast MRI screening has high direct and indirect costs.
- Current breast MRI protocols time consuming to acquire and read.
- Magnet time up to 40 minutes; several hundred-thousands of images.

Mammography

- Mammographic screening highly standardized relatively simple procedure.
- Clinical examinations infrequent
- Studies interpreted by radiologists who batch read up to 100 mammograms per hour.

New Concept

- Breast MRI to mimic screening mammography.
- Abbreviated MRI protocol:
- Early post-contrast sequence
- Standard image reconstruction (MIP) allows fast overview of the imaging volume
- Expert radiologists interpret protocol.
- Numerous pulse-sequence protocols used and most mimic

Goal

- Reduce image acquisition time
- Reduce reading time
- Increase access to screening breast MRI.

Methods

- Prospective IRB-approved reader study
- Conducted over 18 months (January 2009 to June 2010), followed by 2-year validation period.
- Primary objective to investigate whether abbreviated MRI protocol sufficient to identify breast cancer in a screening cohort.

Methods

- Secondary objective- compare diagnostic accuracy and cancer yield of abbreviated protocol(AP) with those of regular diagnostic breast MRI protocols in same individuals.
- Predicted AP would be associated with reduced diagnostic accuracy.
- Acceptable to lose some sensitivity of regular screening breast MRI in exchange for acquisition and interpretation speed.

Inclusion Criteria

- Consecutive women referred for screening breast MRI on clinical history.
- Degree of familial risk categorized as mild, moderate, or high based on BRCAPRO
- Included personal history of breast cancer but only assessed contralateral breast in analysis

Methods

- Women imaged between days 6 and 12 of menstrual cycle.
- Normal clinical examination on MRI day
- Normal or benign digital mammogram
- Negative or benign ultrasound study needed for women with heterogeneously or extremely dense breasts

Pulse Sequences

- Pre-contrast axial T1-weighted gradient echo images
- Post-contrast axial T1-weighted gradient echo images
- Sequence 1 images subtracted from sequence 2 images to yield first post-contrast subtracted (FAST) images
- Fast images fused to yield MIP sequence

Methods

- FDP = AP, plus the non-subtracted and subtracted images of the remaining four post-contrast phases of the dynamic series and additional coronal T1-weighted and axial T2-weighted pulse sequences.
- Bilateral two-view full-field digital mammography (plus additional views and spot magnification views where appropriate) performed and double read.
- Systematic whole-breast screening ultrasound performed using dedicated equipment

Reader Study

- Prospective image interpretation after each MRI examination.
- Two experienced readers (18 and 6 years experience, annual MR caseloads 800/year)
- Blinded to clinical histories
- AP images read 1st (MIP 1st) then FDP

Results

- 443 initial screens; 163 had two annual screening rounds = 606 breast MRI studies
- Mean and median age = 54.2 and 52.6 years, one third premenopausal; two thirds postmenopausal.
- All patients had digital mammography
- High-frequency ultrasound, with negative or benign results performed in 427 of 606 screening rounds

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Results

- ***MRI Acquisition Time:***
- AP 3 minutes.
- FDP 17 minutes.

- ***Time to Read:***
- MIP 2.8 seconds
- AP 28 seconds.
- Time to read the FDP not measured.

Results

- Eleven breast cancers diagnosed in the 606 annual screening round (4 DCIS; 7 invasive carcinomas)
- Additional cancer yield of 18.15 per 1,000 screening rounds
- Breast cancer incidence of 11 of 443 (25 per 1000)
- All invasive cancers small T1 N0; median size 8 mm.
- Distribution of nuclear grading of invasive cancers as well and DCIS skewed toward high-grade lesions
- No interval cancers

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Results

- No difference in sensitivity (91%) between AP and FDP
- NPV 99.8% for MIP and 100.0% for complete AP and FDP readings
- No difference between specificity and PPV for AP reads vs. FDP (94.3% v 93.9% and 24.4% v 23.4%, respectively).

Implications and Questions

- FAST MRI proof of concept demonstrated
- No decrease in diagnostic performance
- Reimbursement and utility challenged
- Shorter scanning and interpretation times = decreased cost/ study but offset by increased volumes
- Applicable to US rads who read less?
- Change in ACR BMRAP?
- ACRIN study planned

Paper 4

- Assessing Improvement in Detection of Breast Cancer with Three-dimensional Automated Breast US in Women with Dense Breast Tissue: The SomoInsight Study
- Brem RF et al.
- Radiology 2014: DOI: http://dx.doi.org/10.1148/radiol.14132832

Background

- Mammography sensitivity as high as 85%, but as low as 48% in women with extremely dense breasts.
- Breast density independent risk factor- estimates of relative lifetime risk 2.8 to 6.0
- Risk increases in proportion to percentage breast density
- >1/2 women under 50 and 1/3 women 50 or older with breasts >50% dense.
- Around 28%–30% of breast cancers associated with breast density vs. approximately 5%–10% due to *BRCA1* or *BRCA2* gene.

Background

- Supplementary breast cancer screening indicated for segments of population
- MRI proven benefit for high risk population
- US screening for high risk patients unable to undergo MRI screening
- US screening for normal risk population with dense breasts?

Background

- Handheld screening breast US increases detection of small, node-negative breast cancers in women with dense breasts.
- Most studies focused on high-risk women with additional risk factors for breast cancer.
- Reliability of handheld US for screening controversial- false-positive rate, variability between operators, considerable physician time required for acquisition.

Background

- 3D automated breast sonography (ABS) posible solution for intermediate-risk women with dense breasts.
- With ABS each breast imaged in sections with automated 15.4-cm 14–6-MHz linear-array transducer.
- Images reconstructed coronally and viewed at dedicated workstation
- Average interpretation time =2.9 minutes.
- Purpose of study to determine improvement in breast cancer detection
- ABS+ screening mammography vs. screening mammography alone is asymptomatic women with dense breasts.

Methods

- All sites one ABS device (somo.v U-systems)
- Multi- institutional IRB- approved study from 2009 to 2011.
- Included asymptomatic women 25 years and older with heterogeneously (50%–75% dense) or extremely (> 75% dense) dense breast parenchyma .
- Women with a history of lumpectomy, contralateral mastectomy, breast augmentation, or implants were included.

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Imaging

- Standard digital CC/ MLO views per screening protocol
- Trained tech performed ABS US study
- Each breast imaged in three views with automated 15.4-cm 14–6-MHz linear-array transducer,
- Up to 1000 2D images acquired in transverse plane; breast imaged in three parts: the central (AP), lateral, and medial portions
- Additional obtained as necessary to cover entire breast.
- Standardized review process uses coronal plane for quick navigation through the breast, plus “survey mode,” (similar to cine and allows rapid review of many images).
- Acquisition time for each view approximately 60 seconds; total examination time about 15 minutes.
- Images reconstructed in coronal plane and were 3D for radiologist interpretation

Interpretation

- Screening mammograms- interpreted prospectively by one of 39 radiologists at 11 clinical sites. (BI-RADS 0,1,2). BI-RADS category 3 rating assigned in small number of patients (19 patients, 0.1%). None had cancer.
- Breast density assessed by radiologist and BI-RADS classified : type 1 (“almost entirely fat”), type 2 (“scattered fibroglandular densities”), type 3 (“heterogeneously dense”), or type 4 (“extremely dense”).

Interpretation

- Screening mammographic images reviewed first without ABS
- BI-RADS risk assessment assigned, recorded and locked
- same investigator interpreted the ABS images with screening images.
- BI-RADS risk assessment category assigned to ABS images; final combined impression (mammo + ABS) recorded
- Routine management (BI-RADS 1 and 2) or immediate management (BI-RADS 0,3,4,5) recommended
- BI-RADS 0,3,4,5= recall

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Interpretation

- To minimize inter-observer variation:
- Radiologists Mammography Quality Standards Act certified.
- All radiologists participated in standardized training program (Web-based training, Web-based one-on-one training, and on-site training with radiologist experienced in ABS) prior to study initiation.

Follow-up

- immediate management= recommendation from either individual mammographic assessment or combined assessment.
- Women with normal, benign, or probably benign findings followed up for 12 months (88% compliance)
- Only cancers detected as a result of original screening, (screening mammography or ABS) were considered screening-detected cancers. (Interval cancers not included)

Results

- 2301 recalls- 1957 from combined read, 344 from screening mammography alone.
- 13,107 had negative mammogram; 2407 (18%) recalled from combined read
- From recalls 112 breast cancers identified:
- 82 identified by mammography
- 30 cancers identified with ABS alone (21%).

Cancer Results

- ABS-only detected cancers more likely to be invasive vs. mammo-only detected (28 of 30, 93.3%) versus 62.2% (51 of 82), with P = .001.
- Larger percentage of invasive low-stage cancers (IA, IB) were detected with ABS alone compared with screening mammography (20 of 30, 66.7%) versus 45.1% (37 of 82).

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Supplementary Cancer Detection Yield

- Mammography and ABS- yield of 7.3 cancers per 1000 women screened
- Mammography alone- 5.4 cancers per 1000 women screened
- Difference in yield- 1.9 detected cancers per 1000 women screened
- Mammography alone- increase in recall rate- 150.2 per 1000 women screened
- Combined approach- 284.9 per 1000 screened

Results

- 26.7% sensitivity increase for combined approach vs. mammography alone
- 13.4% decreased specificity for combined approach vs. mammography alone.
- For combined approach- increase in biopsy rate 36.0 per 1000 women screened
- PPV1 decreased more with combined approach- 3.6% versus 2.6% mammography alone
- PPV3 decreased more with combined approach- 14.0% versus 9.8% for mammography alone

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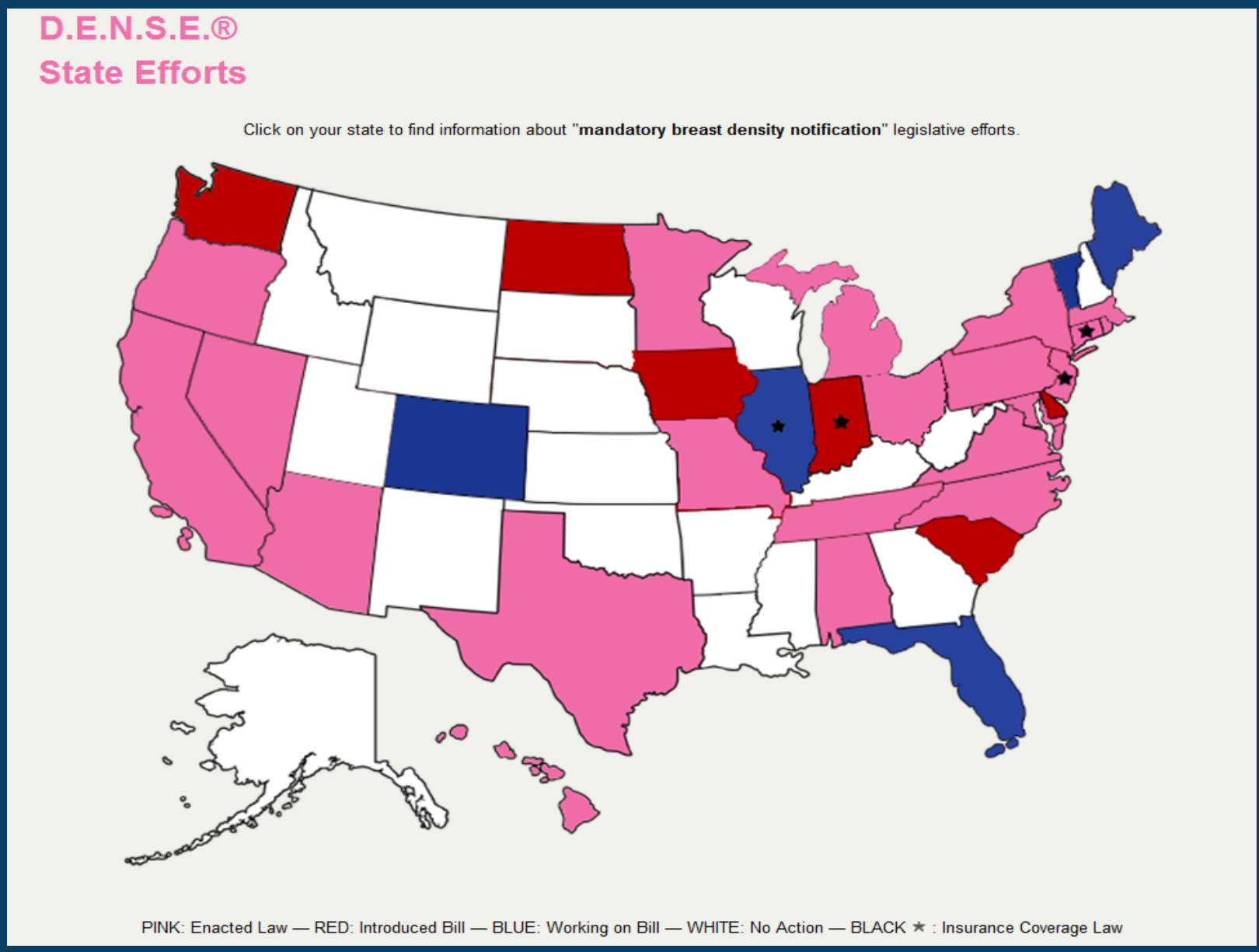
Conclusion

- MRI limited by high cost, relative lack of availability, variable patient tolerance, and the requirement for contrast material injection
- US inexpensive, well tolerated and no ionizing radiation.
- Increase cancer detection with supplementary ABS= 1.9 cancers per 1000 women screened,



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Implications

- 20 states (as of February 2015) with breast density legislation
- Only 4 states mandate insurance coverage for screening breast US in women with dense breasts
- Federal breast density bill introduced (February 2015); no mandated insurance coverage
- More pressure to do breast US? (women and competitors)
- FAST MRI alternative?

Paper 5

- Factors Associated with Repetitive Strain, and Strategies to Reduce Injury Among Breast-Imaging Radiologists
-
- Thompson AC, Kremer Prill MJ, Biswal S et. al.
- J AM Coll Radiol. 2014 Nov;11(11):1074-9

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Purpose

- To investigate prevalence of repetitive strain injury (RSI) in breast imagers
- Examine factors associated with RSI
- Determine strategies to reduce injuries

Methods

- Survey to 2618 SBI physician members in 2012
- 727(28%) response
- Pain levels before and after digital imaging measured
- Association between RSI and work trends analyzed

Methods

- Survey based on “Ergonomic Survey” instrument
- Dept. position, digital vs. analog use, hours/day at PACS workstation
- Hours/day in awkward position, current RSI and prior Dx of repetitve strain syndrome(RSS)

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Additional Information

- Age information grouped 5 year intervals <30->65
- Pain sites/discomfort relating to work tasks
- Use of ergonomic devices at work- mouse/peripheral input device, adjustable chair, adjustable table

Methods

- Univariate and multivariate LR done.
- Assess association between RSI symptoms and:
- Ergonomic score index, desire for ergonomic training, age, number of hours in awkward position or number of hours at computer/PACS workstation.

Results

- 584/727 (80%) used breast imaging RWS/PACS
- 18% with ergonomic mouse/PID
- 56% with adjustable tables
- 92% with adjustable chairs
- 87% no ergonomic training; 85% wanted it

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Results

- 60% with RSI
- 33.3% RSI's treated
- Most common sites- neck>wrists>elbows

Results

- Odds of current RSI symptoms correlated with:
- Decreasing age (p=.0004)
- More hours working/day (p=.0006)
- More hours in awkward position (bent wrist , stooping) (p<.0001)

Results

- Increased pain after switch to PACS (p<.001)
- If used ergonomic training/ergonomic mouse/chair/table then decreased pain (p<.001)
- Of 438 rads who used ergonomics, 392 continued with 1/more devices
- For 1 ergonomic device used, 38% less likely to report RSI symptoms
- 630 no prior training; if had current symptoms or prior Dx/ Rx for RSS more likely to want training vs. those without prior symptoms/injury

Discussion

- Other studies (all radiologists) with similar results- Boiselle PM, J Am Coll Radiol 2008;5:919-23.
- 80% in Boiselle study improved RSS Sx after ergonomic training
- Similar location of injuries with breast imagers vs. all radiologists
- Increased RSI prevalence in younger breast imagers- working more hours? Change in age distribution over time?

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Summary

- Prevalence of current RSI symptoms =(60.2%); RSS= (33.3%).
- 80% used RWS; 18% used ergonomic mouse/peripheral input device, 56% used adjustable tables, 92% used adjustable chairs
- 13% participated in ergonomic training
- 85% non-participants interested in ergonomic training if available.

Summary

- Statistically significant trend for odds of current RSI symptoms to increase with: decreasing age, greater number of hours spent working each day and greater number of hours spent in awkward positions (wrist bent, stooping)

Summary

- Increase in pain level after implementation of PACS workstation,
- Decrease in pain level after ergonomic training, use of ergonomic mouse, PID adjustable chair, or adjustable table.

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Summary

- Improved ergonomics may help prevent RSIs
- Advise radiology departments take aggressive action to prevent radiologist injury through work-based ergonomic training and ergonomic changes in the reading room.

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