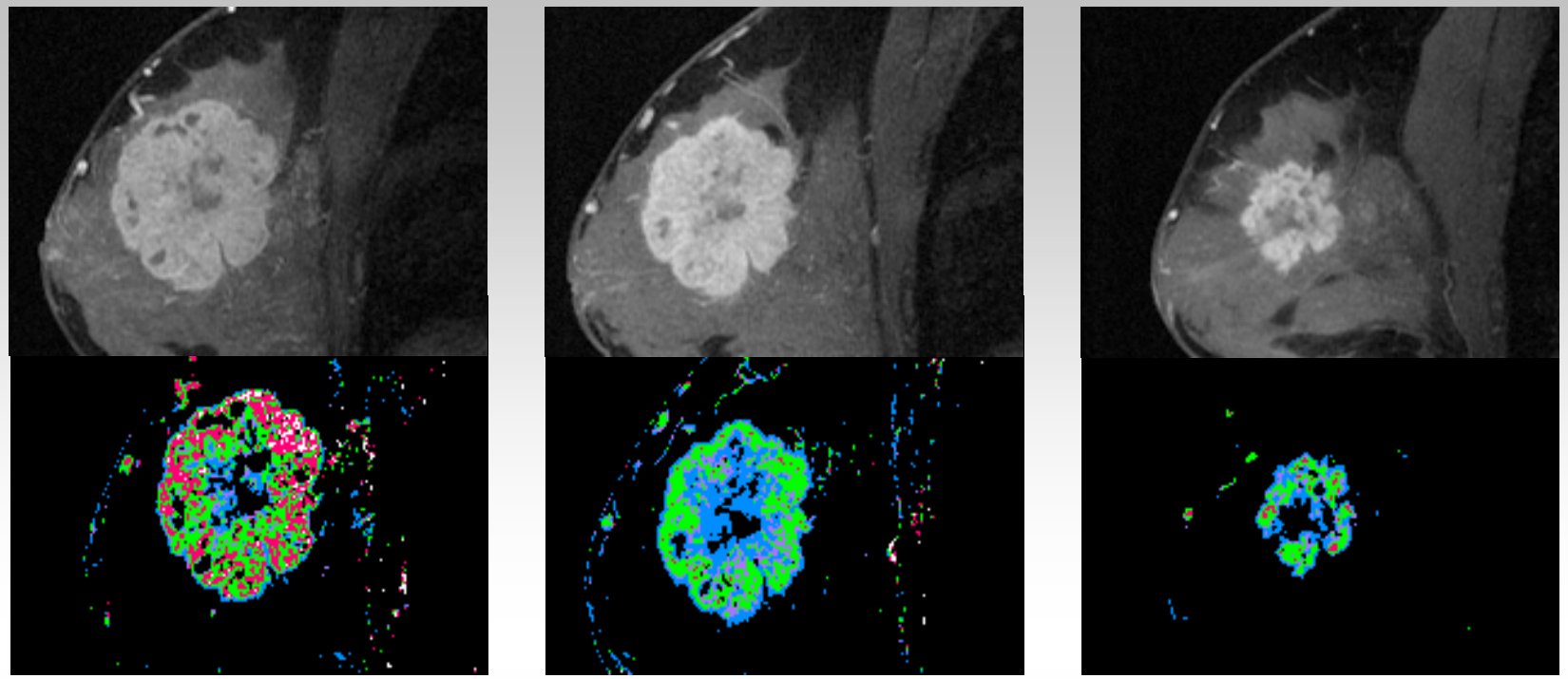


The Challenge of Integrating Information and Improving Care: The Breast Cancer Example

Laura Esserman, MD MBA

Professor of Surgery and Radiology

Director, Carol Franc Buck Breast Care Center

Clinical Challenge

- Integration of imaging, molecular tools, clinical trial data into tools to optimize therapy
- Why is it a challenge?
  - Cancers are heterogeneous and molecular/ imaging phenotypes have
    - Different outcomes
    - Respond differently to pharmaceutical agents,
    - Need different treatment strategies
    - Need tools for complex decision making to optimize outcome
  - Each research field evolves separately
    - Integration is not a priority and may be a “distraction”
  - Integration in the clinical care setting is key
    - Systems for integration are lacking

Problem

- Culture
- Resources
- Lack of availability of tools, systems
- Translation
  - Is about transforming science into information for decision support
    - For physicians, and patients and physicians together
  - Translational science is usually not about decision support

Culture

- Little motivation to share
  - Optimize assay of choice, present, and publish
  - Easier to stay within your field (easier to control)
  - Little credit for group science, collaboration
- Fear of integration/access to data (loss of control)
  - Corrupt data for final trial analysis
  - Trial design culture is around randomization, blinding, not allowing investigators or scientists to see data until data is mature (requires 3-6 yr product life cycle)
  - Correlative science, QI design is necessarily different
- No one takes ownership of or gets reward for creating tools for integration, sharing
- Common data platforms not considered critical
  - For sending and receiving images to colleagues
  - For clinical trial groups

Lack of Resources

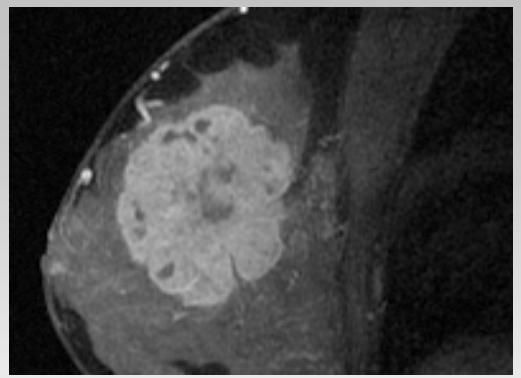
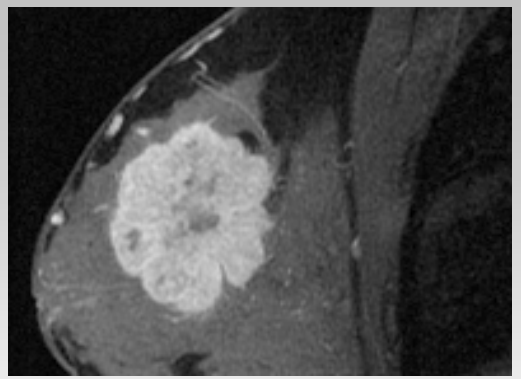
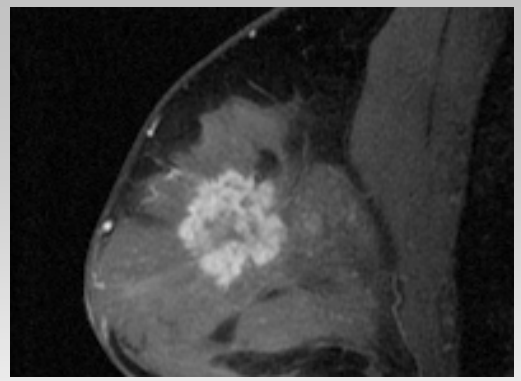
- Lack of common tools
- Resources, grants for informatics not directed toward integration
  - Informatics budgets are often devoted to solving specific problems (bioinformatics)
  - Many groups devoting resources to build the same tools
  - No budget to bring in teams to design informatics support

Lack of Availability of. . .

- Integrated Data platforms for assays, imaging
- Common data platforms for imaging
  - Can’t send MR films from one hospital to the next
  - Common data platforms for viewing, distributing and sharing images
- Clinical systems that
  - Integrate information across platforms (array, imaging, clinical data)
  - Facilitate multidisciplinary communication, collaboration
  - Explicitly support the delivery of quality care, and support or enable quality improvement
  - support the availability of critical information at the point of care

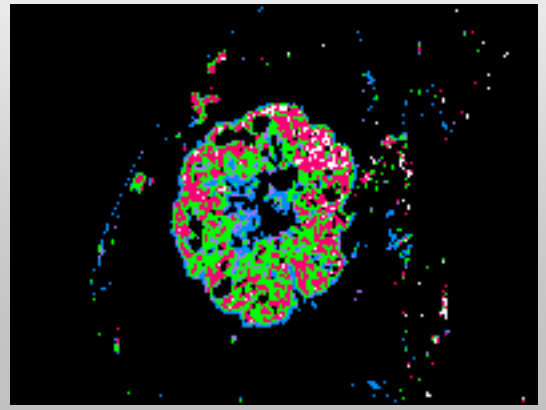
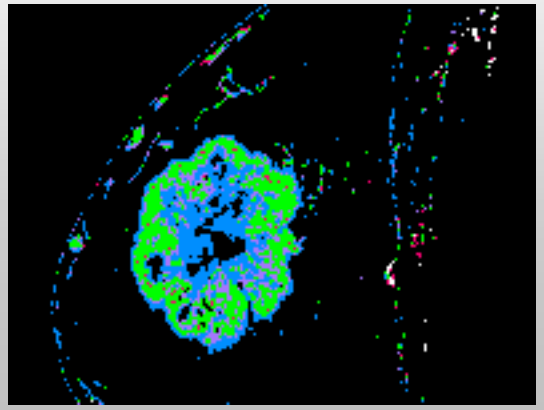
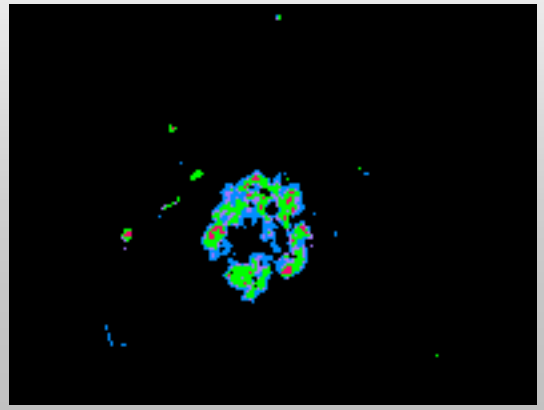
Potential Solutions

- Platform, web portal to integrate all data from correlative science trial
  - I SPY TRIAL example
    - Integration of molecular biology, imaging, clinical science
    - Illustrative problems: data sharing; lab trak; resources
- Prototype Development of systems to support quality of care, quality improvement, shared decision making, tailoring
  - Center of Excellence (DOD): systems to tailor treatment to biology preference and performance
  - Development of tools for shared decision making: patient physician decision aids

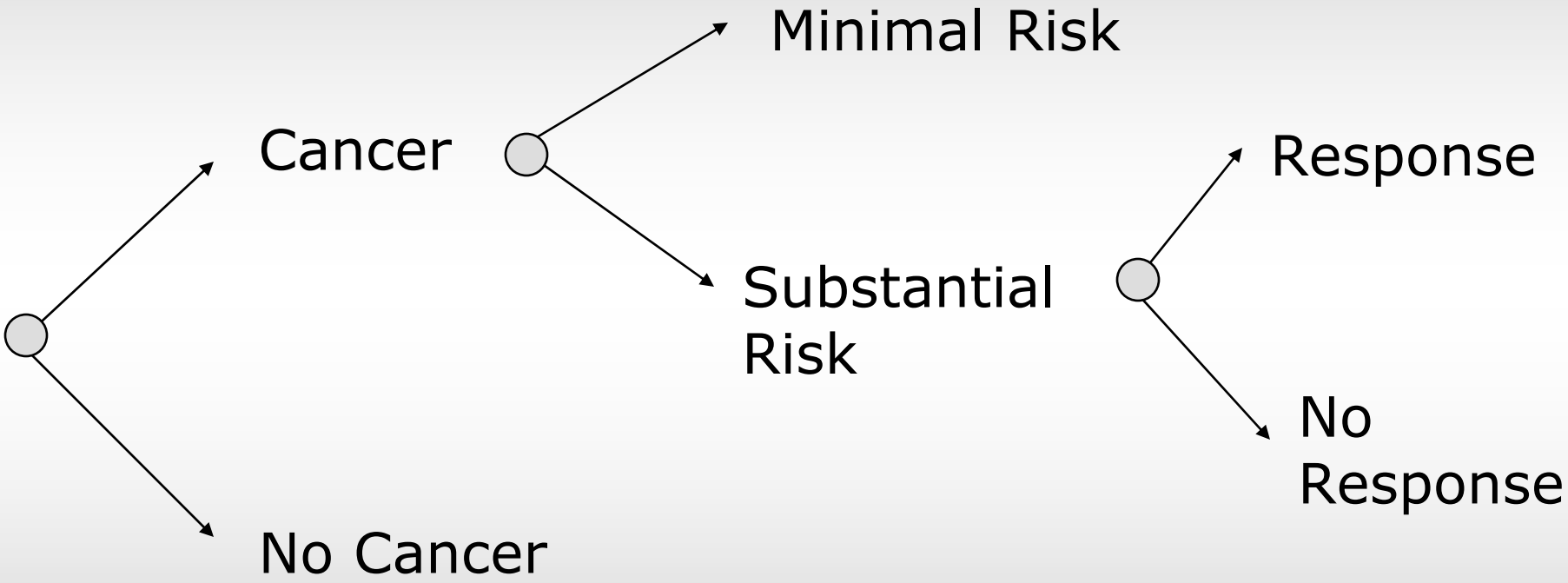




All Roads to Tailored Therapy for Breast Cancer Lead through the Neoadjuvant Paradigm

I SPY TRIAL

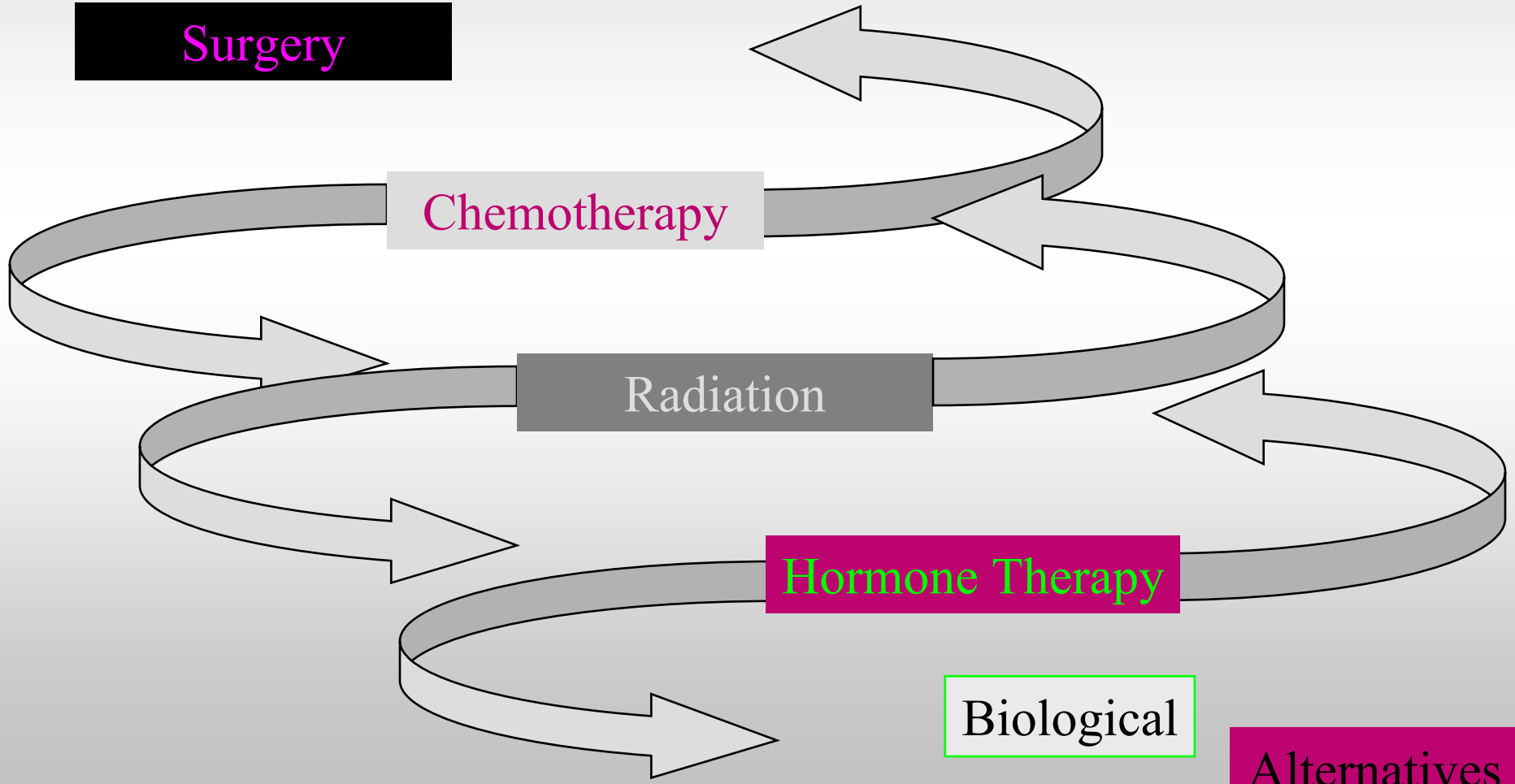




Critical Decision Points



Molecular tools should be integrated into the context of care with the goal of finding thresholds that change clinical decisions

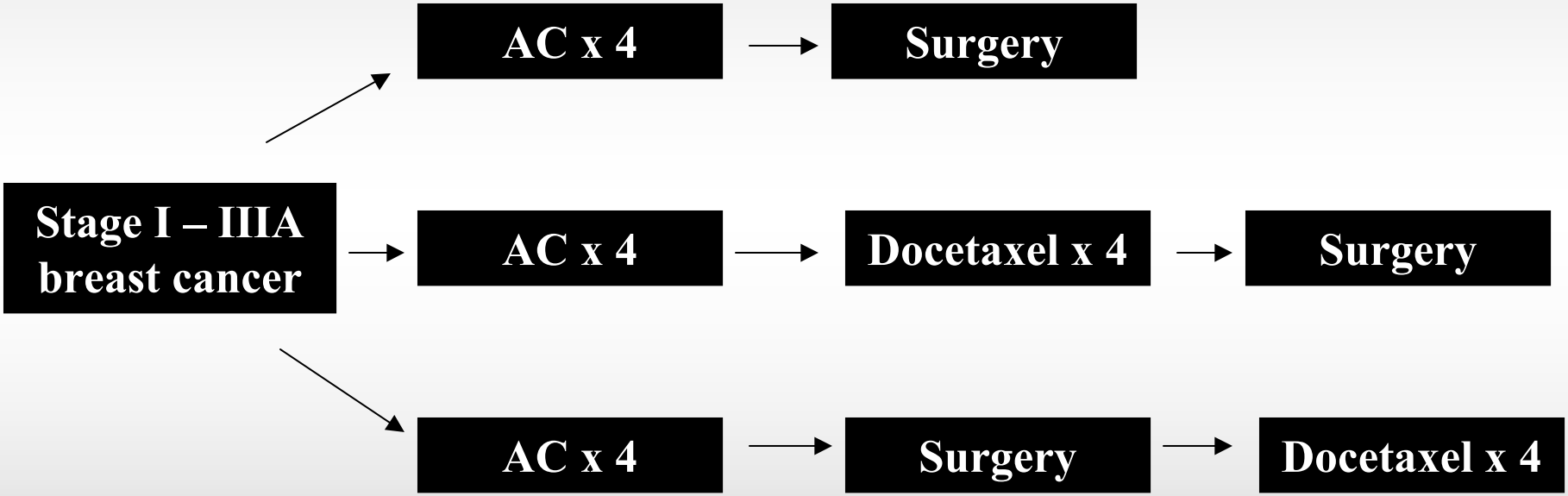
Breast Cancer Treatment Building Blocks



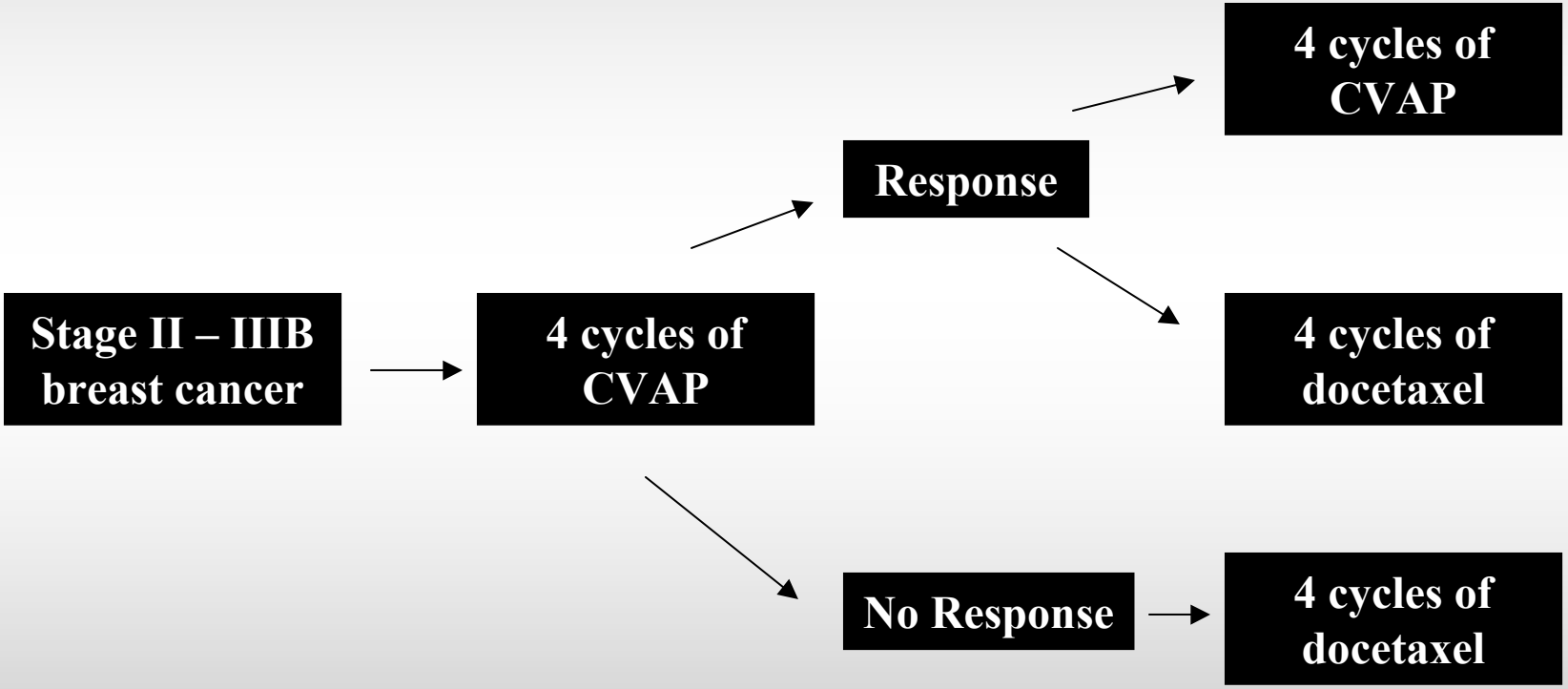
Neoadjuvant therapy

- Order of therapy is not important
  - Timing does not affect survival
- Tumor size and lymph node status retain predictive value after neoadjuvant therapy
- Response to therapy, however, is critical in determining outcome
- Results of response to neoadjuvant therapy impacts practice
- acceptable surrogate if consistent with other data

NSABP B-27 Trial:
Increase in CR with Taxol used as evidence of benefit



Aberdeen Protocol:
Study designed around response to therapy



Pathologic Response to Therapy

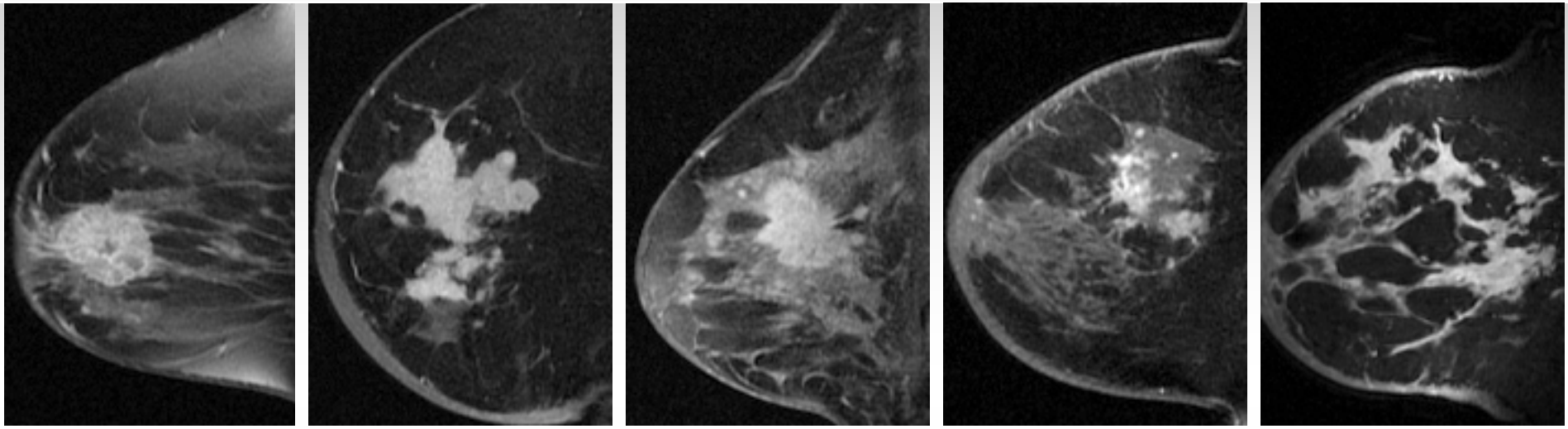
Is the most important predictor of survival after neoadjuvant chemotherapy

Assessing that response requires surgical excision and removal of surrogate

Pilot Data on MRI
from UCSF

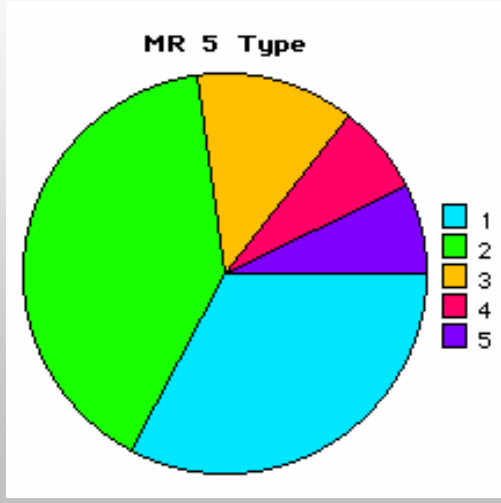
- 74 patients with LABC (1996-2001)
  - Median follow-up 2.5 years
- Neoadjuvant Chemotherapy
  - 4 cycles of Adriamycin (60 mg/m2) and Cytoxan (600 mg/m2)
  - One pt was lost to follow-up
- Serial breast MRI was used to estimate change in longest tumor diameter (LD)
- MR: TARGET technique was used on a 1.5 Tesla machine

MRI Reveals Several Phenotypes

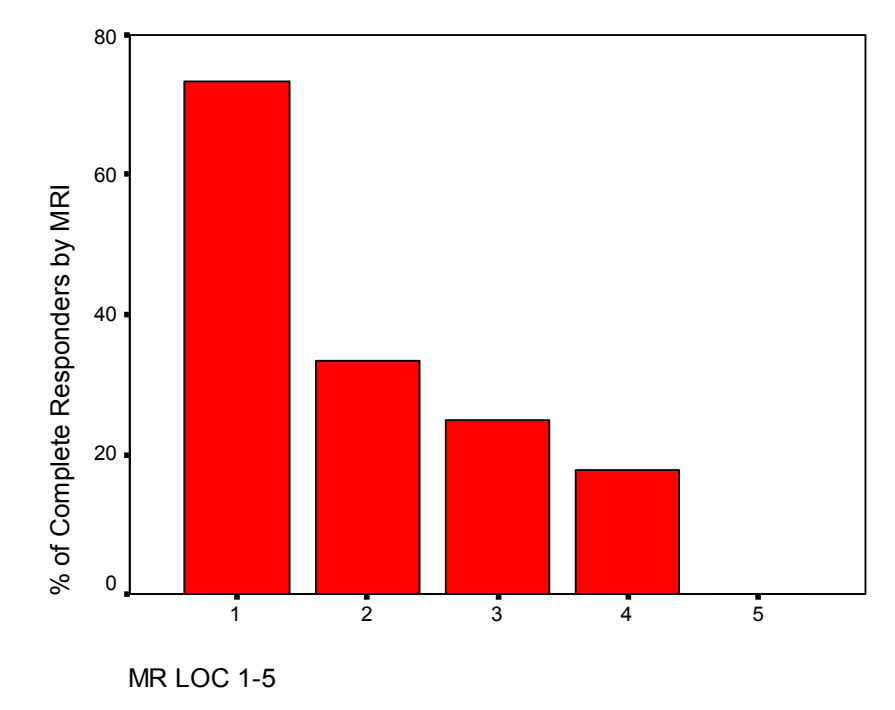


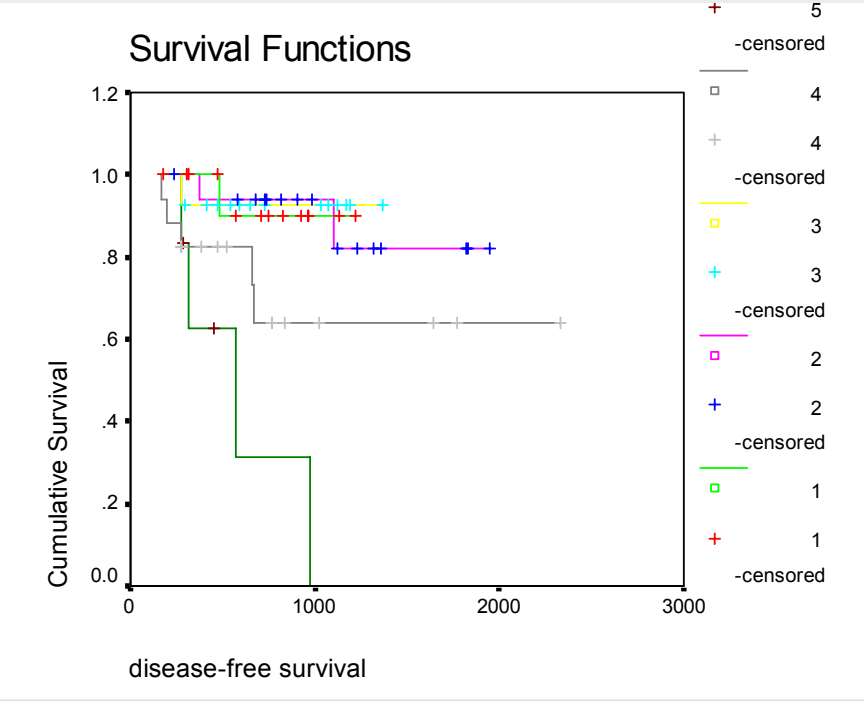
1 2 3 4 5

1: Single predominant mass with identifiable rim, displacing
2: Nodular pattern, irregular borders
3: Diffuse infiltrative pattern
4: Patchy enhancement
5: Septal spread



Response to Chemotherapy by MR Phenotype

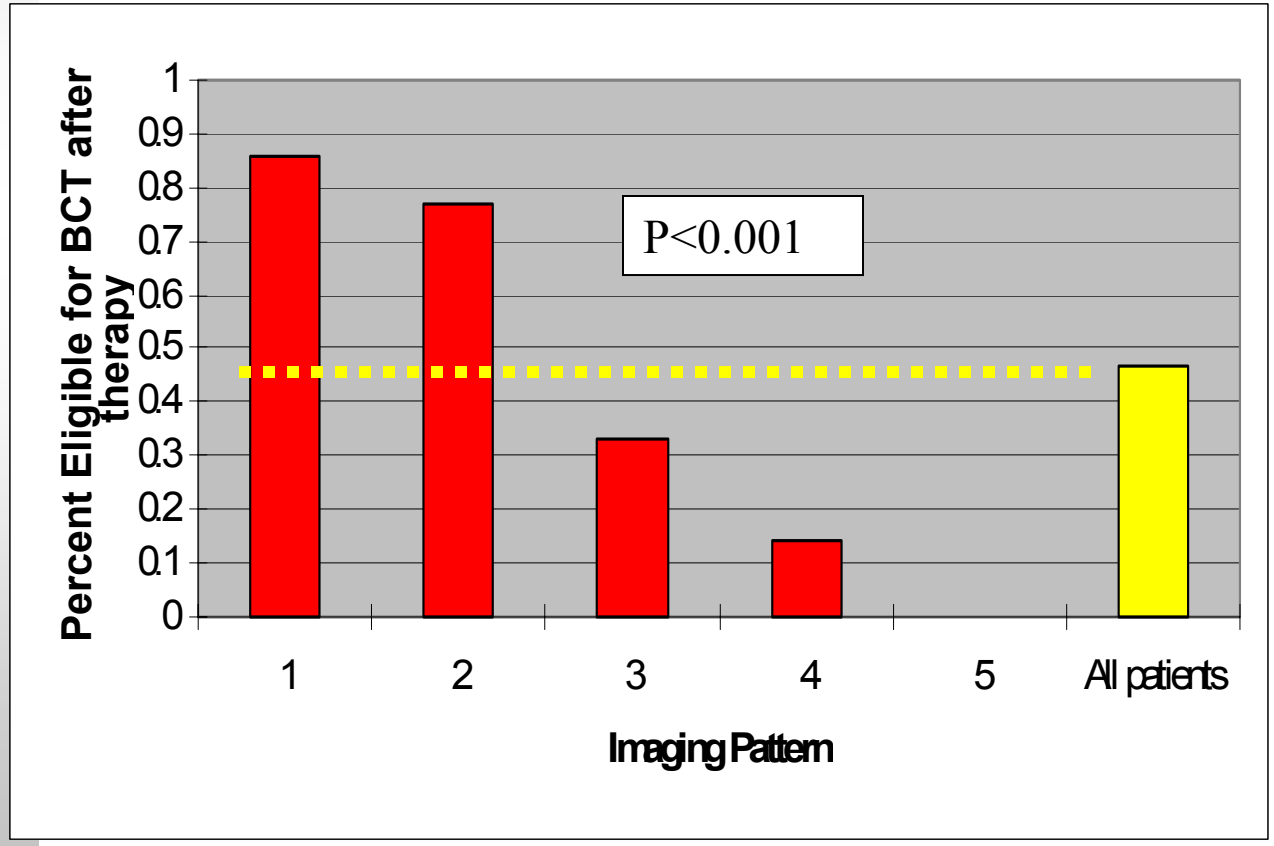




more circumscribed = more likely to respond

MR Type predicted who could have Breast Conservation

Percentage of patients in each imaging pattern who were eligible to undergo BCT based on post-therapy MR diameter <4cm.



Prior Probability for BCT: 47%

Posterior Probability (post MR)

1: 86%,

2: 77%,

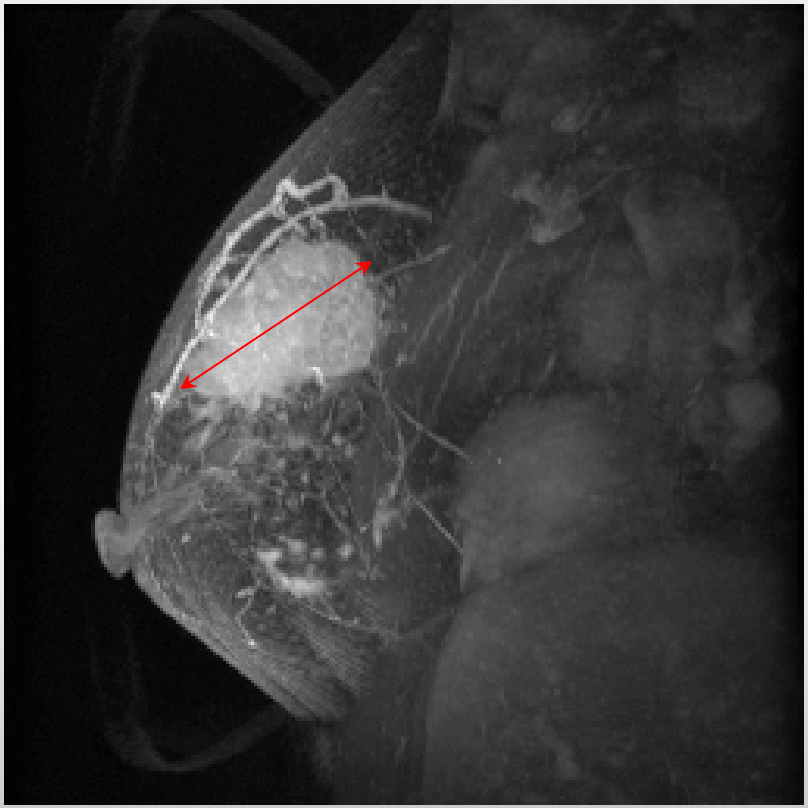
3: 33%,

4: 14%

5: 0%.

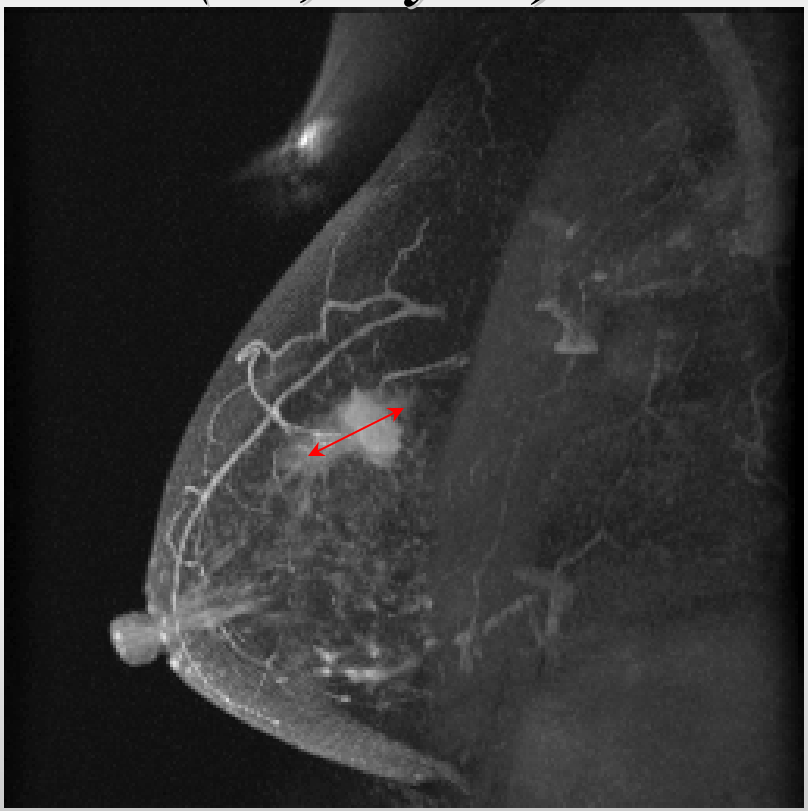
MRI allows measurement of longest dimension pre/post therapy

Pre-chemotherapy



LD=47 mm

Post-chemotherapy
(AC, 4 cycles)



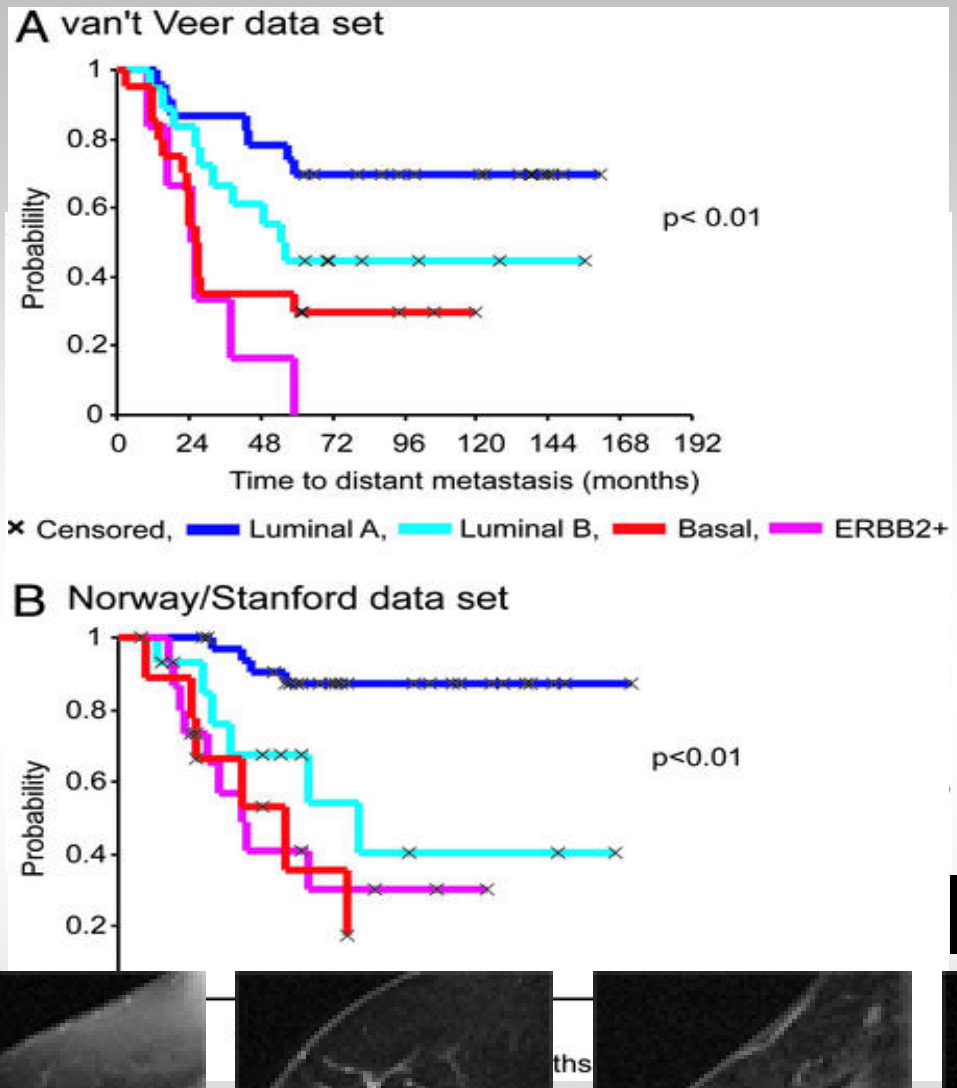
LD=16 mm

Lessons from UCSF pilot MRI study

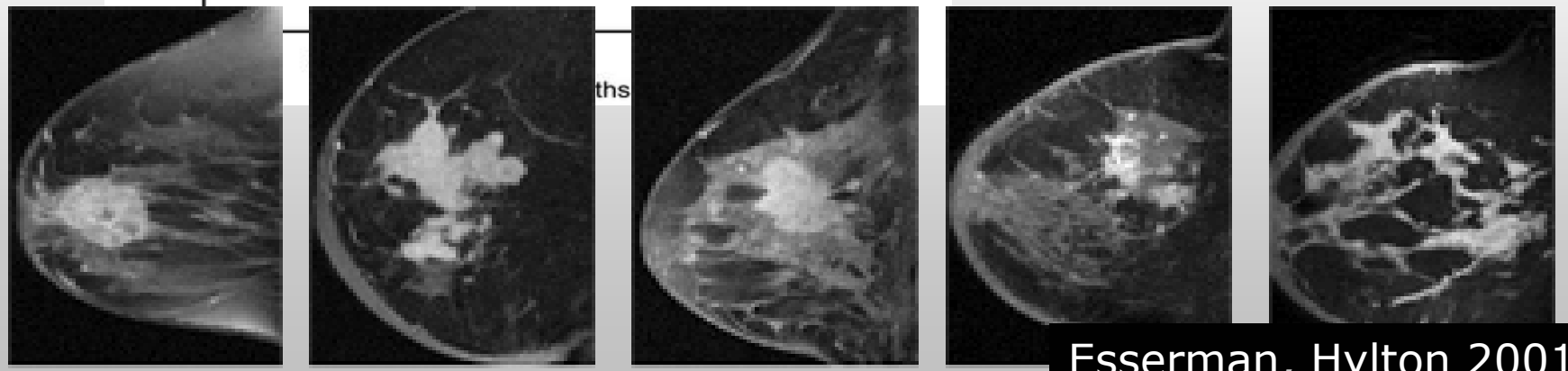
- MRI captures size and tumor morphology over the course of neoadjuvant treatment
  - MR type strongly predicts response and recurrence
  - MR type was the only marker AT DIAGNOSIS that predicted response
  - Longest diameter does not capture density changes- volume measurement needed
- MR size more accurate than clinical exam
  - Provides opportunity to “normalize” response
- Initial and final tissue samples needed for comparison of best, worst responders
  - Lacked ability to integrate imaging with molecular markers

cancers are not the same

Expression arrays show that tumors arise from different cell types, and that these tumor types have different outcomes



Perou PNAS 2003

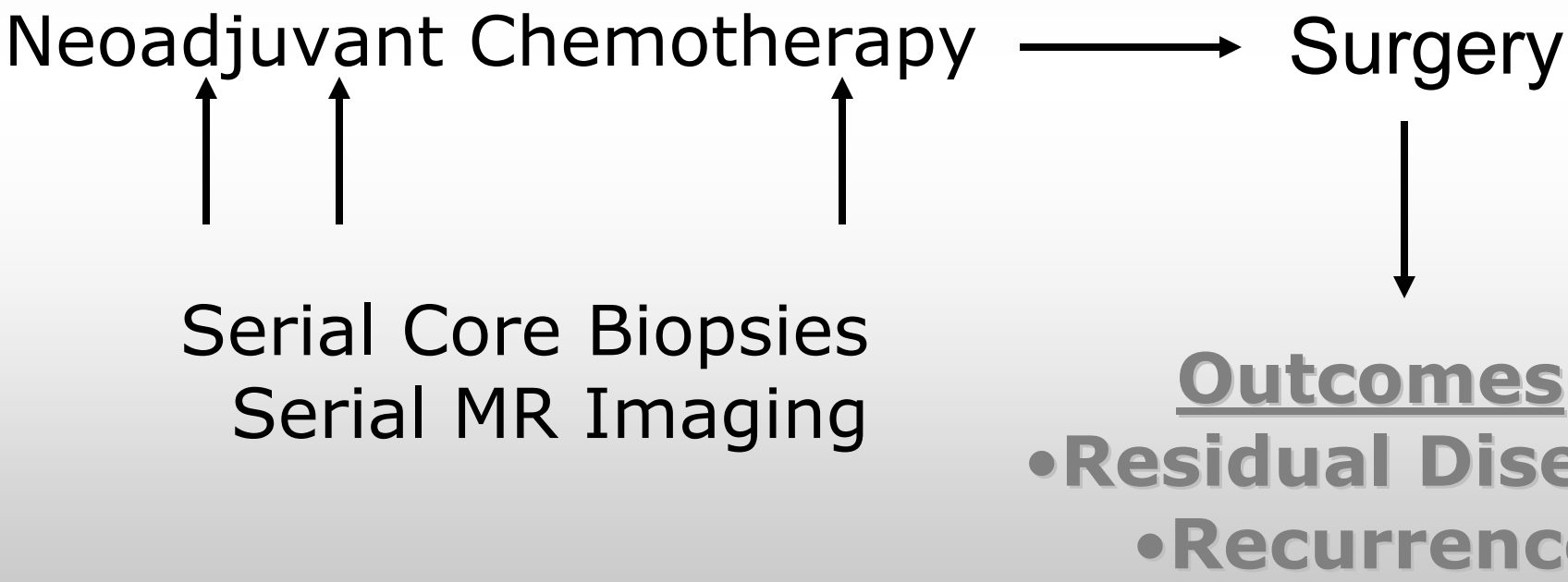


Esserman, Hylton 2001

Neoadjuvant Studies

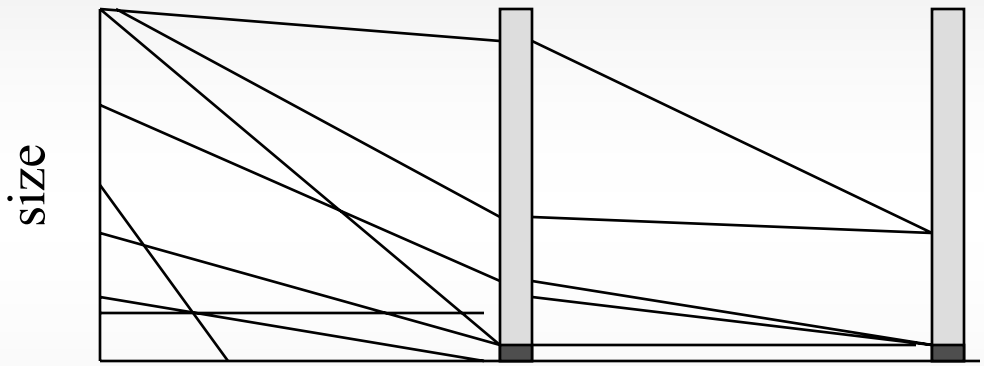
- Potential to make a difference with few patients in a short time frame, but . . .
- Barriers
  - Most conducted as single institution studies
    - But few patients at each institution with large tumors
  - correlative science harder in multiple institutions
  - Surgeons see patients first and operate
  - Individual treatments common

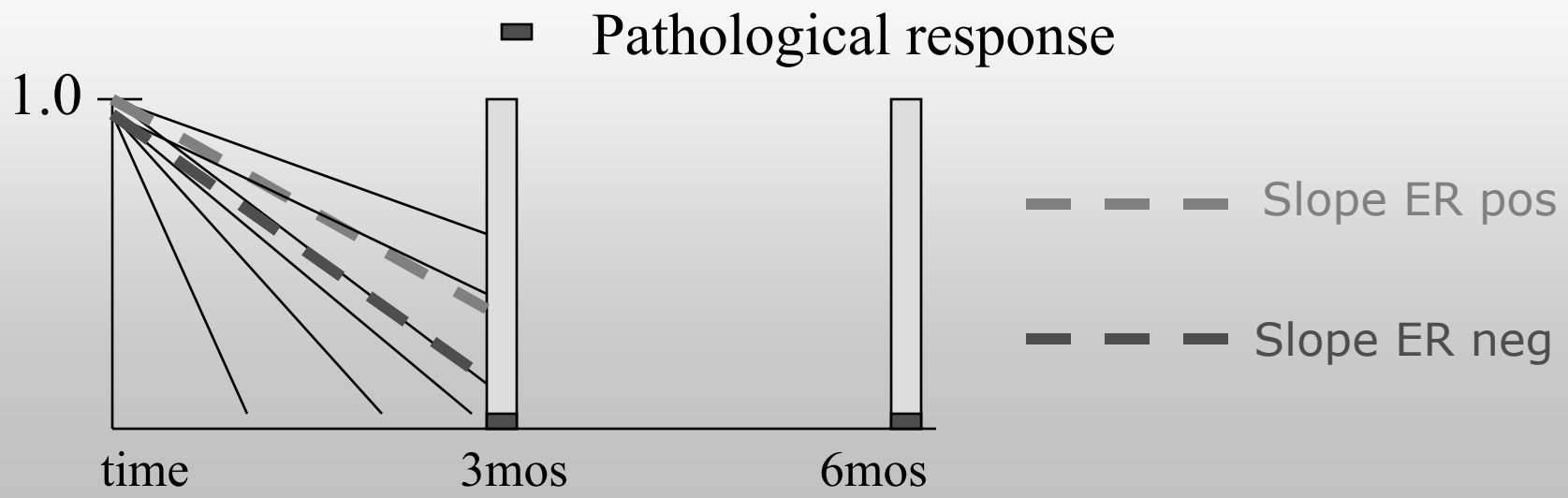
Trial Design



"Pathologic Response" is a single point in time-may not be best measure:

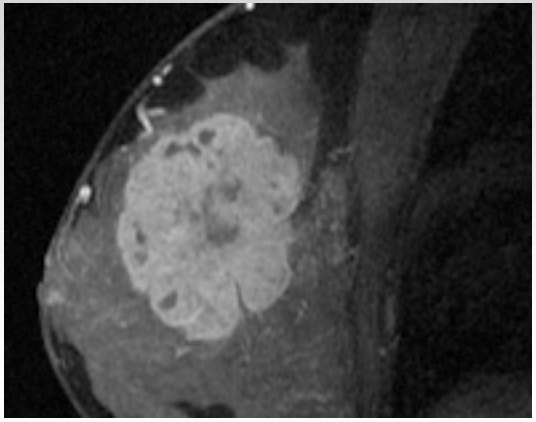
Imaging allows the opportunity to "normalize" and look at slope of response

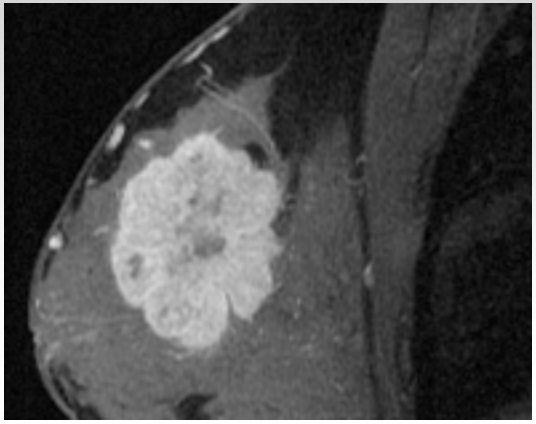


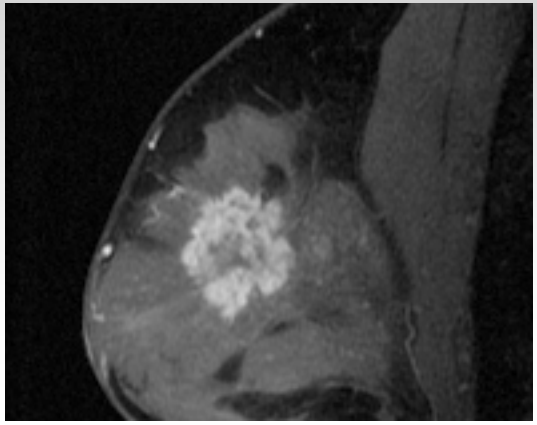


Volumetric/Vascular Response Assessment

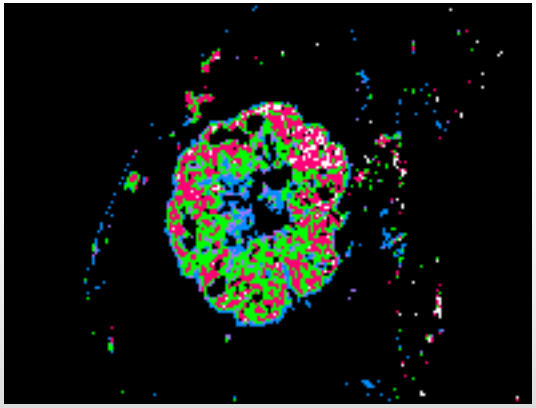
S1

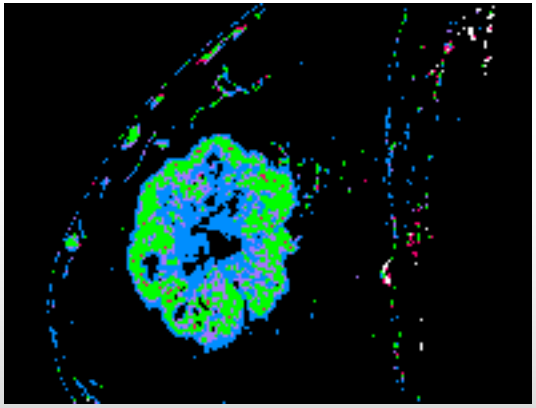


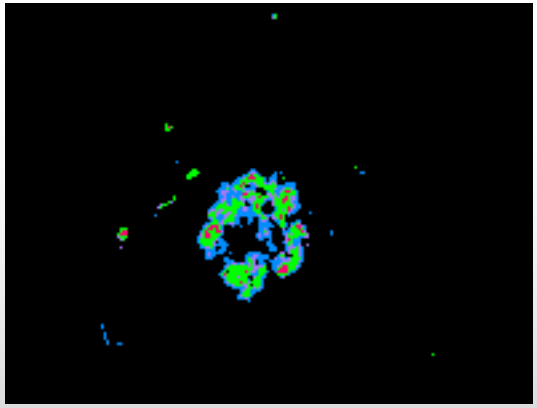




SER





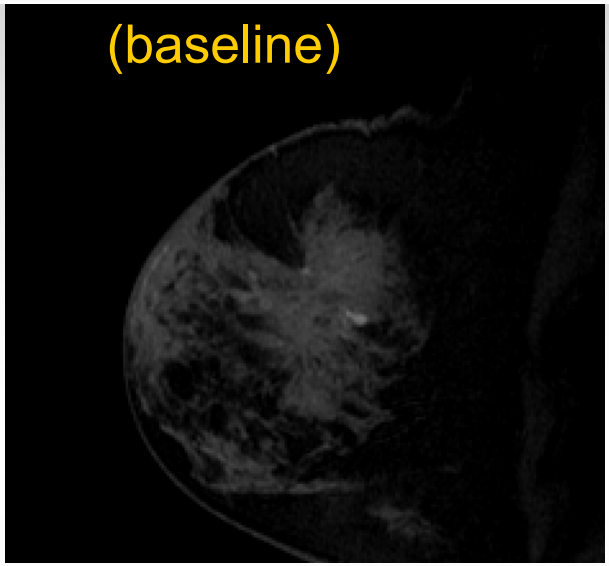


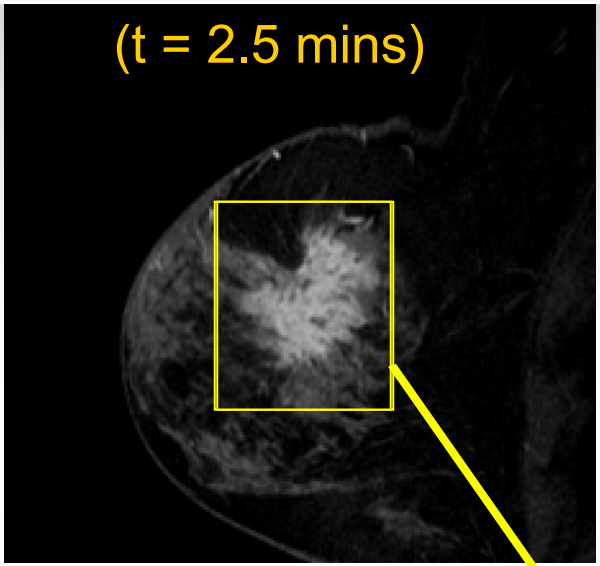
Baseline (pre-chemo):	
peak SER	*= 2.1*
Volume	*= 65 cm³*
%Red+White	*= 41%*

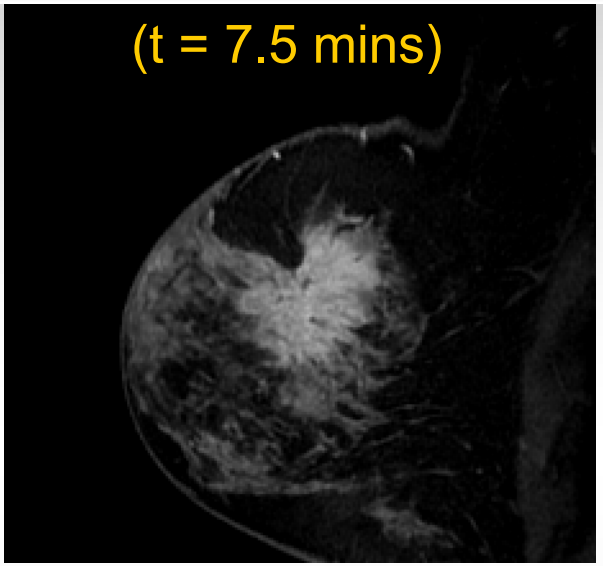
Post 1-cycle AC:	
peak SER	*= 1.5*
Volume	*= 42 cm³*
%Red+White	*= 3%*

Post 4-cycles AC:	
peak SER	*= 1.6*
Volume	*= 4 cm³*
%Red+White	*= 16%*

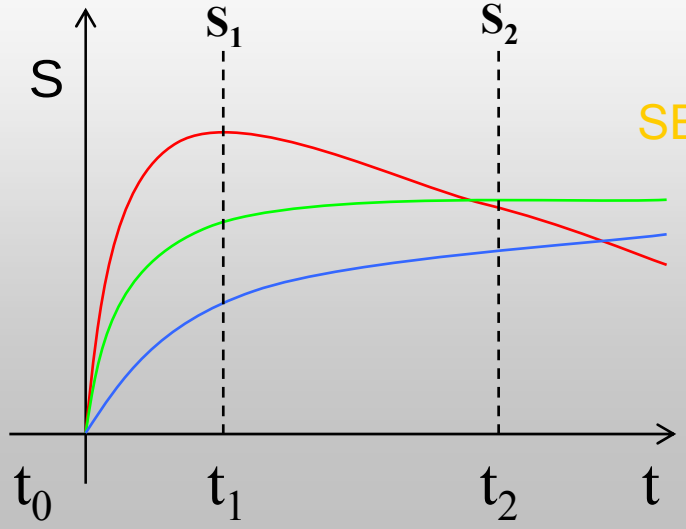
Measurement of Tumor Volume and Vascularity





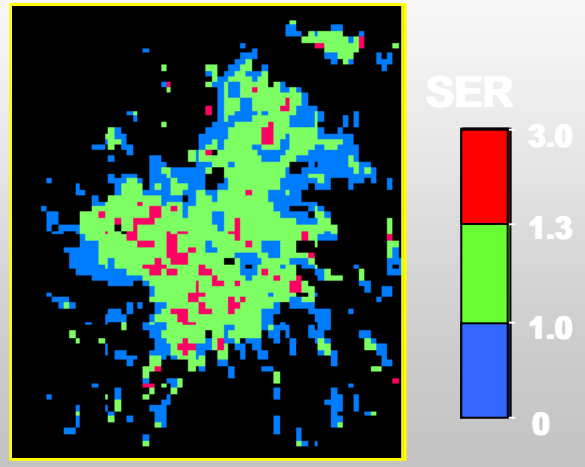


Signal enhancement ratio (SER):



$$SER = \frac{(S_1 - S_0)}{(S_2 - S_0)}$$

$$PE = \frac{(S_1 - S_0)}{(S_0)}$$



CALGB INTERSPORE ACRIN

Investigation of
Serial studies to
Predict
Your
Therapeutic
Response with
Imaging and
And
moLecular analysis

I SPY WITH MY LITTLE EYE . . . . . . A BIO-MARKER BEGIN-ING WITH X . . . .

CALGB 150007/150012
InterSPORE/ACRIN6657
NCICB

MRI and Molecular Markers in patients undergoing neoadjuvant chemotherapy for locally advanced breast cancer

UCSF

UNC

U Penn

Georgetown

U of Alabama

U Washington

U Texas Southwestern

Sloan Kettering (MSKCC)

. . . U Chicago

Hypotheses

. . .

1. Breast Cancer is Heterogenous
2. Molecular and Imaging Markers will predict response to therapy and determine outcome

Tools

MR Imaging, IHC, Genomic and Expression Analyses

Purpose

Identify women with a poor outcome at the time of diagnosis, so that targeted novel therapeutics can be introduced early in the course of treatment

Clinical Study Design

Required:

common MR platform;

common clinical protocol;

willingness to share samples;

multiple funding sources;

Four years to set up. . .

Serial Acquisition of Images, Tissue, Serum to Monitor Response

Clinical Study

Anthracycline → Taxane → Surgery & RT → Tam if ER+

MRI

Tissue: Core or Surgical

Serum: Specific Markers

Tissue/ serum proteomics

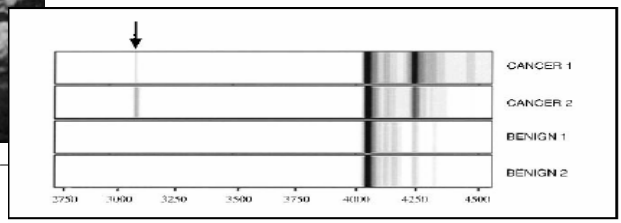
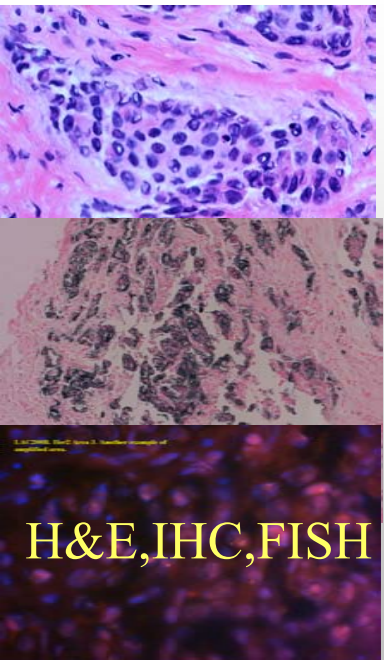
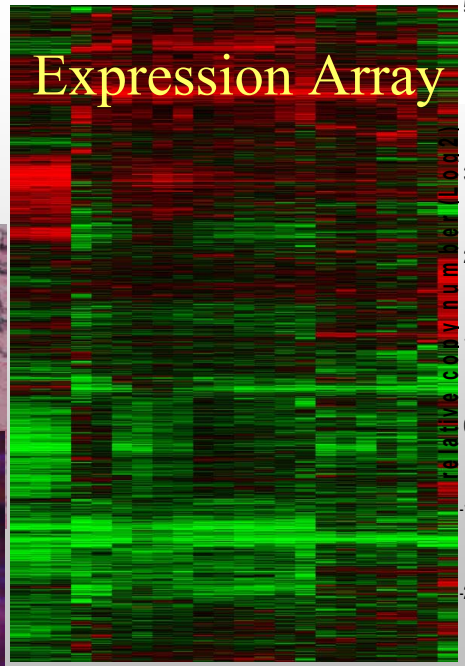
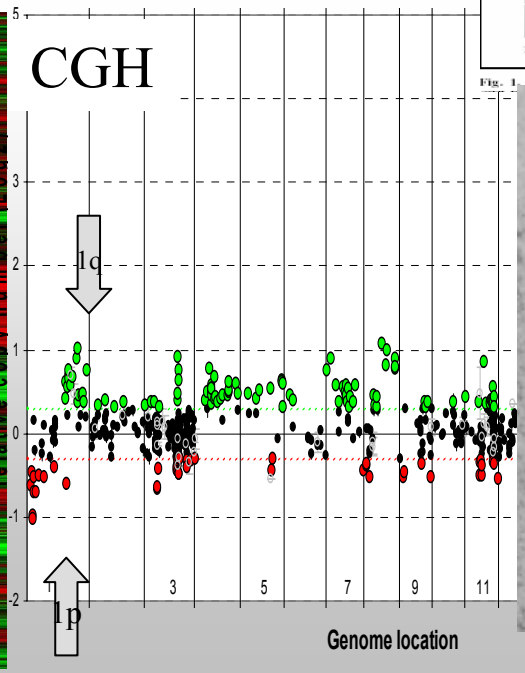
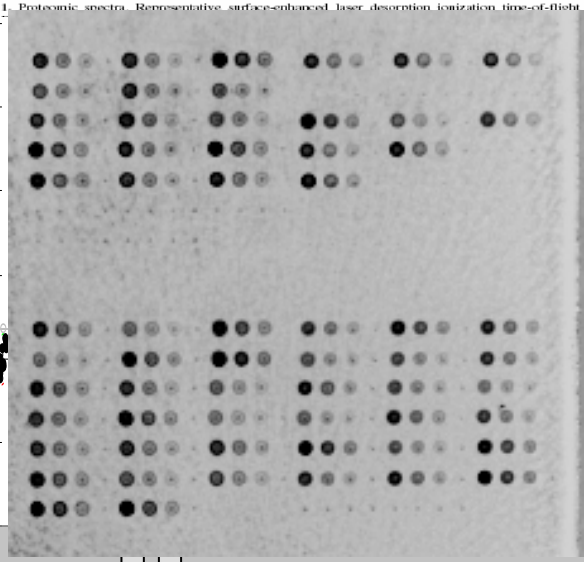


Fig. 1. Proteomic spectra. Representative surface-enhanced laser desorption ionization time-of-flight









Total Accrual: 107

Inst Name	Accrual
University of Pennsylvania Medical Center	13
Georgetown University Hospital	3
University of North Carolina	19
Memorial Sloan Kettering Cancer Center	11
University of Alabama at Birmingham Medical Center	18
University of Texas Southwestern	6
University of California San Francisco	37

Accrual as of June 18, 2004
(1.5 years)

2640 specimens

Tools for Tracking Data

- *Lab Trak*
  - *System originally designed by CALGB*
  - *Web Based Version (tracking) available 8/01*
  - *Supports tracking of specimens*
  - *Supports standards, data acquisition, results*
  - *BUT*
    - *Not integrated with results*
    - *No longer open source: BioNumerick owns web front end . . .*
- *ACRIN*
  - *Central archiving and processing*
    - *reader studies to assess reproducibility*
  - *On-line registration, image transfer*
  - *No standard platform for image processing and analysis*
    - *Hylton, Lehman AVON NCI partners grant?*

NCICB has stepped up to the plate to help develop tools for integration

Goals for Analysis

1. Quality Control
   - sufficiency of tissue cores
   - RNA, DNA quality
   - IHC quality
2. Cross Platform Validation
   - Her2 IHC→ FISH→Expression Array→CGH→proteomics→serum
3. Assay Validation
   - p53 conformal mutation analysis vs. p53 IHC
4. Identify Robust Predictors of Response
   - confirmation across assay platforms
5. Identify non-invasive predictors of molecular features
   - MRI phenotypes (LOC) vs. Expression Array cell types
6. Identify/predict therapeutic alternatives

Response Markers

Early: **primary tumor**	Intermediate: **primary tumor**	Long term: **systemic**
clinical size change	clinical size change over Rx	3 Yr disease free survival
MRI size change at 3 v *longest diameter* *volume*	MR size change after Rx *longest diameter* *volume*	3 Yr overall survival
	Residual disease at surgery *no invasive* *≤1 cm invasive* *>1 cm*	

Predictors of Response

PREDICTORS OF RESPONSE: Baseline, 24-72 hours, Post Rx				
Imaging	**Specific markers**		**Arrays**	**Serum**
MRI	**IHC**	**FISH**	**Genomic**	proteomics
Phenotypes	EGFR, Her-2	EGFR	**Expression**	markers
SER (angiogenesis)	cyclin D,E, p21	Her-2	cell types	
	lkB, Topo 2		**Protein Lysates**	
	Ploidy			
	CD 34			

Summary of Markers

- **Volume Response**
  - MRI
- **Cell Types**
  - Luminal and basal (expression); LOC (imaging)
- **Angiogenesis**
  - CD 34, SER by MRI
- **Proliferation and Cell Death**
  - e.g. Ki67,proteomic lysates, p21, cyclin E,D1,
- **Molecular profiles**:
  - DNA copy number, expression arrays
- **Specific Therapeutic Targets**
  - e.g. ER, PR, erbB2, EGFR, Topo 2 etc.
- **Proteomic Profiles**
  - Serum, tissue phosphoproteins, proteomic imaging

Functional Goals of Web Portal

1. Data entry for assay results
2. Linkage of sample results across platforms
3. Integration of systems
    a. Specimen Tracking (Lab trak)
    b. Results Repository (Cooperative Group Data/CDE, Molecular Assays)
    c. Analysis tools (CaINTEGRATOR)
4. Facilitation of work flow for trial/treatment (FUTURE)

Neoadjuvant Trials as a platform for change

Requires infrastructure and culture change

NCI Informatics

- Operationalize data sharing
  - Levels of access to data by password
- Integrate data analysis with results repository
- Agreement to release data set to public at the conclusion of the trial
- Facilitate viewing of clinical data (images, pathology)
- Facilitate Investigator meetings, review of benchmarks

I-SPY Trial Web Site

The I-SPY Trial

- The Questions:
  - How are we doing? What is the accrual rate by Site?
  - What is the quality of the sample?
  - What is the difference between no-patient response and a good patient response?
  - What is the right surrogate marker?
  - Does the drug work or not?
  - Compare expression data and identify patterns
- The Answers:
  - Embedded in data captured within each data type, in aggregate views of the captured data, and in relationships between each data type
    - Includes quality indicators within each data type and across multiple data types

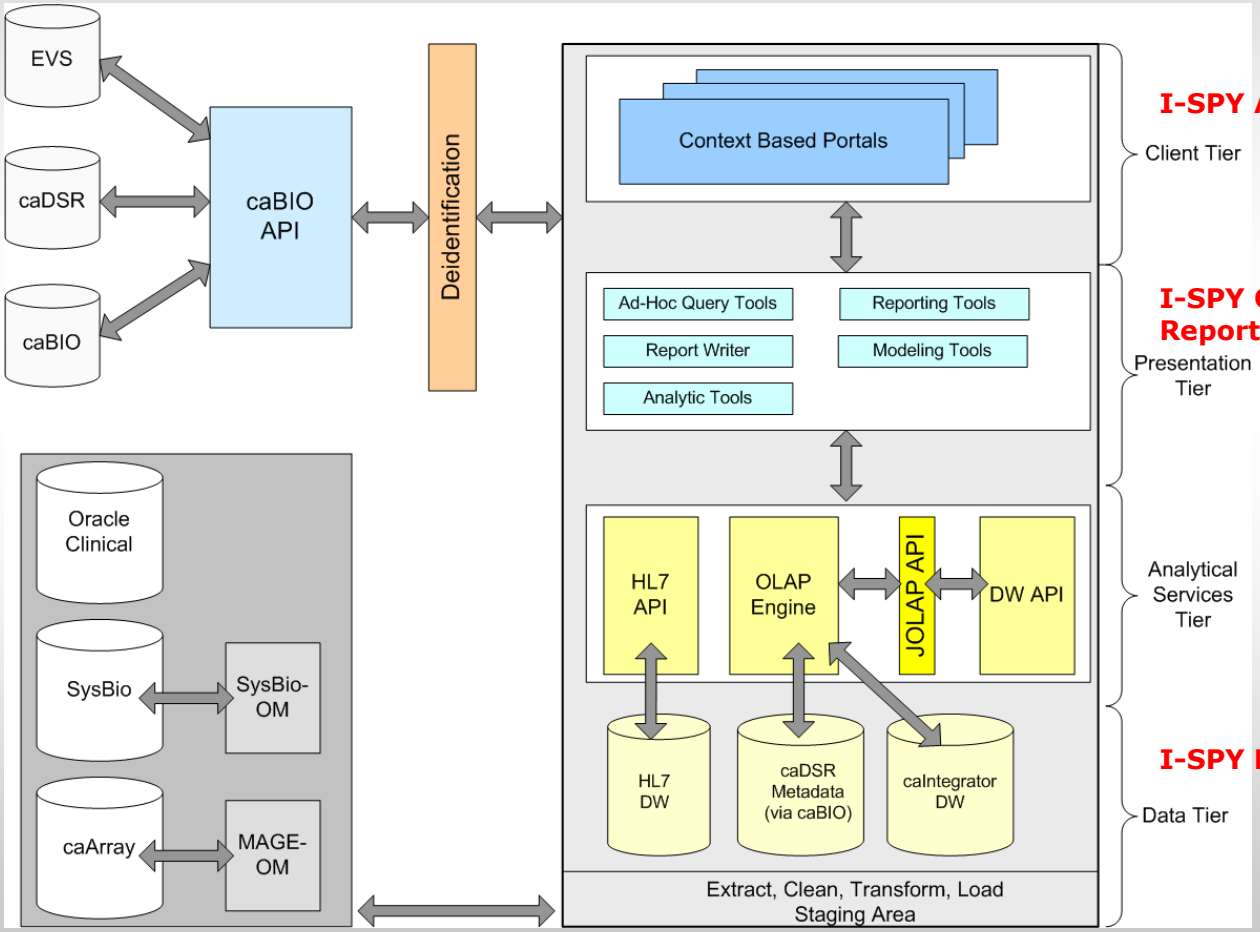
The Challenge

- The capture and integration of diverse data types provided by multiple researchers working on different aspects of the trial
  - Includes the capture of specific and cross data-type quality indicators
- The use of standards (meta-data) supporting the capture of data and interrelationships to facilitate cross data type queries
- The integration of existing applications and analysis tools that may be leveraged to conduct further analytical studies
- The protection (access controls, encryption) of data types and integrated data views
- Assurance that looking at data “early” won’t corrupt results

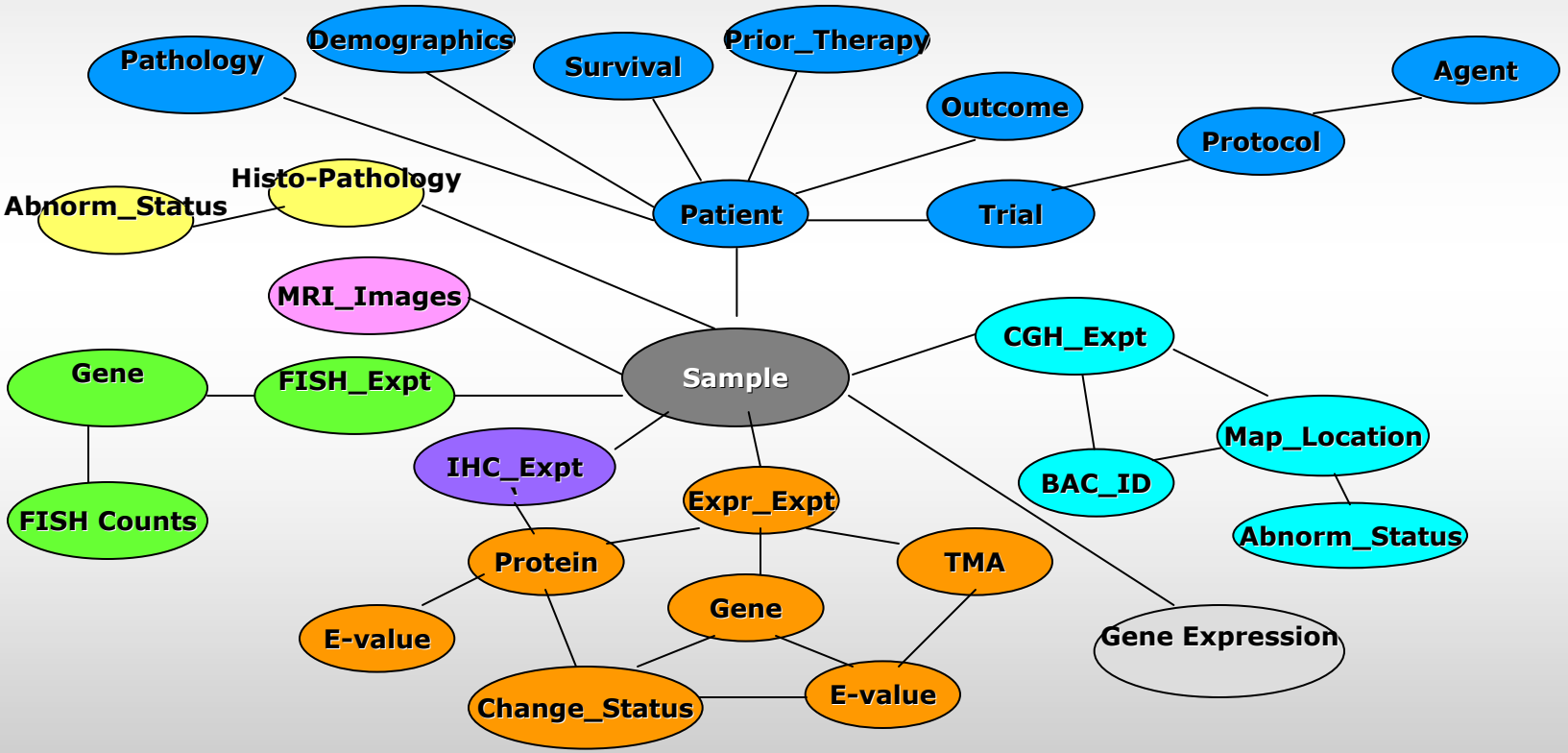
caIntegrator

- caIntegrator is an application framework that allows researchers to access and analyze clinical and experimental data across multiple trials and studies
- caIntegrator facilitates the generation of ad hoc queries and customized reports
- caIntegrator will support data aggregation across patients and samples

caIntegrator Framework



Conceptual Model



Sample question 1: What is the right intermediate marker of response?

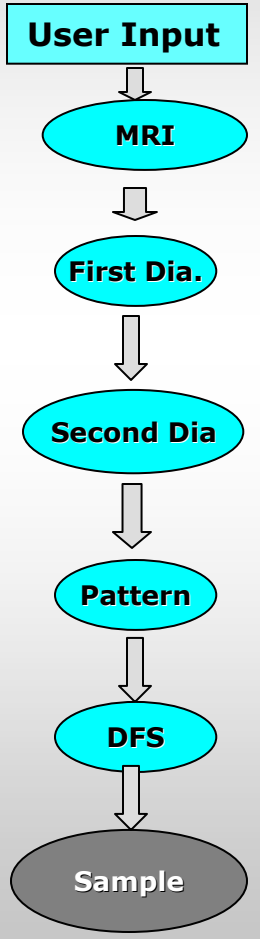
- Question answered by using multiple queries.
- Using MRI as a reliable predictor, correlate with molecular markers
- Sample query to answer this question:
  - Show me data for all patients that have a change in volume after first AC treatment > 30%.
    - Group this data by tumor patterns?
    - Which pattern has the greatest number of patients with a change > 30%.
    - Repeat for the fourth AC treatment?
    - Show me the DFS for these patients and # of lymph nodes present at the time of surgery.

Qn.1) What is the right surrogate marker?

- Data needed to answer query
  - Longest Tumor diameter (M3 Pre-treatment and M4 treatment and post, longest dia. of full extent of disease)
  - Protocol Time Point (M4)
  - Tumor pattern (Morphologic Pattern Classification, M3 & M4)
  - DFS (CALGB Form C-997 From/To dates and Survival Status)

Qn.1) What is the right surrogate marker?

- Data retrieval
  - Get longest diameter from M3
  - Get longest diameter from M4
  - Calculate change in diameter
  - Obtain Pattern and DFS
  - Get Samples

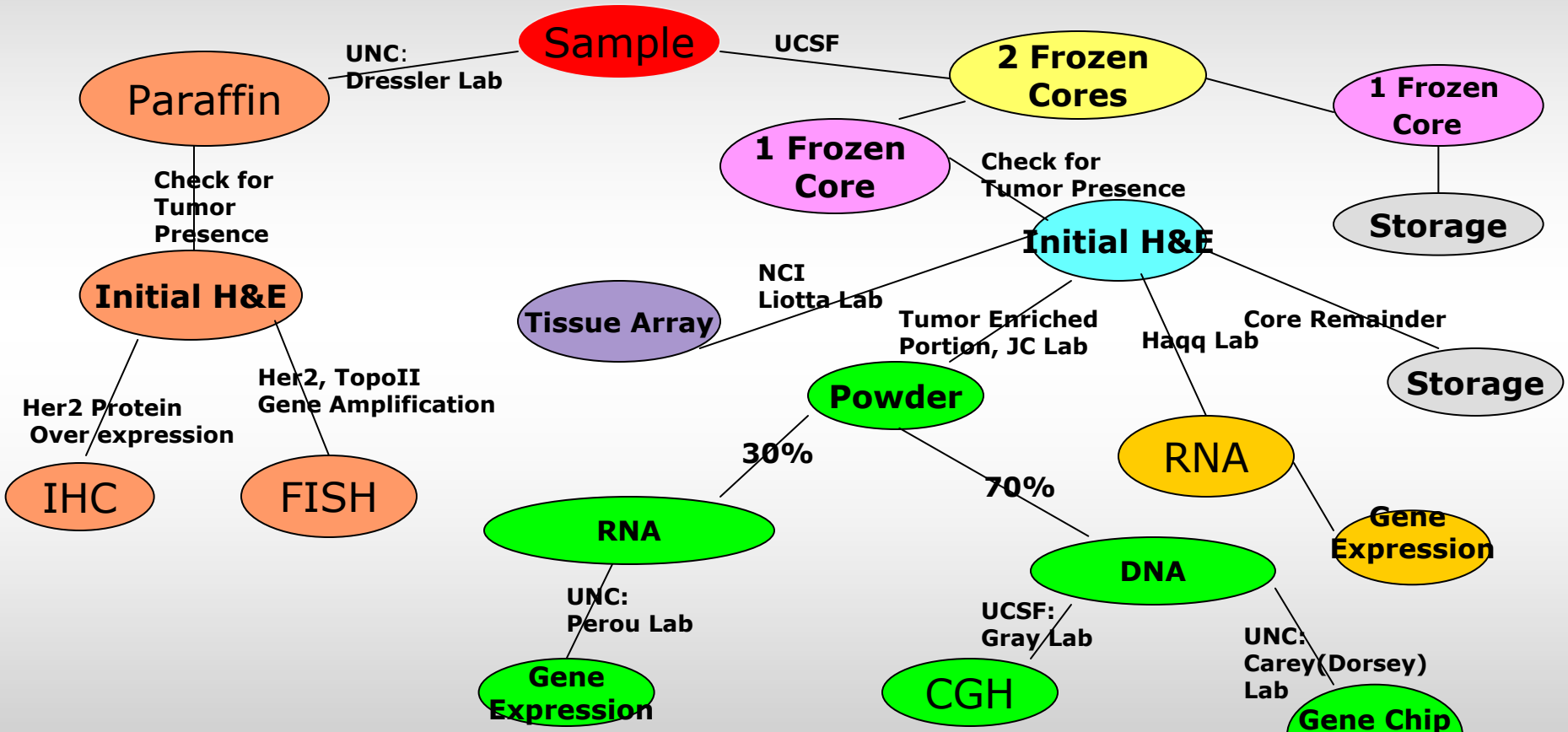


Sample question 2: What is the quality of the sample?

- Biopsy samples:
  1. Frozen core.
  2. Paraffin core.

  Touch preps: collected at the time of core biopsy to maximize the chance of obtaining high quality tumor samples.

Workflow for Sample Cores



Both Perou and Haqq's lab do gene expression experiments, Haqq's has a better technology of doing them, Usually the Perou's lab works on the experiments first, Haqq's lab is only used as a backup.

Frozen Core Quality Indicators

- If the sample(core) is along the bottom of the casette.
- H&E processing to check whether the tumor is present in the cell or not., what is the tumor %?
- Enriched or not?
- DNA yield for doing CGH, how is the quality? Good, ok, or bad?
- DNA amount, volume received: gene chip.
- RNA yield for gene expression, amt?

Paraffin Core Quality Indicators

- This type of samples are used for IHC and FISH experiments.
  1.FISH: gene amplification for HER2 and TopoII.
  2.IHC: protein over expression for HER2.
- Tumor present or not by H&E.
- Quality indicators for FISH:
  1. Fixation: good, bad or ok?
  2. Signal strength for Total Topo II, total HER2 and total Cep17 counts (positive controls, good or bad).
- Quality indicators for IHC:
  1. Fixation: good, bad or ok?
  2. Signal strength for Intensity of the stain.
  3. Percent Positive: SG stain must be >=10% of tumor cells.
  4. Localization: SG stain must be localized to the membrane, or membrane associated.
  5. Distribution of the stain.

Neoadjuvant MRI Correlative Science Trial
Procedure Time Line: Advocate Support

Patient _____

Date _____ Date _____ Date _____ Date _____ Date _____ Date _____ Date _____

48 hrs after AC starts (24-96 hrs)

2 weeks after AC starts

Mammogram

MRI #1

Core Biopsy #1

Serum sample

Core Biopsy #2

MRI #2

MRI #3

Mammogram

6A

SURGERY Date _____

O.R. Tissue Specimens

1 2 3 4 5

Cycle 1 Start AC

Cycle 2

Cycle 3

End AC Cycle 4

Date _____ Date _____ Date _____ Date _____

AC Chemo dates

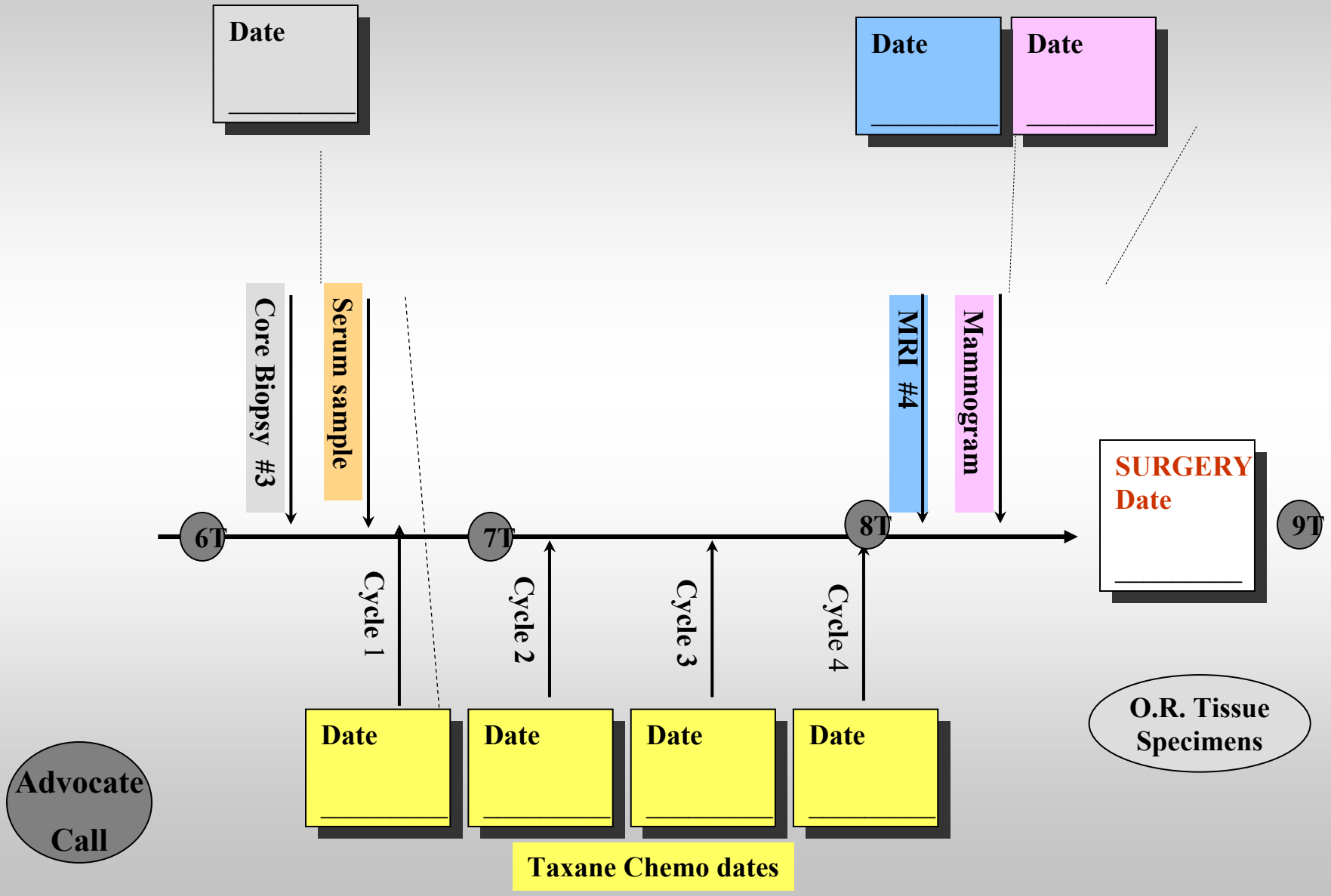
Advocate Call

Start TAXANE

see page 2

Neoadjuvant MRI Correlative Science Trial
Page 2, Taxane arm

Patient _____



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MRI

Nola Hylton

Molecular Profiles

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Many disciplines
Many agencies
education, trust, collaboration

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rioli

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ACRIN

Ben Herman

SPORE

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NCI

Ken Buetow, Sue Dubman, Sharon Settnick

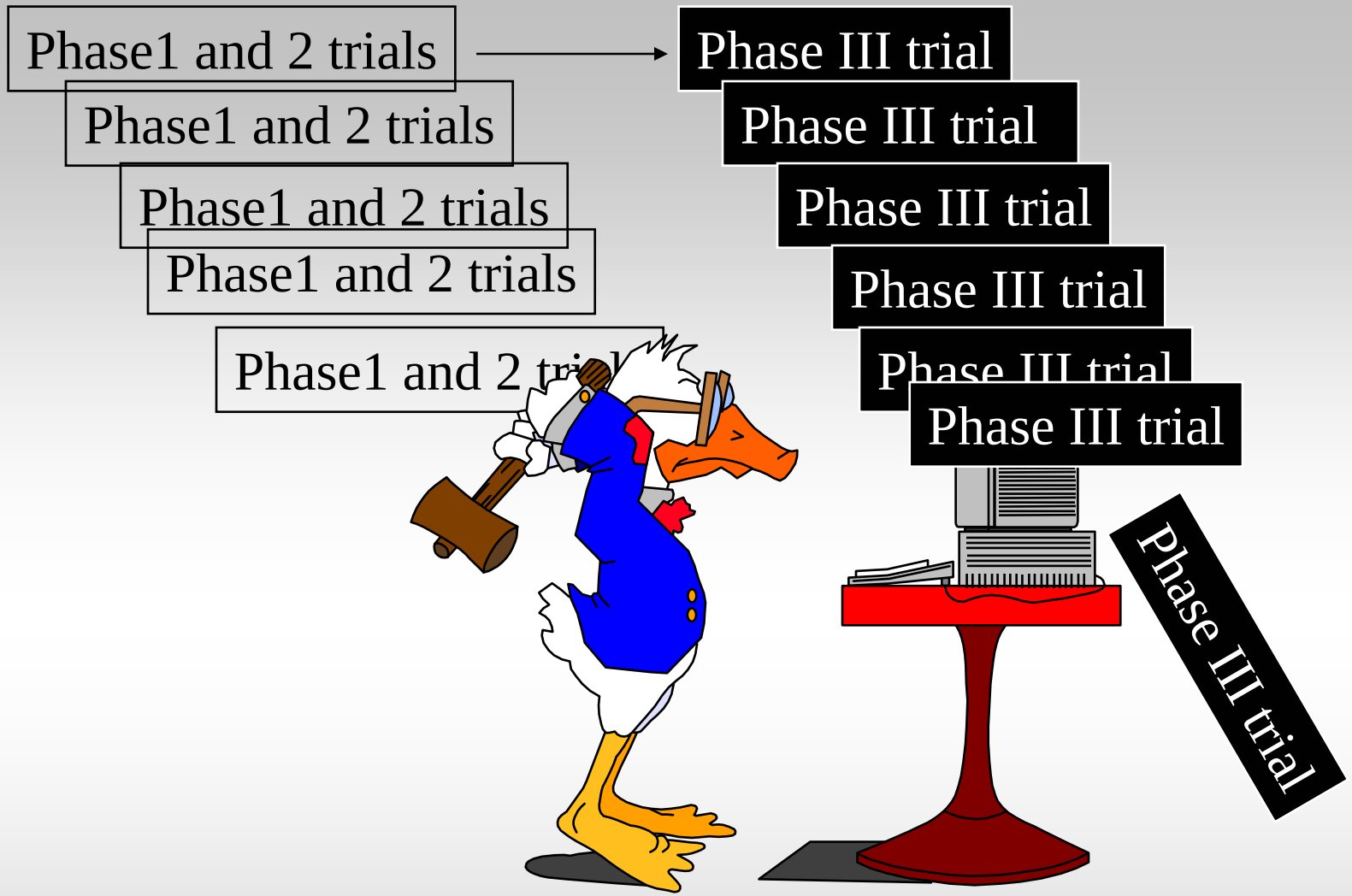
Changing the Paradigm . . .

Use Molecular and Imaging Markers to

- *characterize breast cancer type*
- *predict response to therapy (molecular/imaging)*
- *Validate prediction at 3 weeks by MRI*
- Introduce novel therapeutics for patients with < PR (60% of patients)

We need a new approach to testing new agents in the clinic

Focus on patients at risk for adverse outcome


Phase1 and 2 trials
Phase1 and 2 trials
Phase1 and 2 trials
Phase1 and 2 trials
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Phase III trial
Phase III trial
Phase III trial
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Phase III trial
Phase III trial
Phase III trial

Trials and development of decision support infrastructure

Current Practice

Standard Treatment for All Patients

Future Practice

Tailored Therapies

I-SPY Trial

Ultimately, we need shared decision making tools

to help patients and physicians make decisions together, so both are comfortable with choice of treatment option

ADJUVANT!

Quantitative Estimates of Risk from Your Breast Cancer and Benefits of Therapy

Based on a model by Peter Ravdin MD

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Adjuvant! for Breast Cancer

Patient Information

Age: 68

Comorbidity: Major Prob. (+10)

ER Status: Positive

Tumor Grade: Undefined

Tumor Size: 2.1 - 3.0 cm

Positive Nodes: 0

Calculate For: Mortality

10 Year Risk: 20 Prognostic

Adjuvant Therapy Effectiveness

Horm: Overview 98 (Tamoxifen)

Chemo: Overview 98 (CMF-Like)

Hormonal Therapy: 28

Chemotherapy: 8

Combined Therapy: 34

No additional therapy:

41.2 alive in 10 years.

15.2 die of cancer.

43.6 die of other causes.

With hormonal therapy: Benefit = 3.0 alive.

With chemotherapy: Benefit = 0.8 alive.

With combined therapy: Benefit = 3.6 alive.

Print

Help

Done Internet

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Improving the signal-to-noise ratio

- Decision Analysis
  - Divide and conquer decision into dimensions:
    - Frame, Alternatives, Information, Values
  - Decision tables (pairwise comparisons, look for dominance)

- Adult Learning
  - What are people ready to receive? (Connect to this)
  - Layers of complexity (start simple, detail is optional)

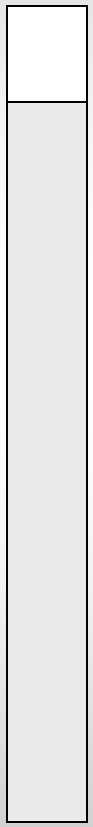
- Cognitive Science (Tufte)
  - Train people on small number of formats, stick to them

- Risk Communication
  - Relative risk presentations are confusing, misleading

Adjuvant - Framing

"90% ten-year survival rate" means that on average, out of 100 women,
90 can be expected to be alive ten years from now
10 can be expected to die.

90%



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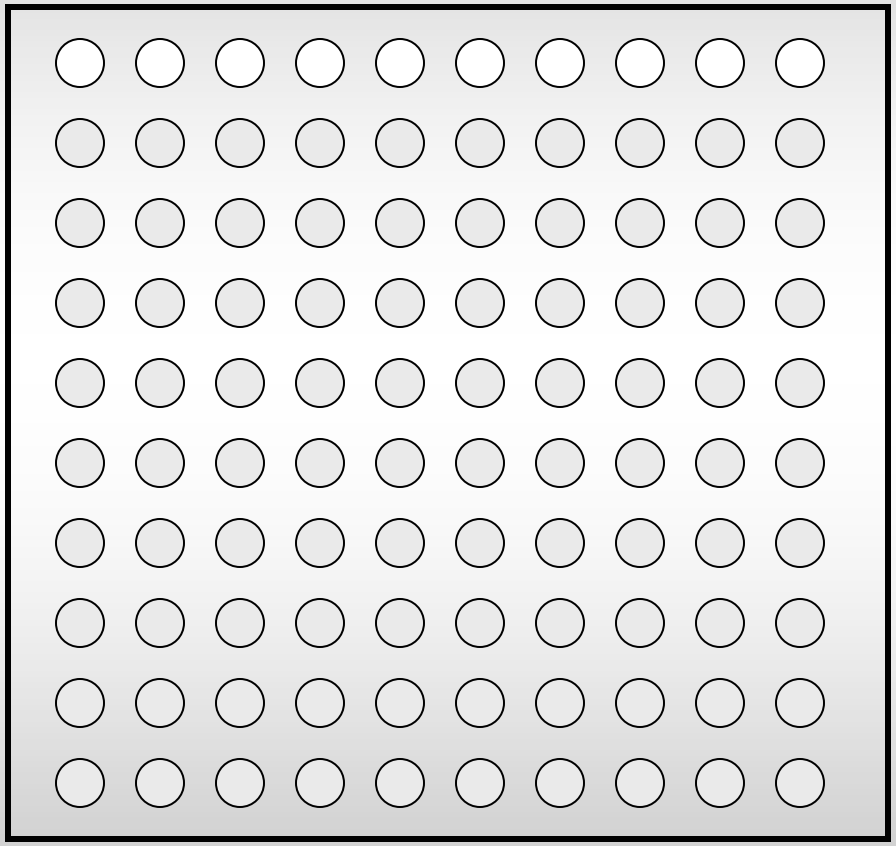


Legend

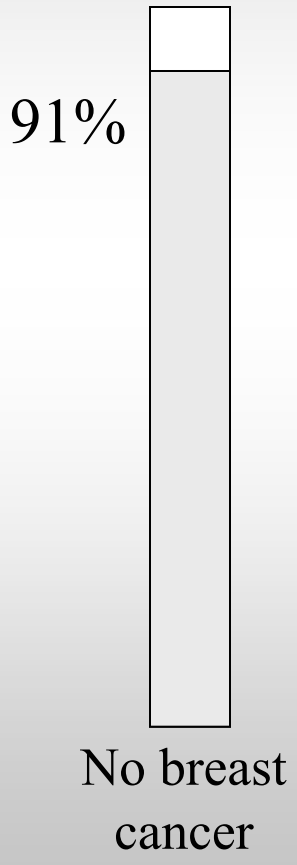
Will be alive at the end of 10 years

Will die some time during the next 10 years

Ten-year survival rates show *how many* women will be alive ten years from now. They do not show *which ones* will be alive or how much longer than ten years these women survive.

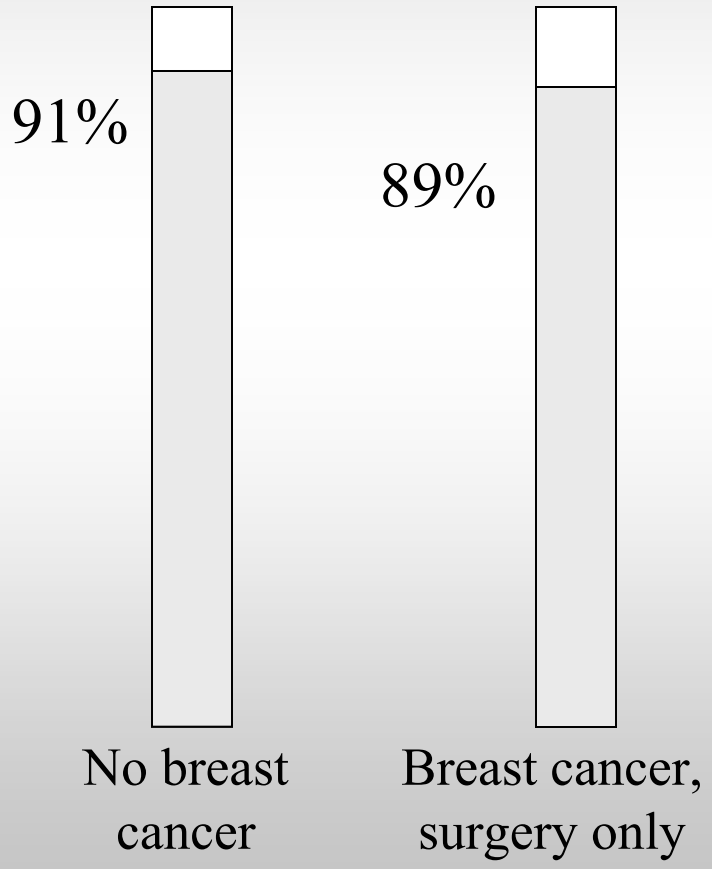
Adjuvant - Baseline

For every 100 women without breast cancer today (otherwise like you)
91 would still be alive in 10 years



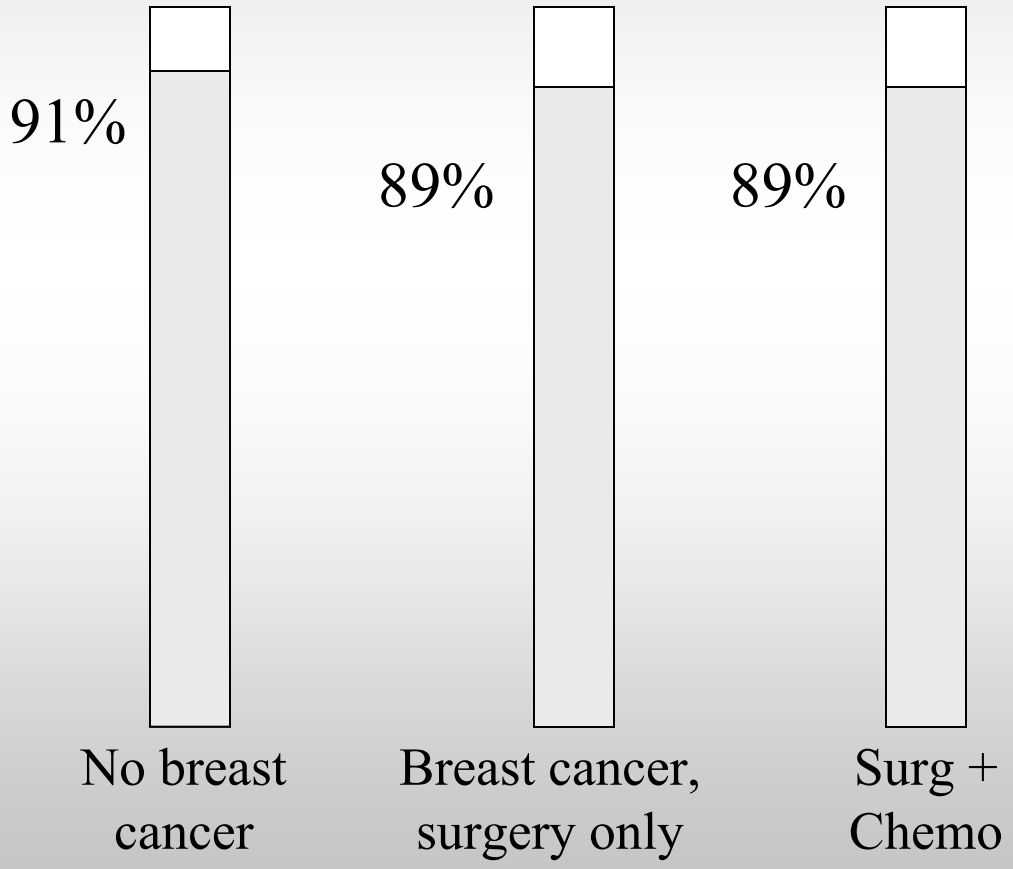
Adjuvant

For every 100 women with breast cancer similar to you, 89 would still be alive in ten years with surgery only



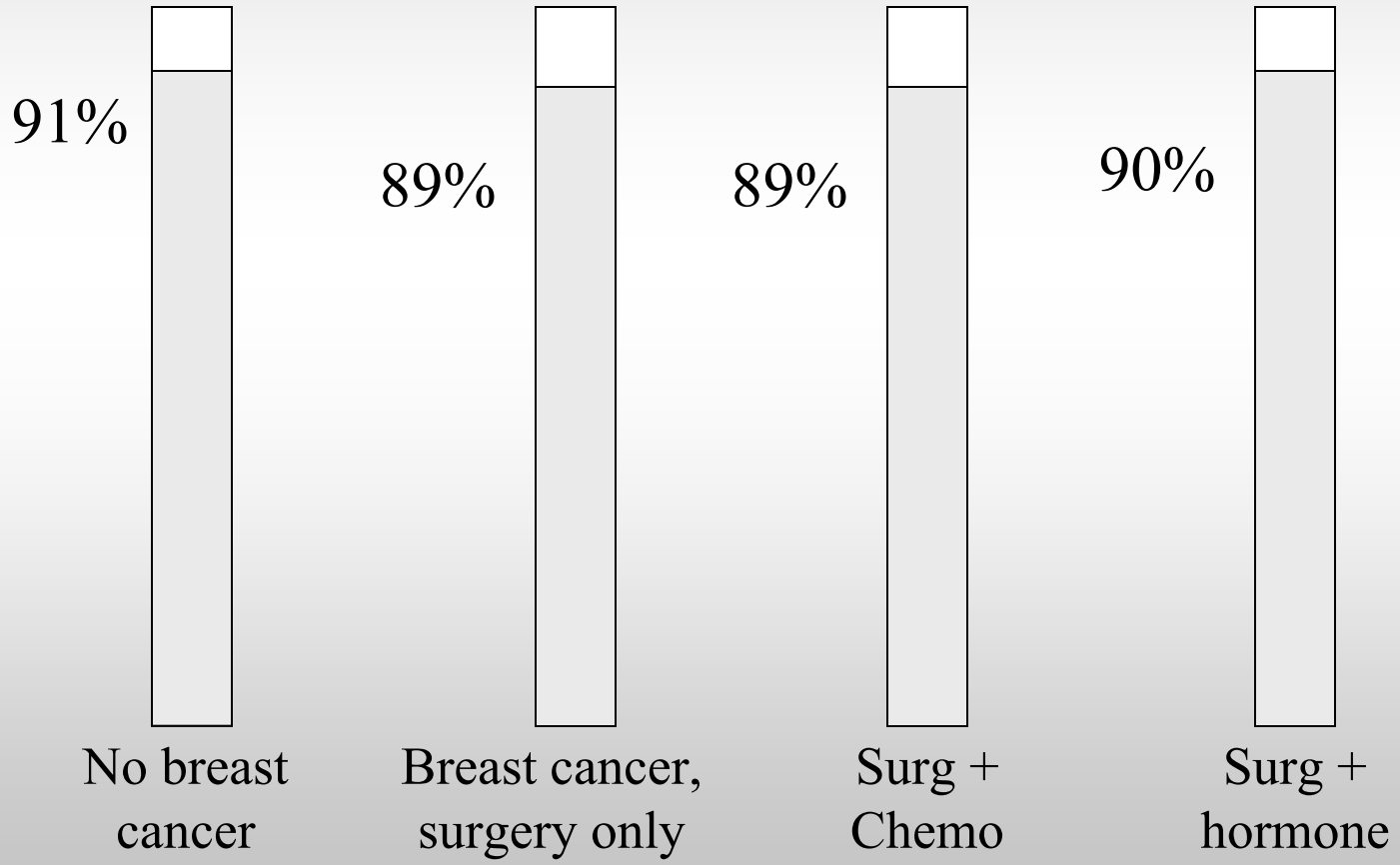
Adjuvant

For every 100 women with breast cancer similar to you,
89 still alive in ten years with surgery alone or surgery plus chemo



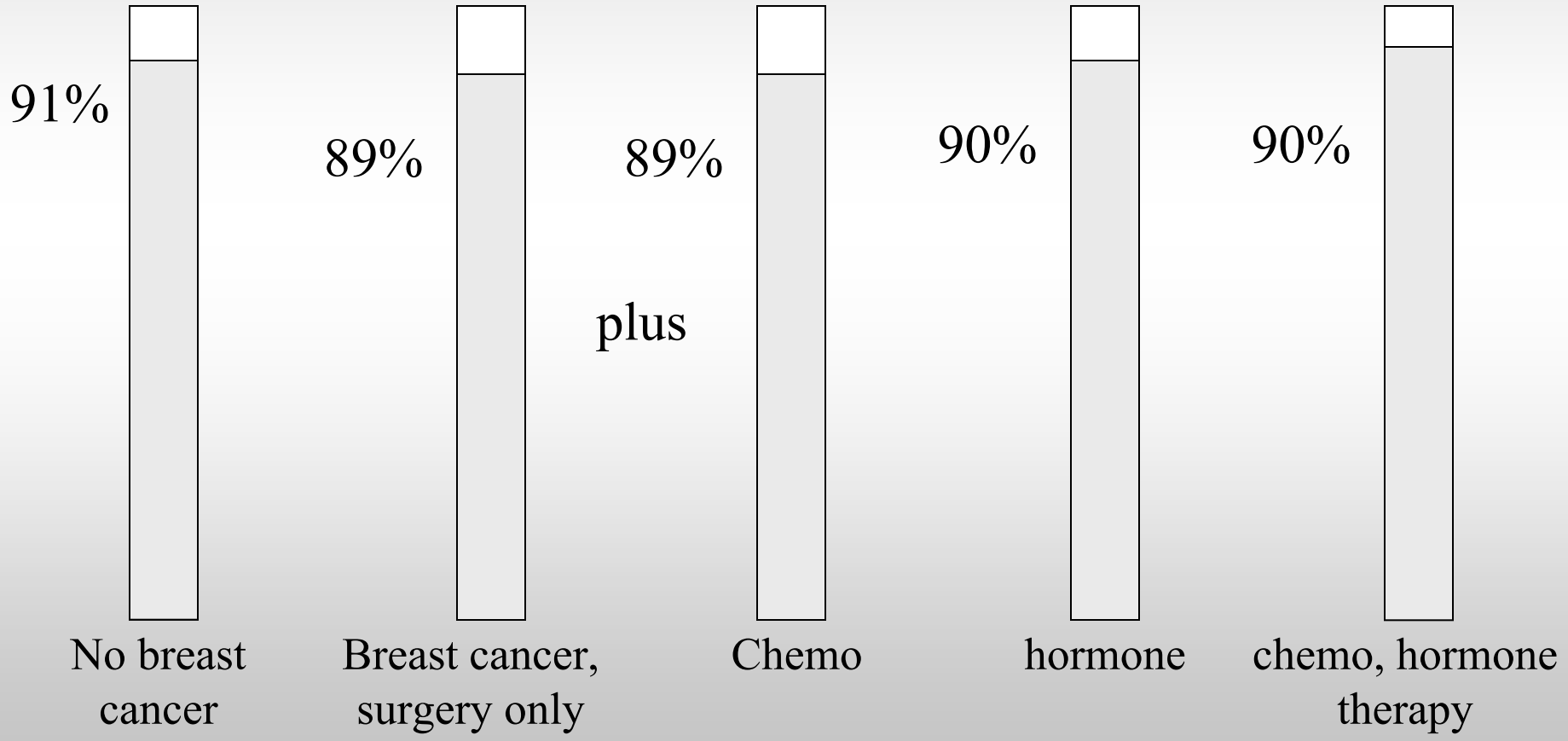
Adjuvant

For every 100 women with breast cancer similar to you,
1 additional woman still alive at 10 years due to surgery + hormone



Adjuvant

For every 100 women with breast cancer similar to you,
1 additional woman still alive at 10 years due to all treatments



Summary Table

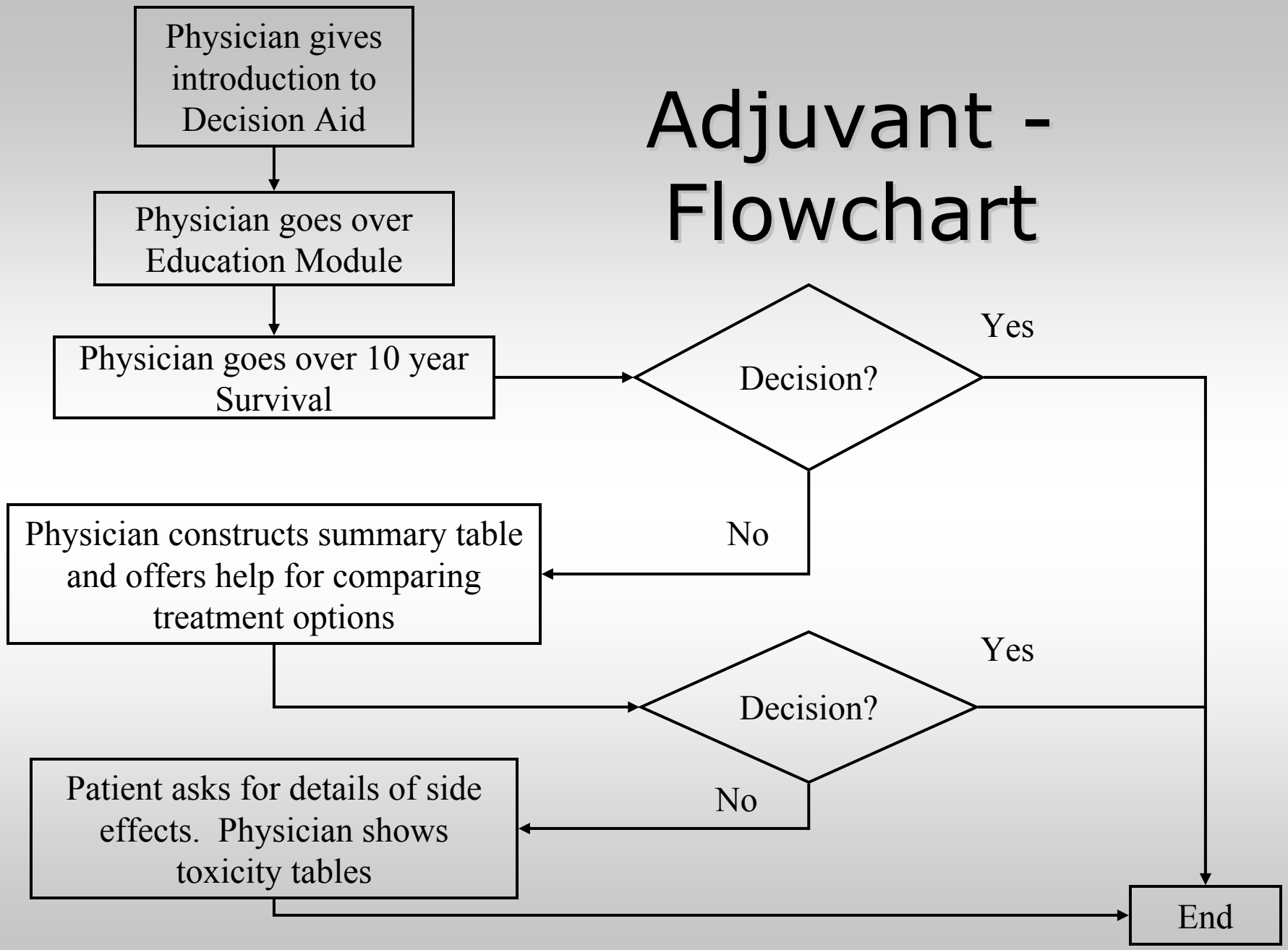
- Qualitative view of risk
  - Rare, low, medium, high
- Type and severity of risk
  - Columns across the top
- Ability to layer detail, drill down

Adjuvant – Summary Detail

High:	50% or greater
Med :	10%-50%
Low :	1%-10%
Rare :	less than 1%
---:	0%

Treatment	Ten year survival rate	Death	Hospitalization	Reduced activity level	Reduced quality of life 1st year	… 2nd year	… 2-5 years
Surgery only	89%						
+ Chemo (AC)	89%	Rare	Low	Rare	High	Rare	---
+ Tam	90%	---	Low	Low	Med	Med	Med
+ Chemo (AC) + Tam	90%	Rare	Med	Low	High	Med	Med

Adjuvant - Flowchart



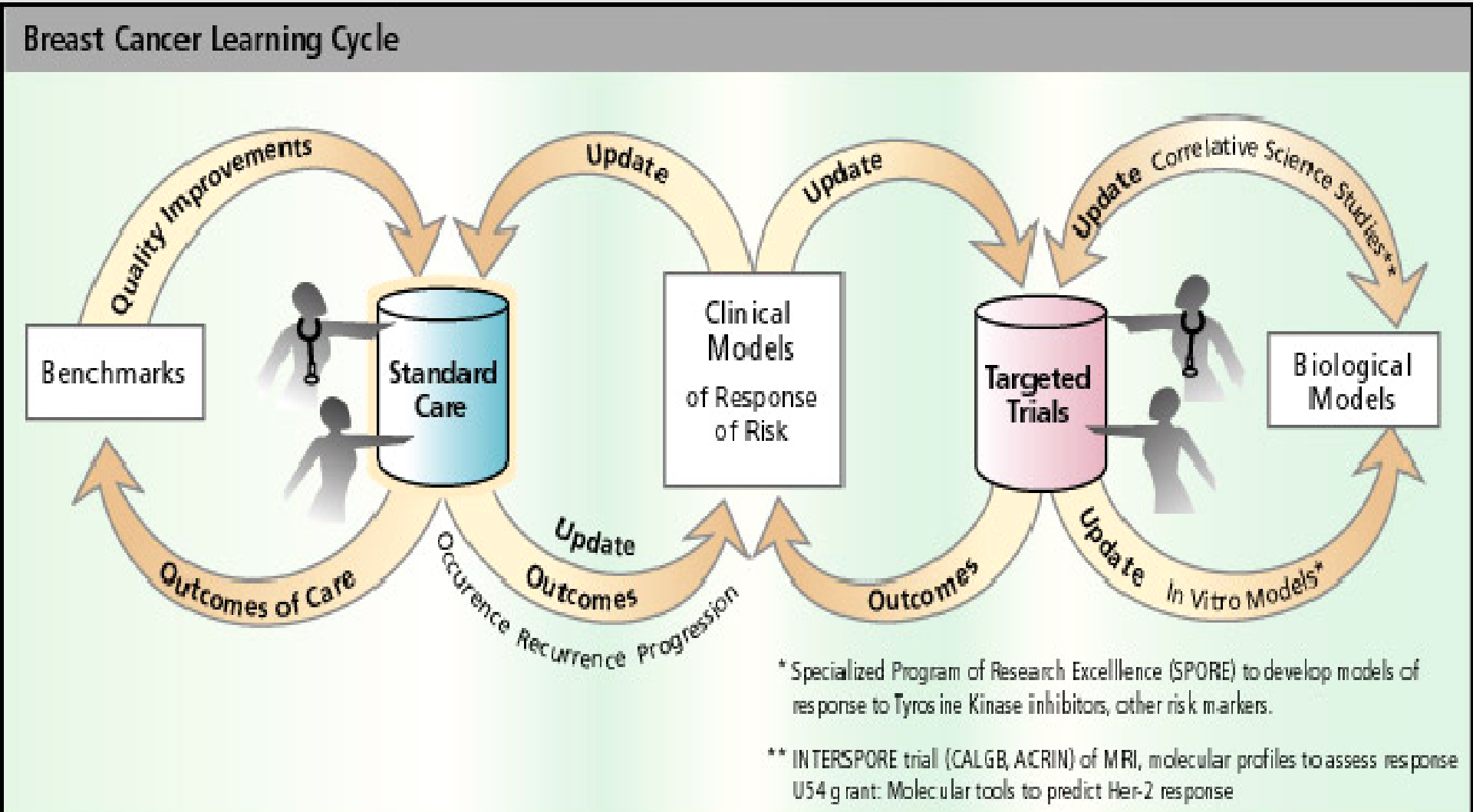
The challenge of Implementing point of care tools

formidable

The Future Will Require Integrated Clinical Systems that Enable Quality Care

- Integrate information across platforms (array, imaging, clinical data)
- Facilitate multidisciplinary communication, collaboration
- Explicitly support the delivery of quality care, and support or enable quality improvement
- Support the availability of critical information, and decision support tools at the point of care

Translation: Integrating Clinical and Research Data



Adjuvant –Tamoxifen Side Effects

Treatment Length: take pill daily for 5 years

Likelihood	Life Impact	Duration	Source	Likelihood
Medium	Reduced quality of life	Treatment	• Vaginal discharge • Hot flashes	• 15 per 100 patients (15%) • 15 per 100 patients (15%)
Low	Hospitalization	A few days	• Blood clots (stroke) • Cataracts (surgery) • Endometrial cancer (hysterectomy)	7 per 100 patients (6.7%)
	Reduced activity level	Recovery from cataract surgery	Cataracts	3 per 100 patients (2.7%)
	Reduced activity level	Long term	Blood clots	3 per 100 patients (2%)
	Reduced quality of life	6+ months after hysterectomy	Endometrial cancer	2 per 100 patients (2%)

Adjuvant – AC Side Effects

Treatment Length: total of 12 weeks = 4 courses x once every 3 weeks

Likelihood	Life Impact	Duration	Source	Likelihood
High	Reduced quality of life	6+ months after end of treatment	• Hair Loss • Fatigue • Muscle/joint pain	• 90 per 100 patients (90%) • 50 per 100 patients (50%) • 5 per 100 patients (5.2%)
High	Reduced quality of life	Treatment	• Nausea • Vomiting • Mouth sores	• 77 per 100 patients (77%)*^ • 43 per 100 patients (43%)*^ • 40 per 100 patients (40%)*
Low	Hospitalization	A few days during treatment	Infection	7 per 100 patients (7%)
Rare	Reduced activity level	Permanent	Heart problems	1 per 100 patients (1%)
Rare	Death	Permanent	Leukemia	2-3 per 1000 patients (0.25%)

*about half of the affected patients have only mild symptoms

^medication to prevent nausea and vomiting is given to all patients

Appendix:

Summary Tables:

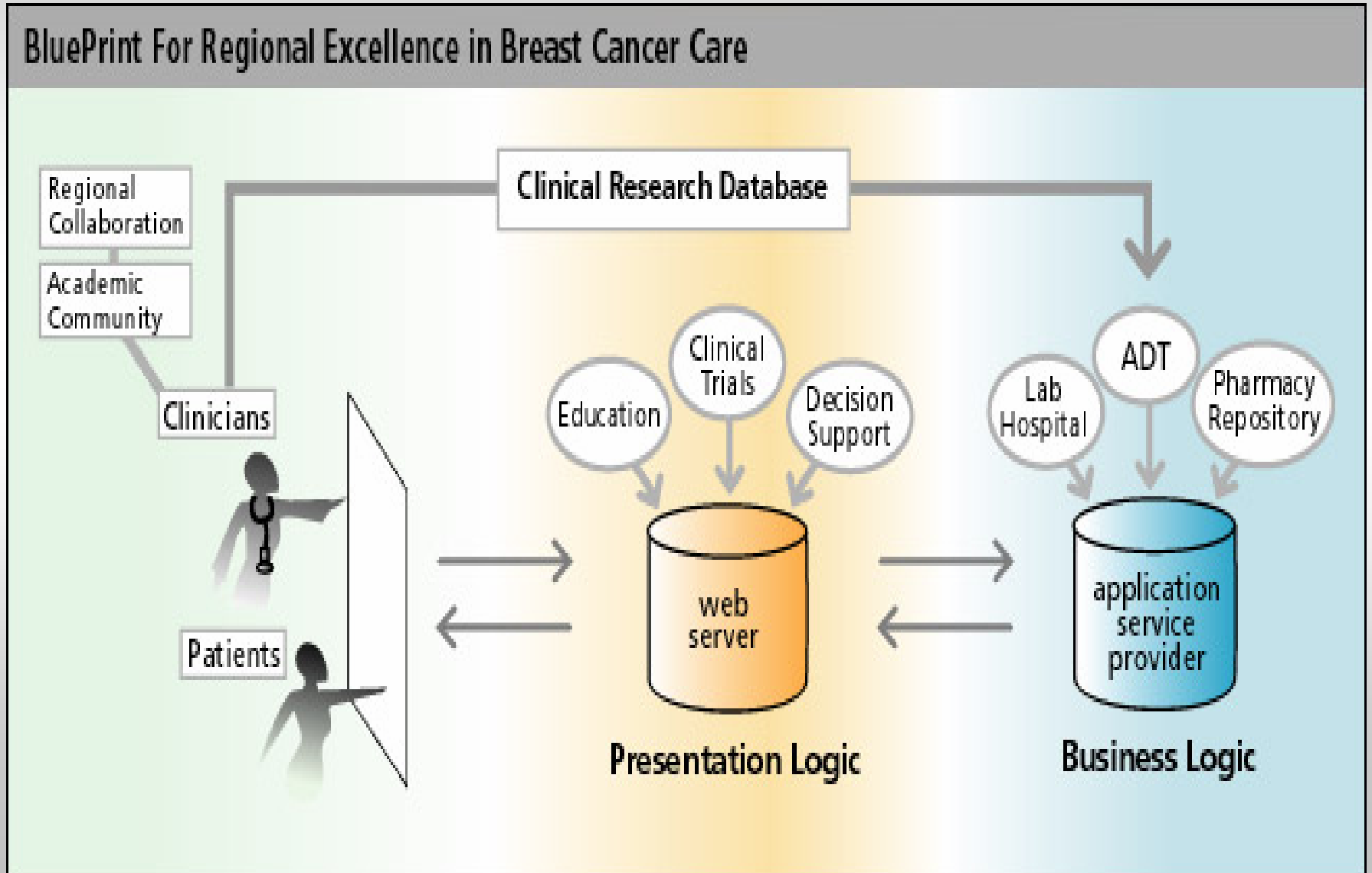
Ages 35-39 AC/ Tam	Ages 40-49 AC/ Tam	Ages 50-59 AC/ Tam	Ages 60-69 AC/ Tam	Ages 70-79 AC/ Tam
Ages 35-39 CMF/ Tam	Ages 40-49 CMF/ Tam	Ages 50-59 CMF/ Tam	Ages 60-69 CMF/ Tam	Ages 70-79 CMF/ Tam
		Ages 50-59 AC/ AI	Ages 60-69 AC/ AI	Ages 70-79 AC/ AI
		Ages 50-59 CMF/ AI	Ages 60-69 CMF/ AI	Ages 70-79 CMF/ AI

Toxicity Tables:

AC				
CMF				
Tam (ages 35-39)	Tam (ages 40-49)	Tam (ages 50-59)	Tam (ages 60-69)	Tam (ages 70-79)
AI				

Point of Care Systems

acurate data capture
decision support



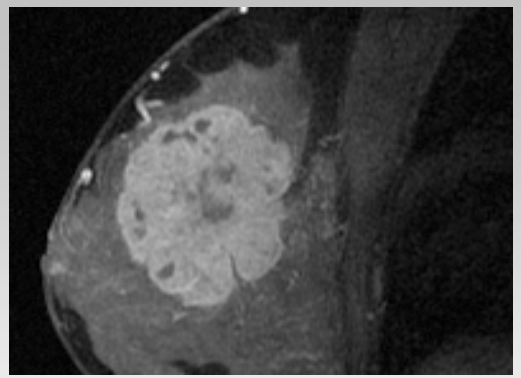
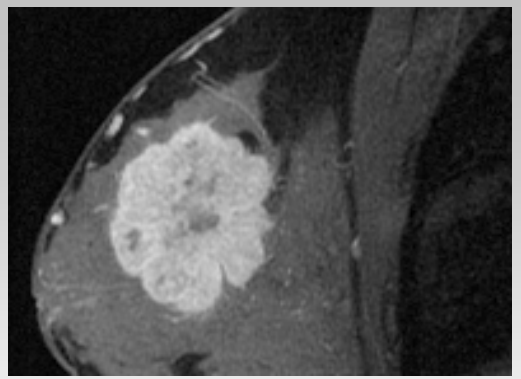
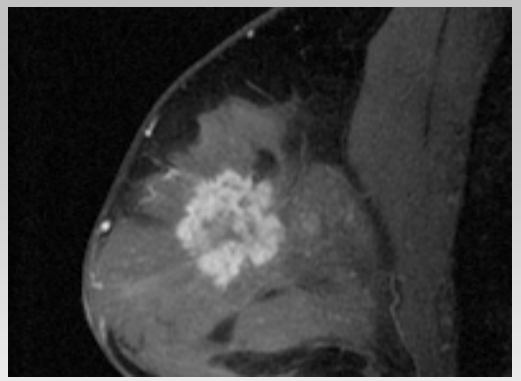

BREAST CANCER
I SPY TRIAL
BREAST CANCER
I SPY TRIAL

. . . and Ethnically Diverse

- Diverse Population
  - Caucasian: 65%
  - Hispanic: 9%
  - African American: 14%
  - Asian: 6%
  - Native American: 1%
- Younger Age Distribution
  - <40: 19%
  - 40-49: 37%
  - 50-59: 33
  - >65: 11%

Tissue Acquisition

- 16 gauge cores
  - 2 frozen
  - 2 paraffin
- Touch preps to assess adequacy
- Additional core for H&E, markers if diagnosis made by FNA, mammo, exam
- Careful correlation of MR findings and final pathology at time of surgical resection

All Roads to Tailored Therapy for Breast Cancer Lead through the Neoadjuvant Paradigm