Health Insurance Portability and Accountability Act (HIPAA) & the Use of Tissue

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How are HIPAA and tissues related?

- Human tissues are critical to translation of research results to the clinic
- Tissue micro-arrays provide large numbers of specimens on a single slide
- Regulations impact our ability to study tissues

Breakthroughs dependent on specimens

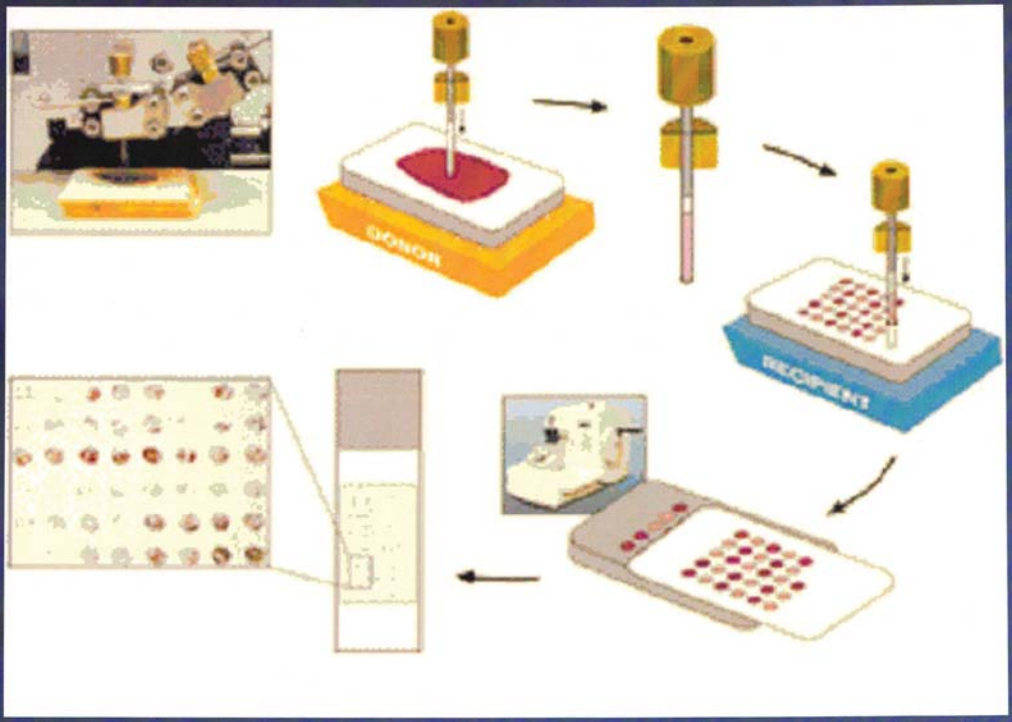
- Targeted therapies
  - Herceptin
  - Gleevec
- New tumor classifications
  - Comprehensive molecular analyses
- Pathway analysis
  - Pharmacogenomics

Breakthroughs dependent on specimens

- Hypothesis generation
  - Model systems
  - Cell lines
- Hypothesis testing
  - Tumors

What is a Tissue Microarray (TMA)?

Tissue microarray construction



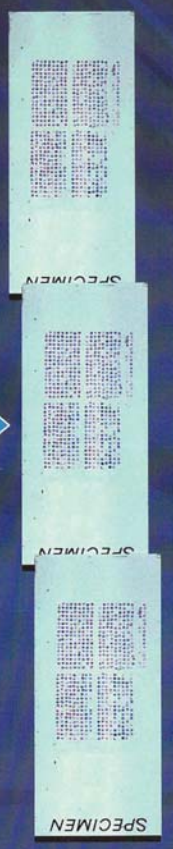
Tumor analysis with tissue microarrays (TMAs)

Tissue Block

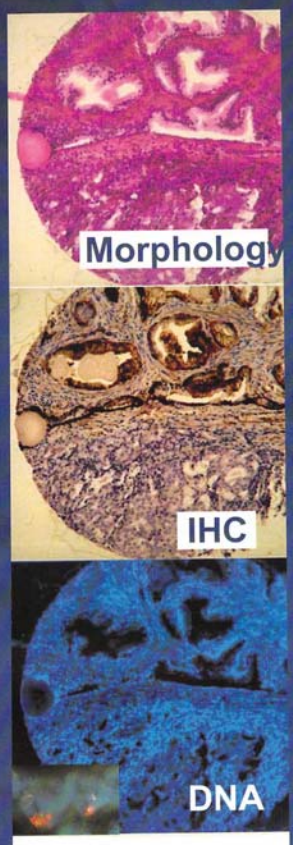
Hundreds of blocks, one case per block.

TMA Block

One block, hundreds of cases per block.



Cut TMA block into multiple slides.



Uses for tissue microarrays

- Estimate/compare prevalence of markers
  - Tumor marker prevalence across stage groups
  - Prevalence of a gene sequence across species
- Examine associations between markers
  - Coordinated expression of two proteins/genes
- Examine association between marker and time-to-event
  - Does tumor marker predict time to relapse?
  - Does marker predict risk of recurrence or death?

TMA designs can be tailored to meet different needs

- Multiple cores per case
  - To account for cellular and marker heterogeneity
- Arrangement of cores on array
  - To avoid regional effects
- Controls built in
  - Positive and negative for standard markers
  - Fixation & handling controls

CBCTR breast cancer progression TMA

Two TMAs were created, each one composed of non-overlapping sets of specimens.

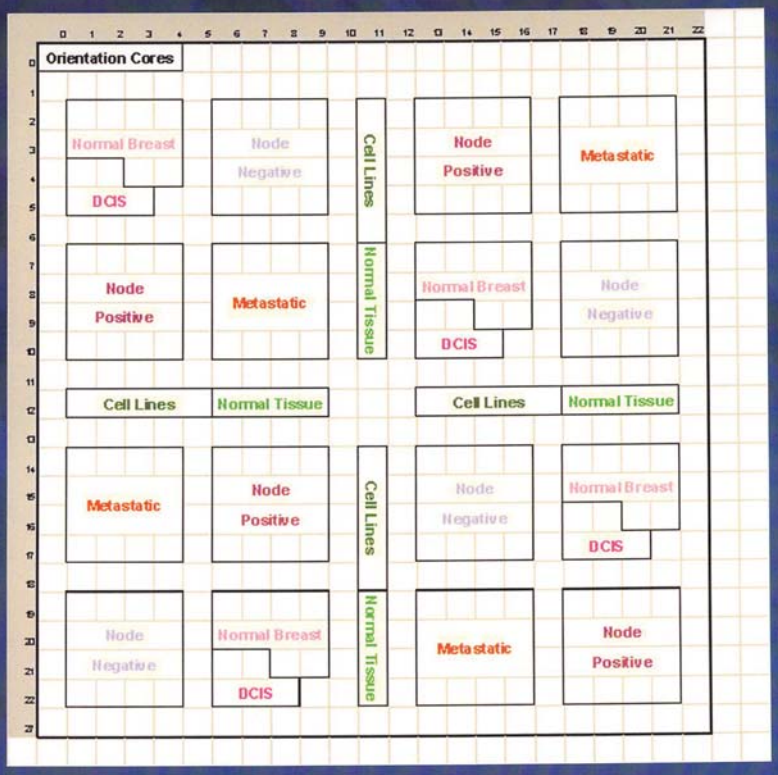
Each TMA was made in quadruplicate.

288 0.6 mm cores/TMA block.

- 20 Normal Breast Specimens
- 20 Normal Breast Adjacent to Invasive Cancer (Matched)
- 20 DCIS Specimens
- 64 Node Negative Specimens
- 64 Node Positive Specimens
- 64 Metastatic Specimens
- 16 Normal Non-Breast Controls
- 20 Cell Line Controls

Difference in prevalence rates detectable with 80% statistical power:

Comparison	1 TMA	2 TMAs
node–/node+	~ 0.24	~ 0.17
normal/invasive (matched)	~ 0.35	~ 0.25



Summary

- TMAs allow parsimonious use of specimens
- TMAs allow efficient studies of biomarkers
- TMAs can be designed to test different hypotheses

Tissue Microarrays and the Impact of Regulations

The privacy rule

- Health Insurance Portability and Accountability Act of 1996 (HIPAA)
- April 14, 2003
- Covered entity
- Protected health information (PHI)
- Authorization

HIPAA versus common rule

- **Common Rule**
  - Only covers federally funded research
  - Protects Human Subjects
  - Focus on reducing risks
  - Requires Consent
  - Sets requirements for IRB review/exemption
  - May apply to research on de-identified data
- **HIPAA Privacy Rule**
  - Applies to all 'covered entities'
  - Use/Disclosure of PHI
  - Requires Authorization
  - Sets requirements for waiver of authorization
  - May apply to research exempt from common rule

Specimens and data In a pre-HIPAA world

- Common Rule
  - IRB approval for "research"
  - Use of anonymous data is not "human subjects research"
  - Research on existing unidentified data may be exempt

Specimens and data in a post-HIPAA world

- Grandfathered
  - Existing studies with consent or waiver before April 14, 2003
- Authorized
  - Patient permission to use data

Specimens and data in a post-HIPAA world

- Waiver
  - IRB or privacy board
- De-identified
  - Remove 18 specified identifiers
- Limited Data Set
  - Remove 16 specified identifers with signed data use agreement
    - Can keep dates and some geographic data (e.g. Zip code)

Issues to consider: de-identification

- Can codes be retained in a HIPAA de-identified dataset?
  - Yes, but
    - Can't include any elements of HIPAA identifiers

Issues to consider: exempt research

- No exempt category under HIPAA
- Different standards for identifiable
  - HIPAA
    - 18 identifiers
  - Common Rule
    - Existing specimens and/or data
    - Recorded in a way subjects cannot be identified directly or through identifiers linked to the subjects

Issues to consider: exempt research

- Does the Privacy rule apply to data that is exempt under the Common Rule (45 CFR 46)?
  - It may if any HIPAA identifiers are included
    - Dates
    - Zipcodes

Issues to consider: use and disclosure of data

- Can researchers receive patient data (PHI) under the privacy rule?
  - Yes, using
    - Authorization
    - any other approach permitted for covered entities.

Implications for using tissue microarrays

- More complicated but possible
  - Authorization impractical
  - Data issues more complicated
    - Dates as identifiers
  - Best solutions
    - Limited data set with data use agreement
    - De-identified if dates not needed