Practical Aspects of CAD Research

Assessment Methodologies for CAD

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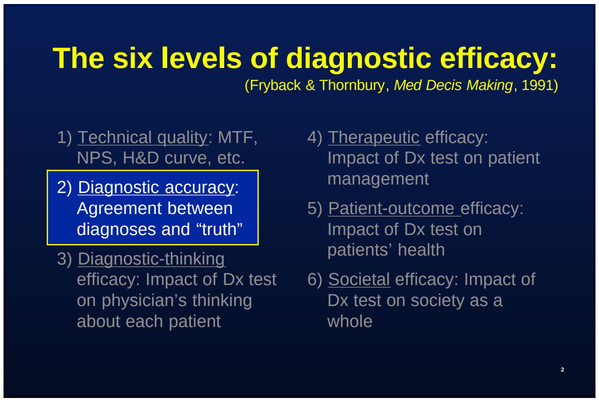


The six levels of diagnostic efficacy:

(Fryback & Thornbury, *Med Decis Making*, 1991)

1) Technical quality: MTF, NPS, H&D curve, etc.

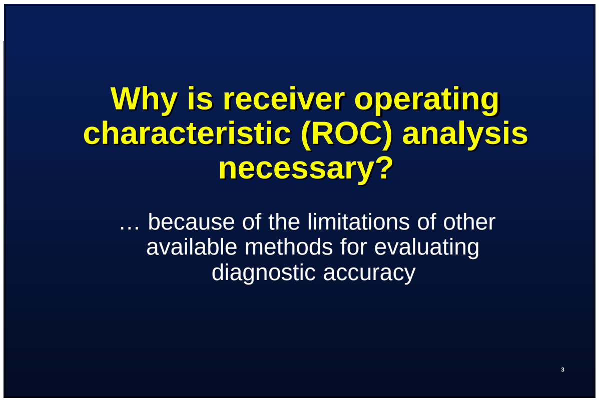
2) Diagnostic accuracy: Agreement between diagnoses and "truth"

3) Diagnostic-thinking efficacy: Impact of Dx test on physician's thinking about each patient

4) Therapeutic efficacy: Impact of Dx test on patient management

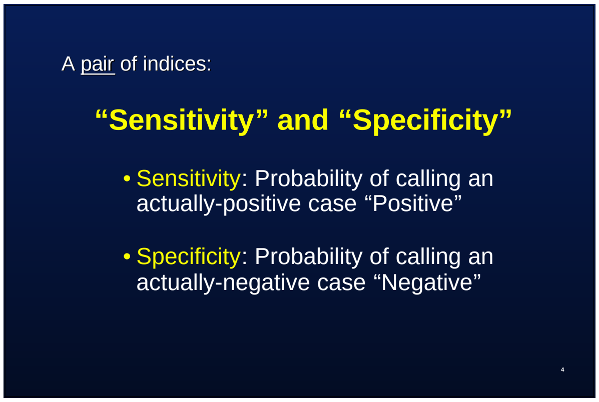
5) Patient-outcome efficacy: Impact of Dx test on patients' health

6) Societal efficacy: Impact of Dx test on society as a whole



Why is receiver operating characteristic (ROC) analysis necessary?

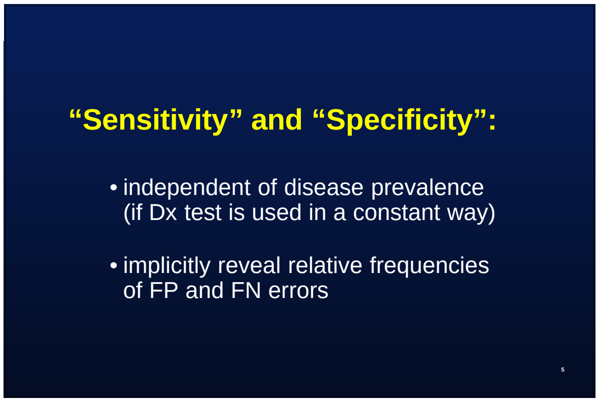
… because of the limitations of other available methods for evaluating diagnostic accuracy



A pair of indices:

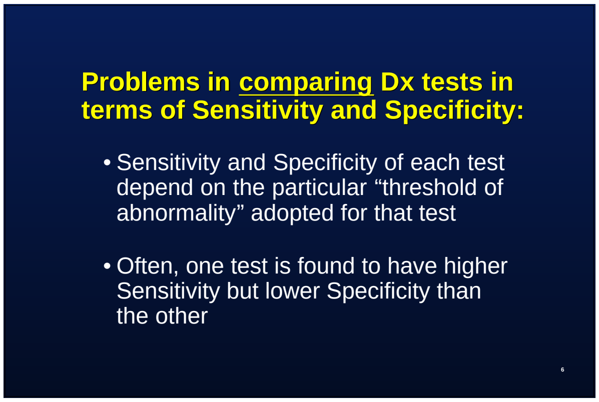
"Sensitivity" and "Specificity"

- Sensitivity: Probability of calling an actually-positive case "Positive"
- Specificity: Probability of calling an actually-negative case "Negative"



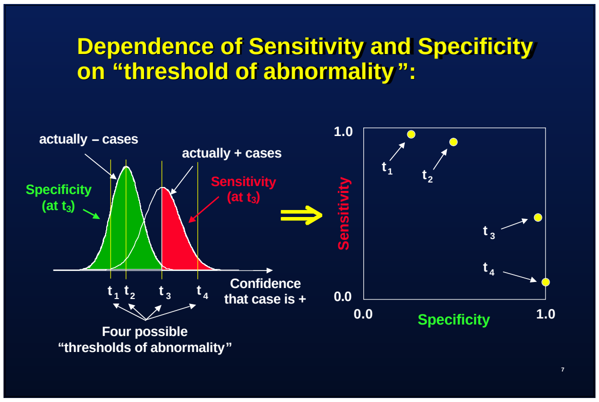
"Sensitivity" and "Specificity":

- independent of disease prevalence (if Dx test is used in a constant way)
- implicitly reveal relative frequencies of FP and FN errors

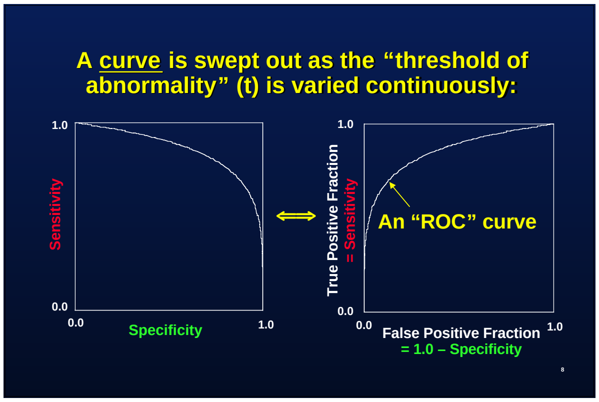


Problems in comparing Dx tests in terms of Sensitivity and Specificity:

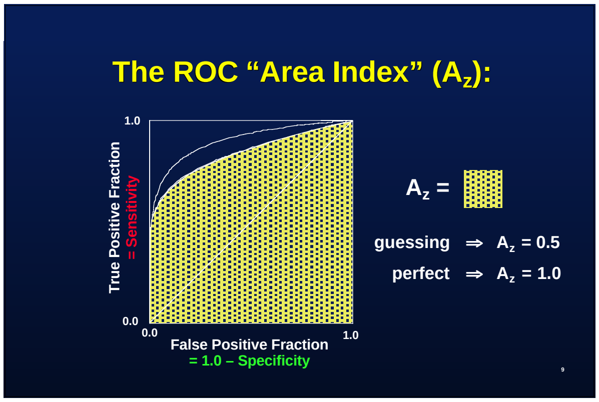
- Sensitivity and Specificity of each test depend on the particular "threshold of abnormality" adopted for that test
- Often, one test is found to have higher Sensitivity but lower Specificity than the other



Dependence of Sensitivity and Specificity on "threshold of abnormality":



A curve is swept out as the "threshold of abnormality" (t) is varied continuously:



The ROC "Area Index" (A_z):

A_z = ▨

guessing ⇒ $A_z = 0.5$

perfect ⇒ $A_z = 1.0$

Interpretations of ROC area (A_z):

- Sensitivity (TPF) averaged over all Specificities (or FPFs) — i.e., average ROC curve height
- Specificity averaged over all Sensitivities
- Probability of distinguishing correctly between a randomly selected actually-positive case and a randomly selected actually-negative case

However ...

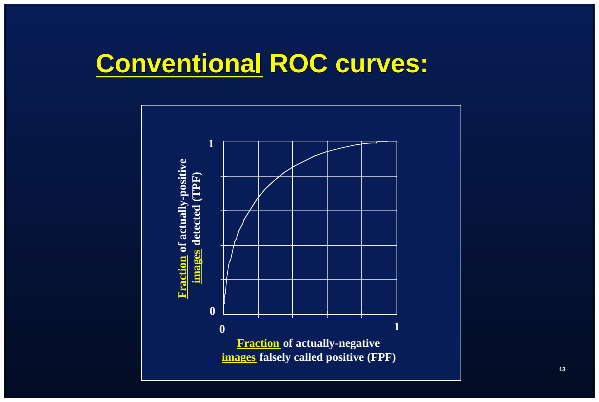
- this global index can be misleading when curves cross and/or there is only one region of interest

Other ROC-based indices of performance

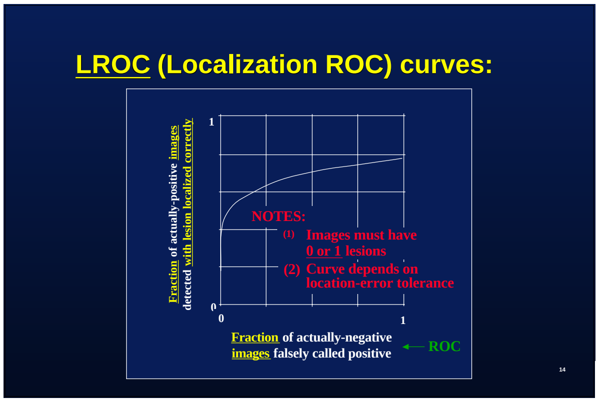
- Partial area below, or to the right of, a segment of the ROC curve (regional)
- TPF at fixed FPF or vice-versa (local)
- Expected utility at optimal operating point (local) — most meaningful but least practical

Generalized ROC analysis :

- Localization ROC (LROC) analysis
- Free-response ROC (FROC) analysis
- Alternative FROC (AFROC) analysis

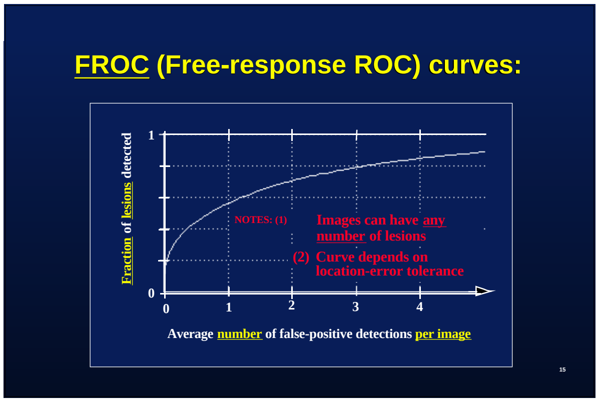


Conventional ROC curves:



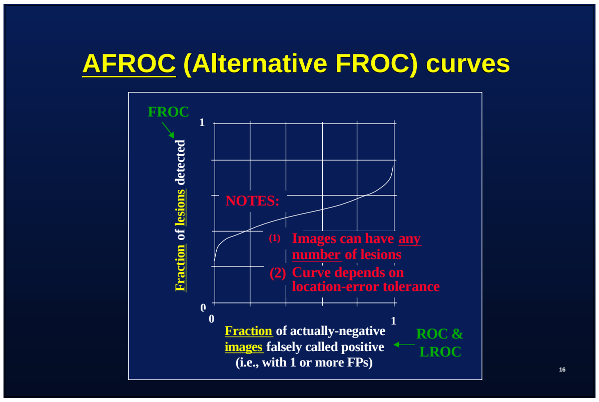
LROC (Localization ROC) curves:

NOTES:
(1) Images must have 0 or 1 lesions
(2) Curve depends on location-error tolerance



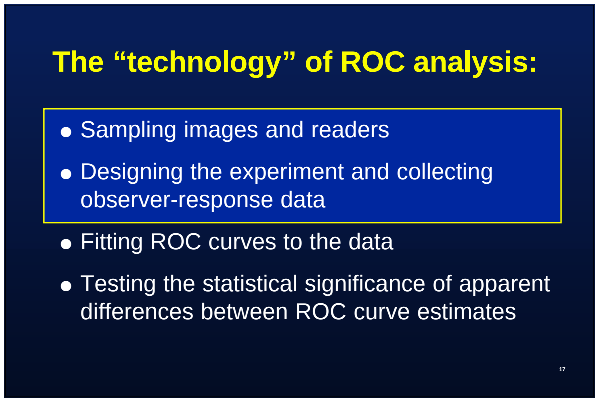
FROC (Free-response ROC) curves:

NOTES: (1) Images can have any number of lesions
(2) Curve depends on location-error tolerance



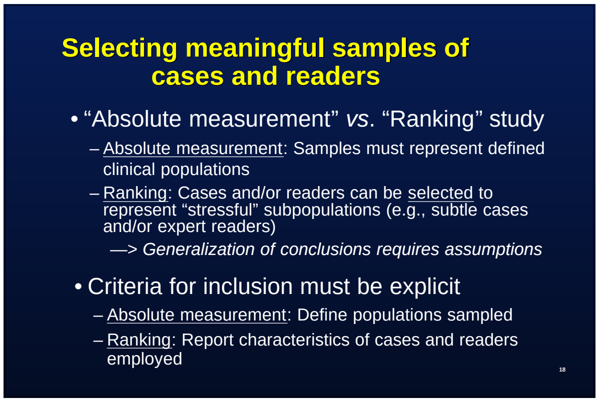
AFROC (Alternative FROC) curves

NOTES:
(1) Images can have any number of lesions
(2) Curve depends on location-error tolerance



The "technology" of ROC analysis:

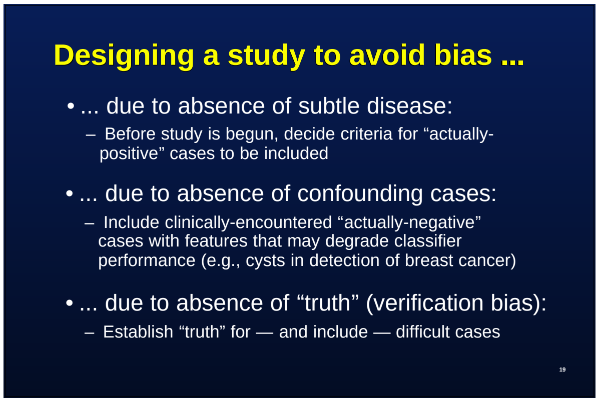
- Sampling images and readers
- Designing the experiment and collecting observer-response data
- Fitting ROC curves to the data
- Testing the statistical significance of apparent differences between ROC curve estimates



Selecting meaningful samples of cases and readers

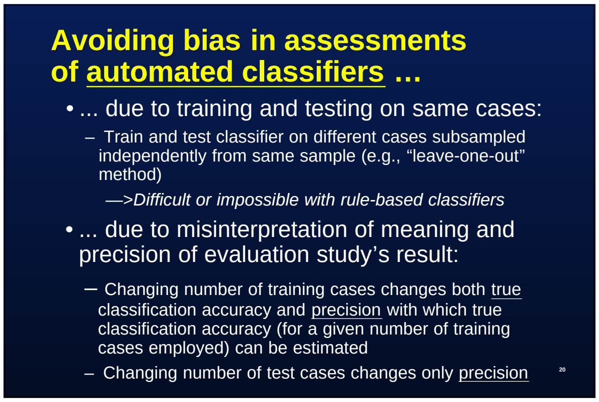
- "Absolute measurement" *vs*. "Ranking" study
  - Absolute measurement: Samples must represent defined clinical populations
  - Ranking: Cases and/or readers can be selected to represent "stressful" subpopulations (e.g., subtle cases and/or expert readers)

    —> Generalization of conclusions requires assumptions
- Criteria for inclusion must be explicit
  - Absolute measurement: Define populations sampled
  - Ranking: Report characteristics of cases and readers employed



Designing a study to avoid bias ...

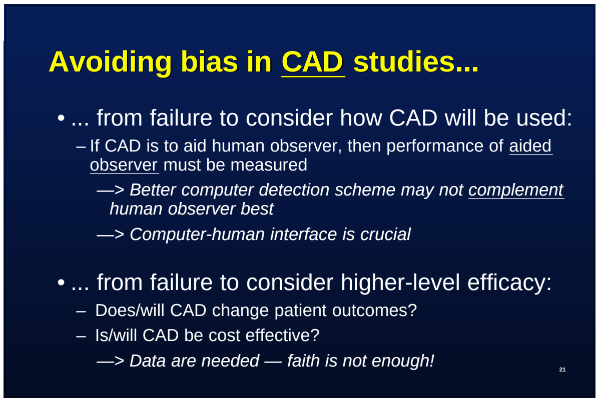
- ... due to absence of subtle disease:
  - Before study is begun, decide criteria for “actually-positive” cases to be included
- ... due to absence of confounding cases:
  - Include clinically-encountered “actually-negative” cases with features that may degrade classifier performance (e.g., cysts in detection of breast cancer)
- ... due to absence of “truth” (verification bias):
  - Establish “truth” for — and include — difficult cases



Avoiding bias in assessments of automated classifiers …

- ... due to training and testing on same cases:
  - Train and test classifier on different cases subsampled independently from same sample (e.g., “leave-one-out” method)

    —>Difficult or impossible with rule-based classifiers
- ... due to misinterpretation of meaning and precision of evaluation study’s result:
  - Changing number of training cases changes both true classification accuracy and precision with which true classification accuracy (for a given number of training cases employed) can be estimated
  - Changing number of test cases changes only precision



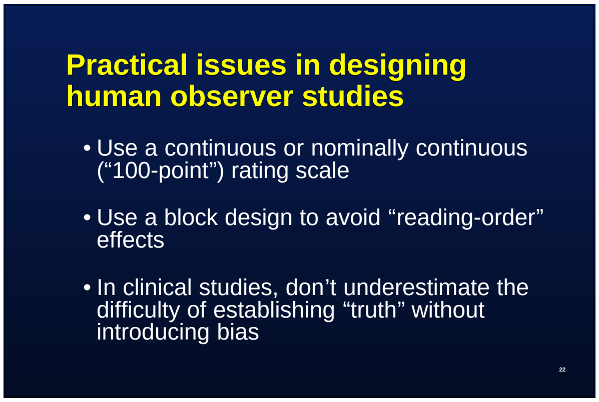
Avoiding bias in CAD studies...

- ... from failure to consider how CAD will be used:
  - If CAD is to aid human observer, then performance of aided observer must be measured

    —> Better computer detection scheme may not complement human observer best

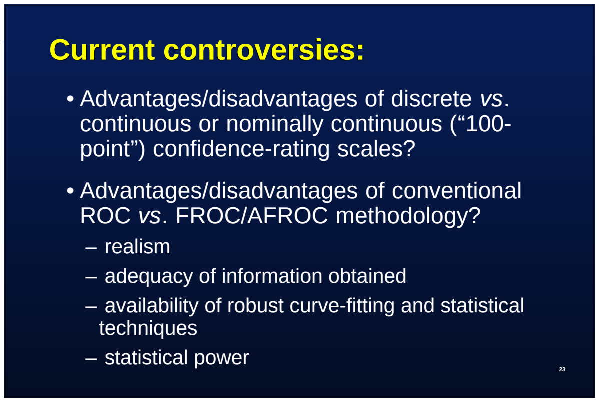
    —> Computer-human interface is crucial
- ... from failure to consider higher-level efficacy:
  - Does/will CAD change patient outcomes?
  - Is/will CAD be cost effective?

    —> Data are needed — faith is not enough!



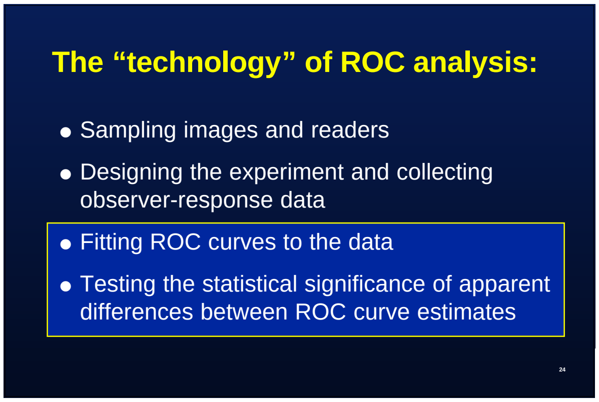
Practical issues in designing human observer studies

- Use a continuous or nominally continuous (“100-point”) rating scale
- Use a block design to avoid “reading-order” effects
- In clinical studies, don’t underestimate the difficulty of establishing “truth” without introducing bias



Current controversies:

- Advantages/disadvantages of discrete *vs*. continuous or nominally continuous (“100-point”) confidence-rating scales?
- Advantages/disadvantages of conventional ROC *vs*. FROC/AFROC methodology?
  - realism
  - adequacy of information obtained
  - availability of robust curve-fitting and statistical techniques
  - statistical power



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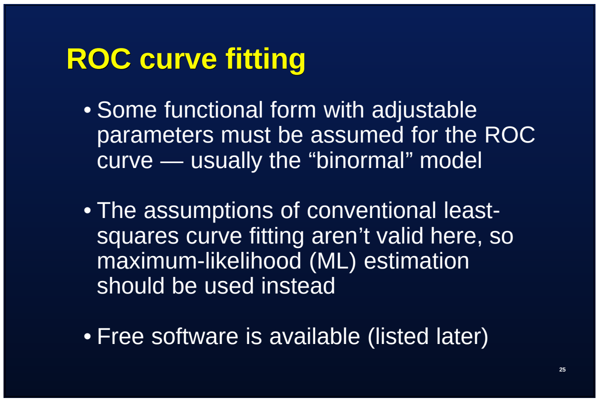
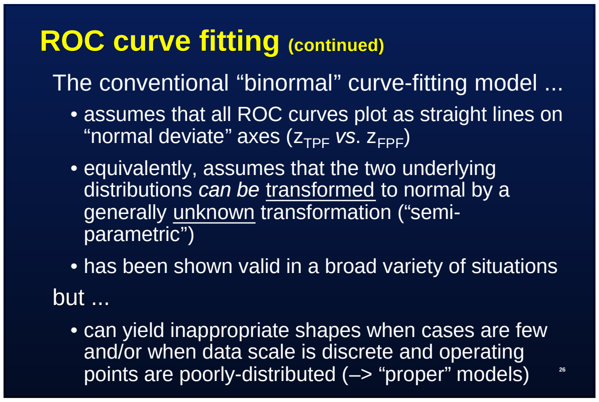


ROC curve fitting

- Some functional form with adjustable parameters must be assumed for the ROC curve — usually the “binormal” model
- The assumptions of conventional least-squares curve fitting aren’t valid here, so maximum-likelihood (ML) estimation should be used instead
- Free software is available (listed later)



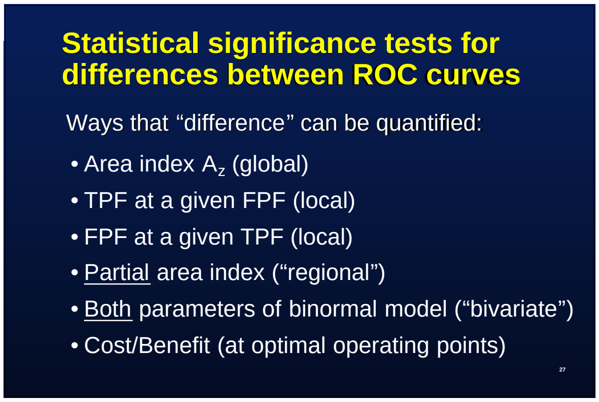
ROC curve fitting (continued)

The conventional “binormal” curve-fitting model ...

- assumes that all ROC curves plot as straight lines on “normal deviate” axes (z_{TPF} *vs.* z_{FPF})
- equivalently, assumes that the two underlying distributions *can be* transformed to normal by a generally unknown transformation (“semi-parametric”)
- has been shown valid in a broad variety of situations

but ...

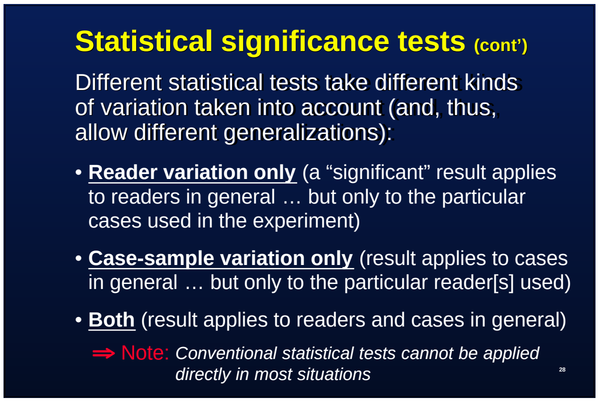
- can yield inappropriate shapes when cases are few and/or when data scale is discrete and operating points are poorly-distributed (–> “proper” models)



Statistical significance tests for differences between ROC curves

Ways that “difference” can be quantified:

- Area index A_z (global)
- TPF at a given FPF (local)
- FPF at a given TPF (local)
- Partial area index (“regional”)
- Both parameters of binormal model (“bivariate”)
- Cost/Benefit (at optimal operating points)

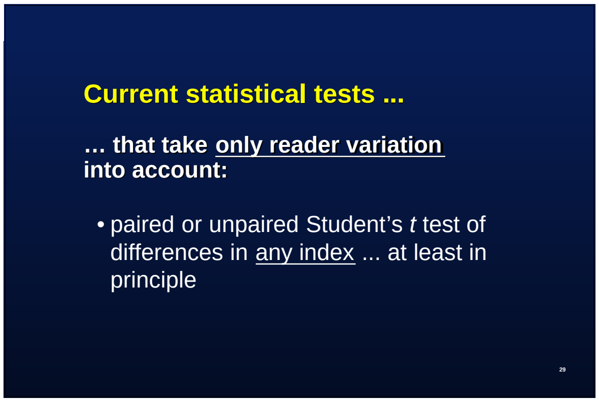


Statistical significance tests (cont’)

Different statistical tests take different kinds of variation taken into account (and, thus, allow different generalizations):

- **Reader variation only** (a “significant” result applies to readers in general … but only to the particular cases used in the experiment)
- **Case-sample variation only** (result applies to cases in general … but only to the particular reader[s] used)
- **Both** (result applies to readers and cases in general)

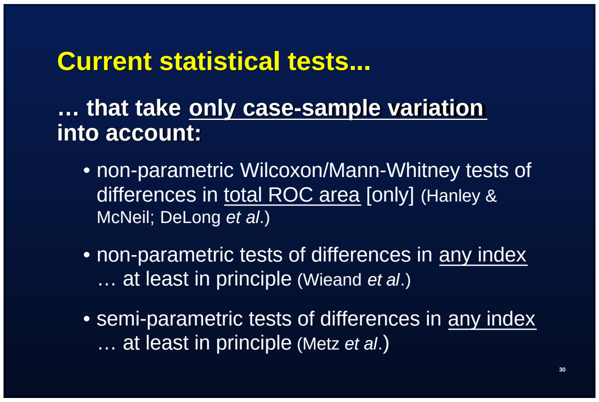
⇒ Note: *Conventional statistical tests cannot be applied directly in most situations*



Current statistical tests ...

… that take only reader variation into account:

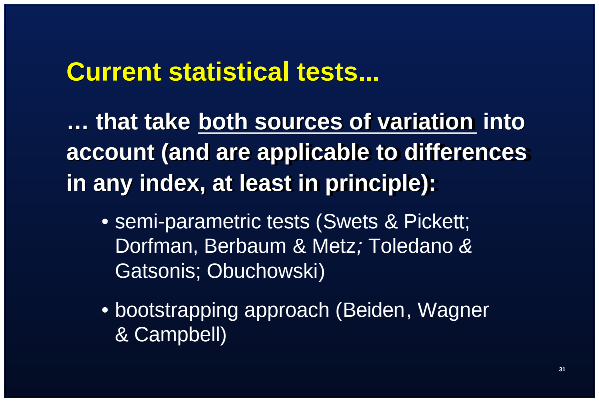
- paired or unpaired Student’s *t* test of differences in any index ... at least in principle



Current statistical tests...

… that take only case-sample variation into account:

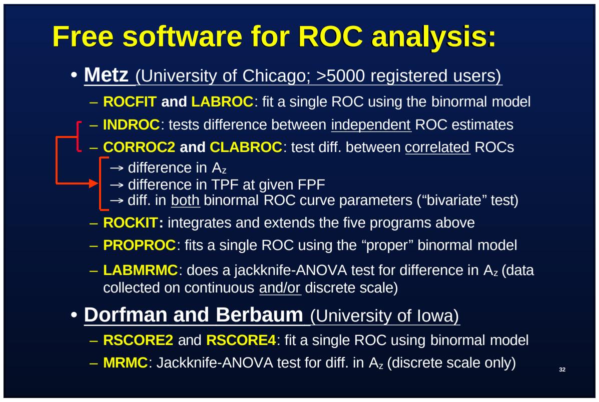
- non-parametric Wilcoxon/Mann-Whitney tests of differences in total ROC area [only] (Hanley & McNeil; DeLong *et al.*)
- non-parametric tests of differences in any index … at least in principle (Wieand *et al.*)
- semi-parametric tests of differences in any index … at least in principle (Metz *et al.*)



Current statistical tests...

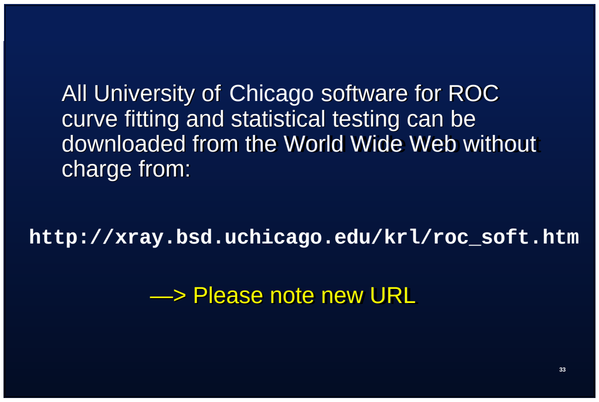
... that take both sources of variation into account (and are applicable to differences in any index, at least in principle):

- semi-parametric tests (Swets & Pickett; Dorfman, Berbaum & Metz; Toledano & Gatsonis; Obuchowski)
- bootstrapping approach (Beiden, Wagner & Campbell)



Free software for ROC analysis:

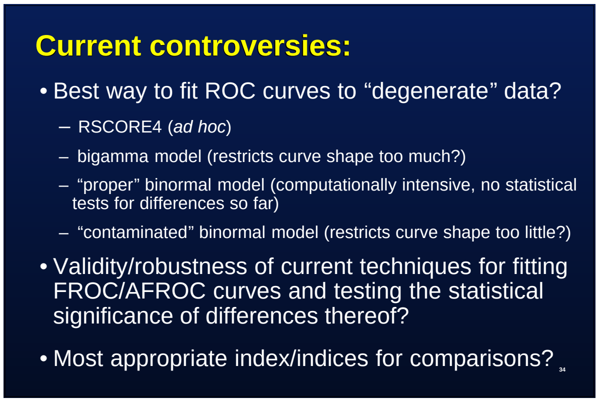
- **Metz** (University of Chicago; >5000 registered users)
  - – **ROCFIT and LABROC**: fit a single ROC using the binormal model
  - – **INDROC**: tests difference between independent ROC estimates
  - – **CORROC2 and CLABROC**: test diff. between correlated ROCs
    - → difference in A_z
    - → difference in TPF at given FPF
    - → diff. in both binormal ROC curve parameters (“bivariate” test)
  - – **ROCKIT:** integrates and extends the five programs above
  - – **PROPROC**: fits a single ROC using the “proper” binormal model
  - – **LABMRMC**: does a jackknife-ANOVA test for difference in A_z (data collected on continuous and/or discrete scale)
- **Dorfman and Berbaum** (University of Iowa)
  - – **RSCORE2** and **RSCORE4**: fit a single ROC using binormal model
  - – **MRMC**: Jackknife-ANOVA test for diff. in A_z (discrete scale only)



All University of Chicago software for ROC curve fitting and statistical testing can be downloaded from the World Wide Web without charge from:

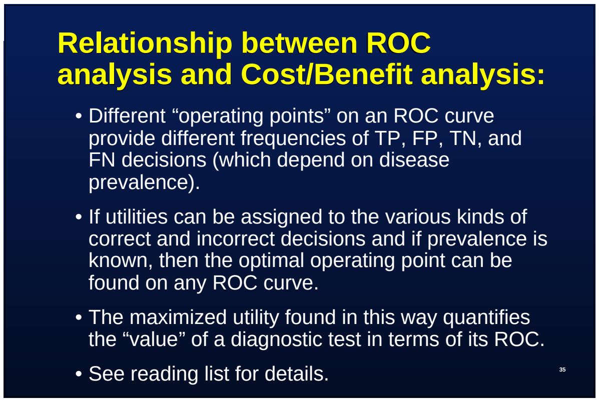
`http://xray.bsd.uchicago.edu/krl/roc_soft.htm`

—> Please note new URL



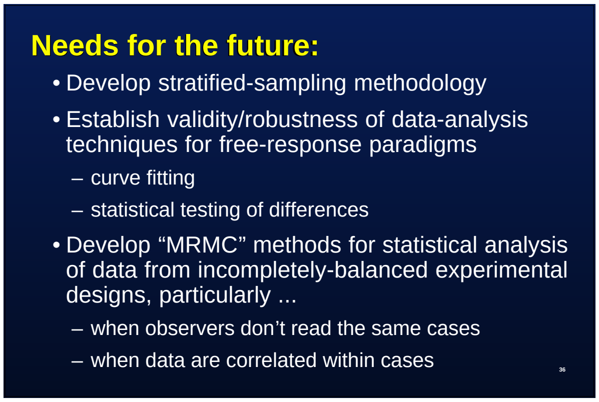
Current controversies:

- Best way to fit ROC curves to “degenerate” data?
  - – RSCORE4 (*ad hoc*)
  - – bigamma model (restricts curve shape too much?)
  - – “proper” binormal model (computationally intensive, no statistical tests for differences so far)
  - – “contaminated” binormal model (restricts curve shape too little?)
- Validity/robustness of current techniques for fitting FROC/AFROC curves and testing the statistical significance of differences thereof?
- Most appropriate index/indices for comparisons?



Relationship between ROC analysis and Cost/Benefit analysis:

- Different “operating points” on an ROC curve provide different frequencies of TP, FP, TN, and FN decisions (which depend on disease prevalence).
- If utilities can be assigned to the various kinds of correct and incorrect decisions and if prevalence is known, then the optimal operating point can be found on any ROC curve.
- The maximized utility found in this way quantifies the “value” of a diagnostic test in terms of its ROC.
- See reading list for details.



Needs for the future:

- Develop stratified-sampling methodology
- Establish validity/robustness of data-analysis techniques for free-response paradigms
  - – curve fitting
  - – statistical testing of differences
- Develop “MRMC” methods for statistical analysis of data from incompletely-balanced experimental designs, particularly ...
  - – when observers don’t read the same cases
  - – when data are correlated within cases

Needs for the future (continued):

- Develop highly efficient approaches well-suited to exploratory analyses
  - Key need is to control for decision-threshold effects
  - Other biases may be acceptable if sufficiently small
- Generalize ROC analysis to handle >2 decision alternatives
  - Must provide an appropriate compromise between complexity and practicality
  - Approaches proposed to date are *not* adequate

An incomplete list of recommended literature on ROC methodology

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- Egan JP. Signal detection theory and ROC analysis. New York: Academic Press, 1975.
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- Wagner RF, Beiden SV, Metz CE. Continuous vs. categorical data for ROC analysis: Some quantitative considerations. Academic Radiol 2001, 8: 328, 2001.
- Wagner RF, Beiden SV, Campbell G, Metz CE, Sachs WM. Assessment of medical imaging and computer-assist systems: lessons from recent experience. Academic Radiol 2002; 8: 1264.

BIAS:

- Begg CB, Greenes RA. Assessment of diagnostic tests when disease verification is subject to selection bias. Biometrics 1983; 39: 207.
- Begg CB, McNeil BJ. Assessment of radiologic tests: control of bias and other design considerations. Radiology 1988; 167: 565.
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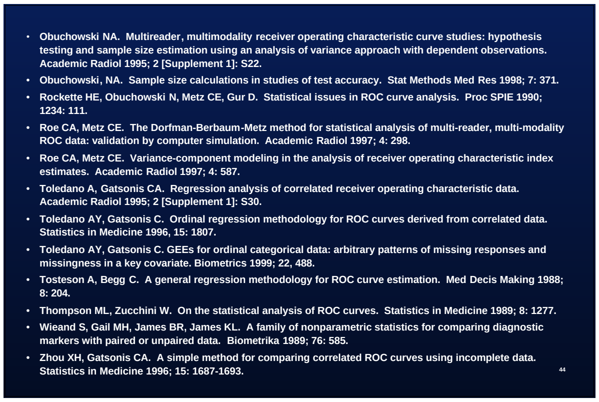

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