

Multi-reader diagnostic imaging case studies: components of variance

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Abstract

In this talk we will introduce the framework for analyzing multi-reader diagnostic imaging case studies. This framework is the launching point for the advanced methods discussed in the other talks of this session. The core of the framework is the accounting for reader variability in addition to case variability in the analysis of diagnostic imaging performance metrics. There are several methods (and software) for representing and estimating the constituent components of variance, and we will summarize a few. The methods are often referred to as multi-reader multi-case (MRMC) variance analysis methods. We will demonstrate MRMC analysis of several real studies and discuss the sizing of future studies.

Keywords

MRMC, AUC, variance, imaging

25 minutes for presentation + 10 for questions

Multi-reader diagnostic imaging case studies: components of variance

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Outline

- Diagnostic Performance
 - Area under ROC curve
- Variance representations
- Sizing a study
 - Using Components of Variance
 - Investigating Study designs
 - Practical vs. Statistical Efficiency

Variance Representations

DBM 3-way ANOVA

– Charlie Metz, University of Chicago



Numerous contributions:
radiological imaging
nuclear medicine
ROC analysis
medical-decision making
computer-aided diagnosis

...
Scientist
Educator
Mentor

- September 11, 1942 - July 4, 2012

Variance Representations

DBM 3-way ANOVA

– Charlie Metz, University of Chicago



Memorial service:
11 a.m. Monday, Aug. 27
Rockefeller Memorial
Chapel, followed by a
reception in Ida Noyes
Hall's Cloister Club.

- September 11, 1942 - July 4, 2012

Diagnostic Performance

- Sensitivity
 - Success rate on diseased cases
- Specificity
 - Success rate on non-diseased cases
- ROC and Area Under ROC curve
 - Tradeoff between Sensitivity and Specificity
 - Interaction btw diseased and non-diseased

Diagnostic Performance Observer Data

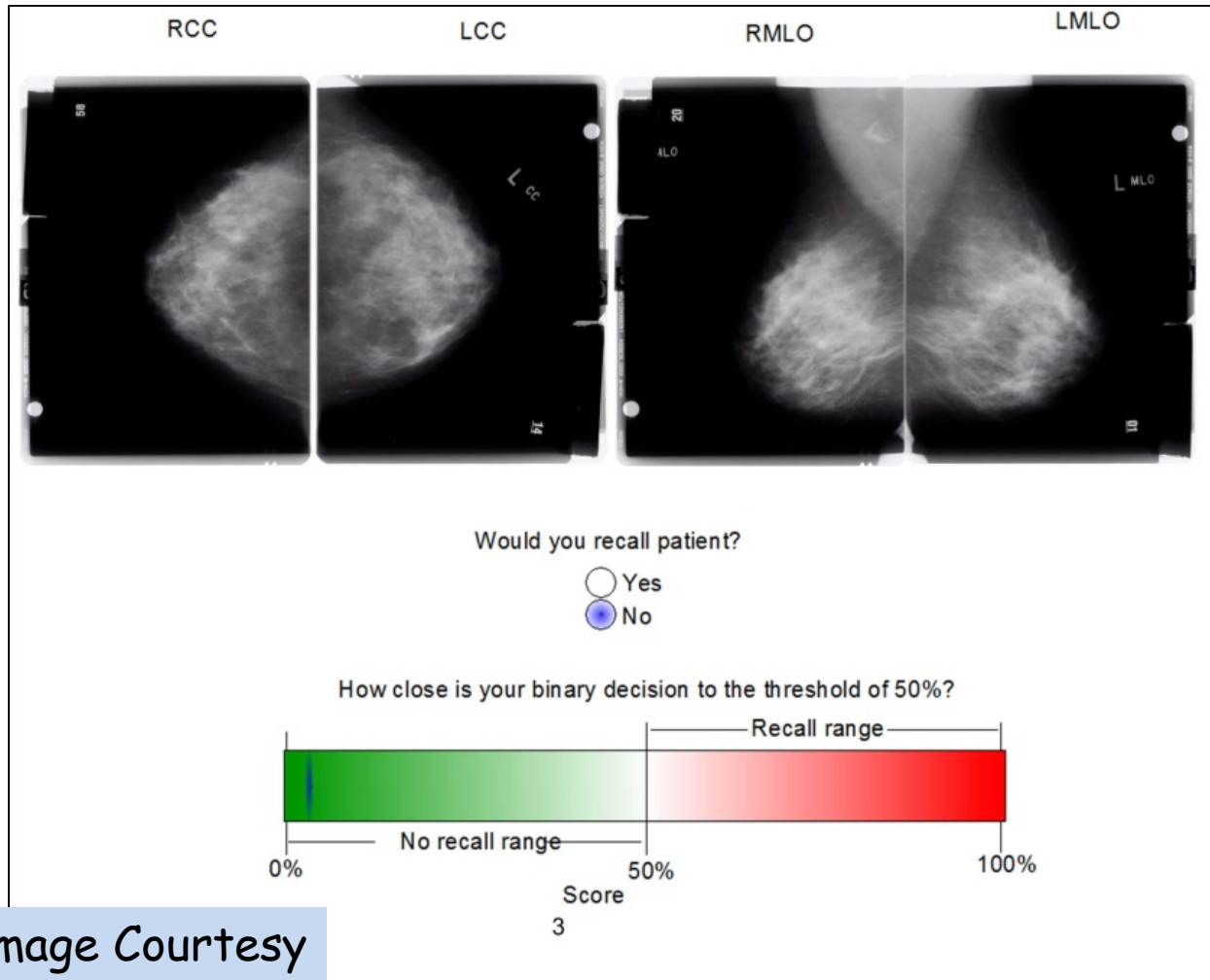


Image Courtesy
Cole and Pisano at MUSC

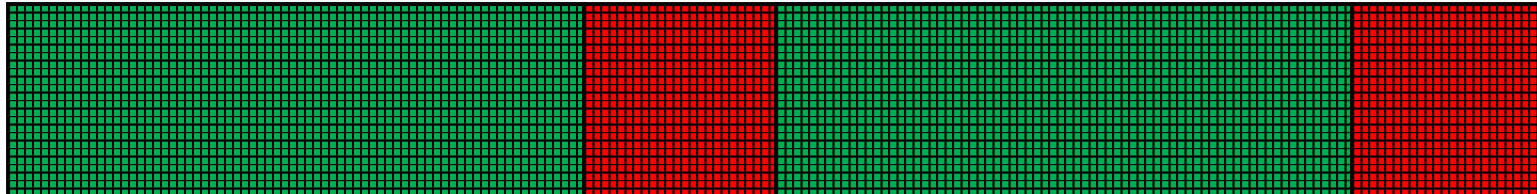
Diagnostic Performance Observer Data

- Fully-crossed study
 - All readers read all cases
 - Readers and cases are paired across modalities

Data Array:
Rows = readers
Cols = cases

Modality 1

Modality 2



Non-Diseased
Cases

Diseased
Cases

Non-Diseased
Cases

Diseased
Cases

Time = 4:00

- Pause
- Previous Time = 5:13

Diagnostic Performance

Reader-averaged AUC

- Focus: Reader-averaged AUC
 - Summary of ROC
 - Reader average of ability to separate
 - Equivalent to probability

Diagnostic Performance

Reader-averaged AUC

- Nonparametric estimator
 - U-stats, Mann-Whitney, Wilcoxon, Trapezoid

$$\widehat{\text{AUC}}_m = \sum_{r=1}^{N_R} \frac{1}{N_R} \left(\sum_{j=1}^{N_1} \frac{1}{N_1} \right) \left(\sum_{i=1}^{N_0} \frac{1}{N_0} \right) S_{mijr}$$

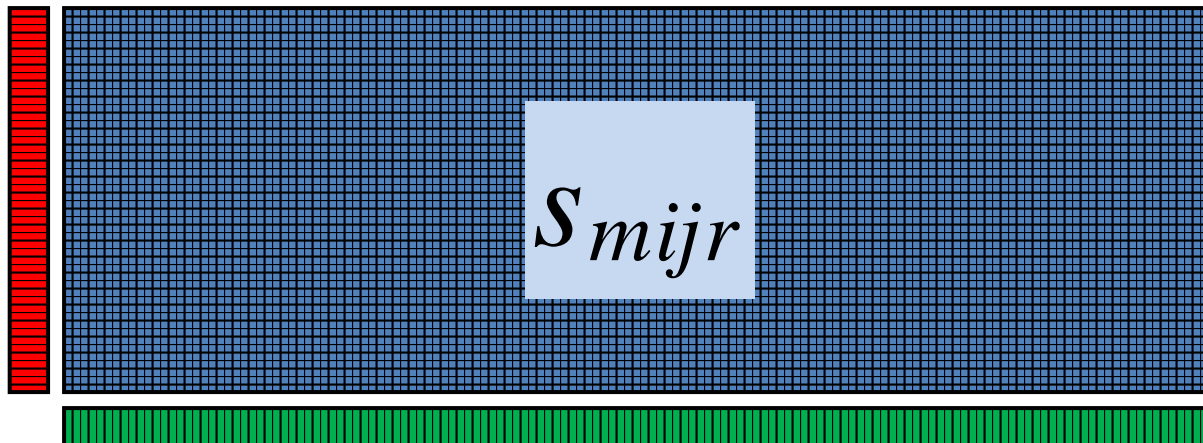
$$S_{mijr} = s(y_{mjr} - x_{mir})$$

m: Modality
i: Non-diseased case
j: Diseased case
r: Reader

$$= \begin{cases} 1 & y_{mjr} - x_{mir} > 0 \\ 1/2 & y_{mjr} - x_{mir} = 0 \\ 0 & y_{mjr} - x_{mir} < 0 \end{cases} ,$$

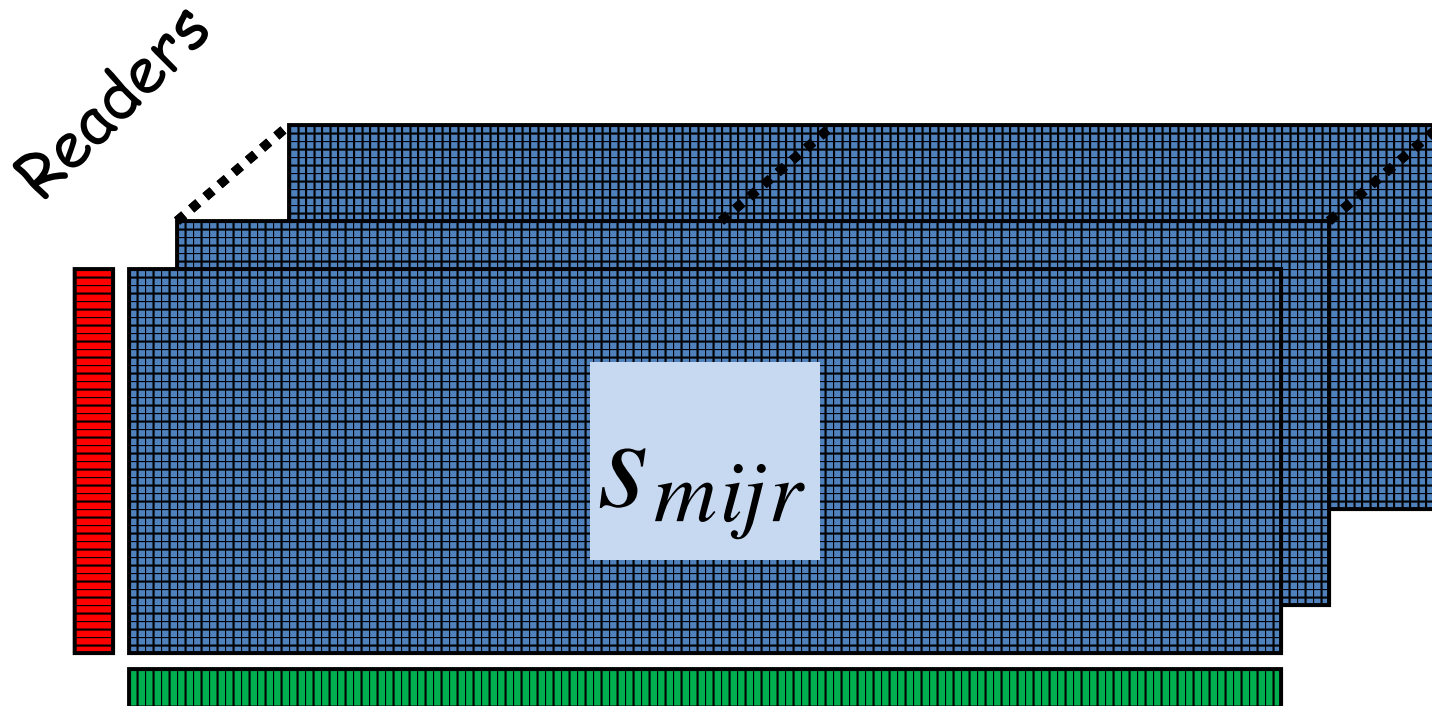
Diagnostic Performance Success Matrix

- One modality m
- One reader r
- Row i : Diseased case
- Col j : Non-diseased case



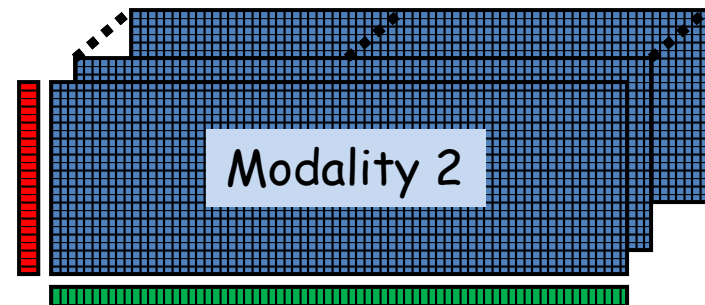
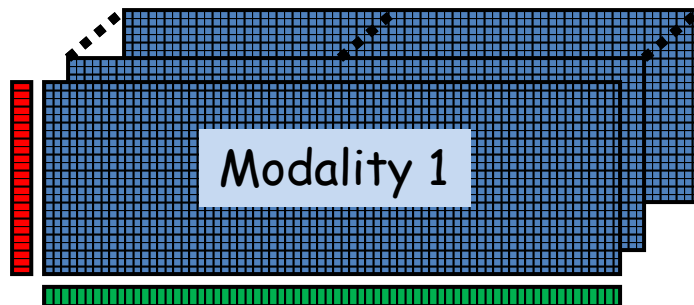
Diagnostic Performance Success Matrix

- One modality
- Multiple readers
- Row i : Diseased case
- Col j : Non-diseased case



Diagnostic Performance Success Matrix

- Multiple modalities
- Multiple readers
- Row i : Diseased case
- Col j : Non-diseased case



Diagnostic Performance

Nonparametric AUCs

- Average elements of Success Matrix

Estimates

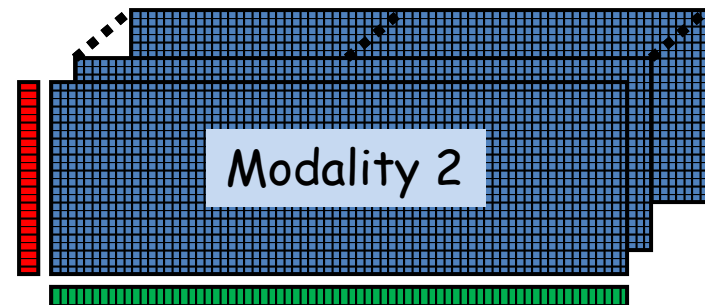
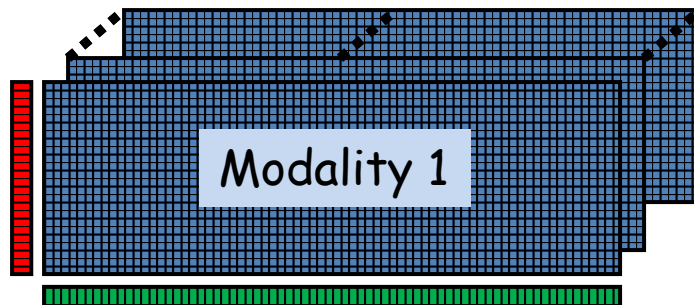
$$\bar{s}_{m\bullet\bullet r} = \widehat{\text{AUC}}_{mr}$$

$$\bar{s}_{m\bullet\bullet} = \widehat{\text{AUC}}_m$$

population quantities

$$E(s_{mijr} | mr) = \text{AUC}_{mr}$$

$$E(s_{mijr} | m) = \text{AUC}_m$$



Time = 6:00

- Pause
- Time=2:30, Total=7:45

Variance Representations

- Main Random Effects
 - case variability
difficulty
 - reader variability
skill
 - reader/case interaction
training
readers reading same cases
- **MRMC**: Multi-Reader Multi-Case Variance Analysis

Variance Representations

- Main Random Effects
 - case variability
Non-disease + Disease + Interaction
 - reader variability
 - reader/case interaction
Non-disease + Disease + Interaction

Variance Representations

U-statistic result

- Single Modality

- Gallas et al. (2009)

$$\text{var}(\widehat{\text{AUC}}) = \frac{\sigma_0^2}{N_0} + \frac{\sigma_1^2}{N_1} + \frac{\sigma_{01}^2}{N_0 N_1} + \frac{\sigma_R^2}{N_R} + \frac{\sigma_{0R}^2}{N_0 N_R} + \frac{\sigma_{1R}^2}{N_1 N_R} + \frac{\sigma_{01R}^2}{N_0 N_1 N_R}$$

Non-diseased cases
Diseased cases
Interaction

No modeling, MVUE

7 components

Variance Representations

U-statistic result

- Two Modalities

– Gallas et al. (2009)

$$\text{var}(\widehat{\text{AUC}}_1 - \widehat{\text{AUC}}_2) = \frac{\sigma_0^2}{N_0} + \frac{\sigma_1^2}{N_1} + \frac{\sigma_{01}^2}{N_0 N_1} + \frac{\sigma_R^2}{N_R} + \frac{\sigma_{0R}^2}{N_0 N_R} + \frac{\sigma_{1R}^2}{N_1 N_R} + \frac{\sigma_{01R}^2}{N_0 N_1 N_R}$$

Non-diseased cases
Diseased cases
Interaction

No modeling, MVUE

Of course, different interpretation for these components of variance from before.

Variance Representations

U-statistic result

- Two Modalities

- Gallas et al. (2009)

$$\text{var}(\widehat{\text{AUC}}_1 - \widehat{\text{AUC}}_2) = \frac{\sigma_0^2}{N_0} + \frac{\sigma_1^2}{N_1} + \frac{\sigma_{01}^2}{N_0 N_1} + \frac{\sigma_R^2}{N_R} + \frac{\sigma_{0R}^2}{N_0 N_R} + \frac{\sigma_{1R}^2}{N_0 N_R} + \frac{\sigma_{01R}^2}{N_0 N_1 N_R}$$

Non-diseased cases
Diseased cases
Interaction

7 components modality 1
 7 components modality 2
 7 covariances

Variance Representations

MLE, Ideal Bootstrap, Method of Moments

- Two Modalities

- Gallas et al. (2009)

$$\text{var}(\widehat{\text{AUC}}_1 - \widehat{\text{AUC}}_2) = \frac{\sigma_0^2}{N_0} + \frac{\sigma_1^2}{N_1} + \frac{\sigma_{01}^2}{N_0 N_1} + \frac{\sigma_R^2}{N_R} + \frac{\sigma_{0R}^2}{N_0 N_R} + \frac{\sigma_{1R}^2}{N_0 N_R} + \frac{\sigma_{01R}^2}{N_0 N_1 N_R}$$

Non-diseased cases
Diseased cases
Interaction

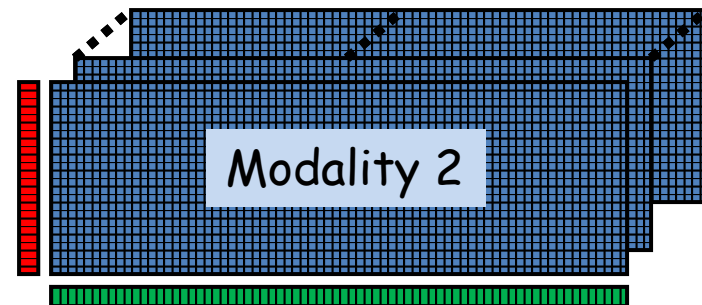
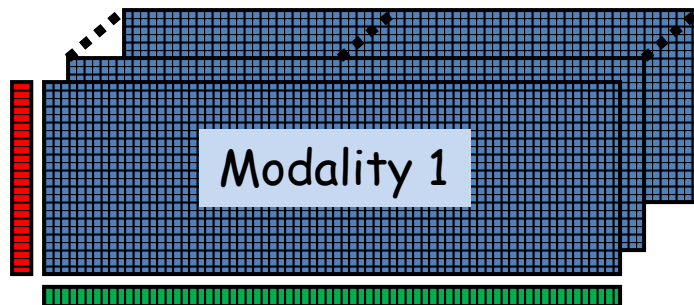
MLE: Assume samples are entire distribution.

Introduce bias for positive variances (components)

Variance Representations

U-statistic result = 4-way ANOVA

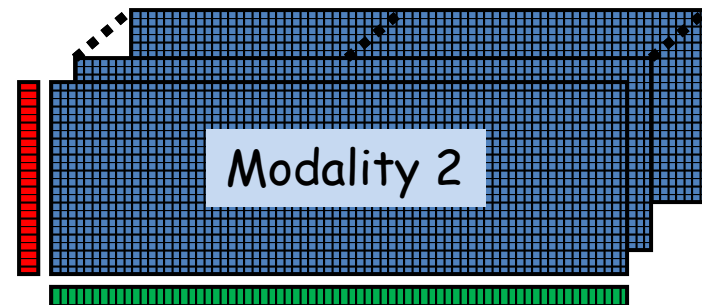
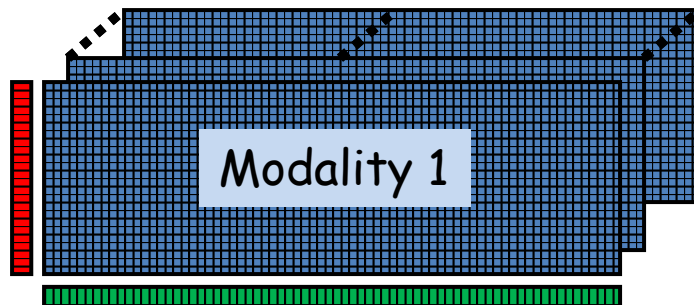
- 4 effects:
 - Multiple modalities (fixed)
 - Multiple readers (random)
 - Rows: Diseased cases (random)
 - Columns: Non-diseased cases (random)



Variance Representations

U-statistic result = 4-way ANOVA


- Caveats:
 - Observed data are success elements
Not strictly independent observations
 - Can specify variances per modality or pool



Time = 9:30

- Pause
- Time=5:15, Total=13:00

Variance Representations ANOVA

- **DBM**: Dorfman, Berbaum and Metz (1992)
 - 3-way ANOVA: modality, readers, cases
 - Jackknife pseudovalues
 - **OR**: Obuchowski & Rockette (1995)
 - 2-way ANOVA: modality, reader
 - Correlated errors
 - **Marginal-Mean ANOVA**
 - **Mm-ANOVA**
 - (Hillis to be submitted)
 - Bridge linking both variance representations
 - Hypothetical 3-way ANOVA no pseudovalues
 - Estimation based on OR
- 

Variance Representations

3-way ANOVA

- Single Modality: DBM & mm-ANOVA

$$\begin{aligned} \text{var}(\widehat{\text{AUC}}) = & \frac{\sigma_{\text{cases}}^2 + \sigma_{\text{mod} \times \text{cases}}^2}{N_{\text{cases}}} \\ & + \frac{\sigma_{\text{readers}}^2 + \sigma_{\text{mod} \times \text{readers}}^2}{N_{\text{readers}}} \\ & + \frac{\sigma_{\text{cases} \times \text{readers}}^2 + \sigma_{\text{mod} \times \text{cases} \times \text{readers}}^2}{N_{\text{cases}} N_{\text{readers}}} \end{aligned}$$

Can also estimate these components from U-statistics or MLE

Diseased and non-diseased effects are pooled

Variance Representations

3-way ANOVA: DBM & mm-ANOVA

- Two Modalities: DBM & mm-ANOVA

$$\text{var}(\widehat{\text{AUC}}_1 - \widehat{\text{AUC}}_2) = \frac{2\sigma^2_{\text{mod} \times \text{cases}}}{N_{\text{cases}}} + \frac{2\sigma^2_{\text{mod} \times \text{readers}}}{N_{\text{readers}}} + \frac{2\sigma^2_{\text{mod} \times \text{cases} \times \text{readers}}}{N_{\text{cases}} N_{\text{readers}}}$$

Can also estimate these components from U-statistics or MLE

Diseased and non-diseased effects are pooled

Variance Representations

2-way ANOVA & Correlated Errors

OR & mm-ANOVA

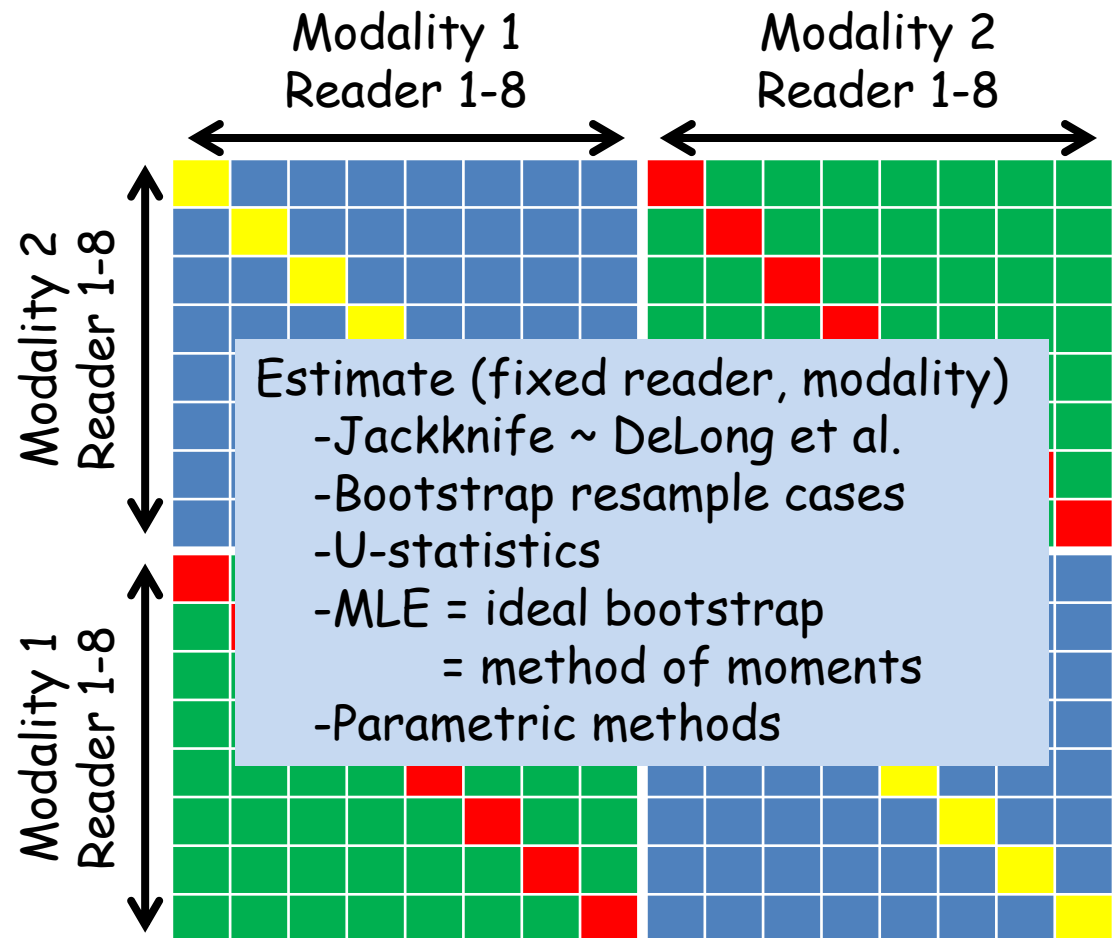
$$\text{cov}(\widehat{\text{AUC}}_{mr}, \widehat{\text{AUC}}_{mr} | mr)$$

Var_ε =
Same modality, same reader

Cov1 =
Diff modality, same reader

Cov2 =
Same modality, Diff reader

Cov3 =
Diff. modality, Diff. reader



Variance Representations

Hillis Marginal-Mean (3-way) ANOVA

- If use U-stats (or MLE) to estimate fixed-reader covariances
- ... then equivalence across variance representations.

Variance in Reader Studies: iMRMC

- <http://www.imrmc.html> (coming to googlecode)

Main author:
Xin He, FDA

Menu

Select an input method:

pilot study...

☒ use MLE estimates of moments to avoid n ☐ Difference

AUC1=0.603 AUC2=0.748 AUC1-AUC2=-0.145 10 Readers, 58 Normal case

Statistical Analysis: sqrt(total var)=0.0161 p-Value=

	N	D	N-D	R	R-N
components	3.11385E-2	2.82052E-2	1.97888E-2	1.00000E-1	1.17546E-1
coeff	1.72414E-2	2.17391E-2	3.74813E-4	1.72414E-3	2.17391E-3
total	5.36870E-4	6.13156E-4	7.41709E-6	1.61604E-4	4.40575E-4

Significant level Effect Size #Re

Sizing Results: = Power(Z test) =

DATA INPUT

DATA
ANALYSIS

SIZE A
TRIAL

Data courtesy of
Jiang at UC.
(Acad Radiol 1999)
Detection of
microcalcifications
in mammography:
Film vs. Film + CAD

Variance in Reader Studies: iMRMC, U-Stats

- <http://js.cx/~xin/mrmc.html>

AUC1=0.603 AUC2=0.748 AUC1-AUC2=-0.145

10 Readers, 58 Normal cases, 46 Disease cases.

Statistical Analysis: $\text{sqrt}(\text{total var})=0.001073$ $t\text{Stat}=4.41$ $df(\text{Hillis 2008})=321.68$ $p\text{-Value}=0.0000$ $\text{Conf. Int.}=(-0.21, -0.08)$

BDG

BCK

DBM

OR

MS

	N	D	N~D	R	N~R	D~R	R~N~D
components	2.58076E-2	2.05323E-2	6.99835E-3	-9.18608E-4	4.2972E-2	7.94478E-2	1.35851E-1
coeff	1.72414E-2	2.17391E-2	3.74813E-4	1.00000E-1	7.2414E-3	2.17391E-3	3.74813E-5
total	4.44958E-4	4.46354E-4	2.62307E-6	-9.18608E-5	3.6158E-5	1.72713E-4	5.09186E-6

Var=0.001073

Variance in Reader Studies: iMRMC, MLE

- <http://js.cx/~xin/mrmc.html>

AUC1=0.603 AUC2=0.748 AUC1-AUC2=-0.145 10 Readers, 58 Normal cases, 46 Disease cases.

Statistical Analysis: sqrt(total var)=0.001567 tStat= 3.65 df(Hillis 2008)= 131.61 p-Value= 0.0004 Conf. Int.=(-0.22, -0.07)

BDG**

BCK**

DBM**

OR**

MS**

	N	D	N~D	R	N~R	D~R	R~N~D
components	3.11385E-2	2.82052E-2	1.97888E-2	1.61604E-3	0.6370E-2	7.20108E-2	1.17546E-1
coeff	1.72414E-2	2.17391E-2	3.74813E-4	1.00000E-1	7.2414E-3	2.17391E-3	3.74813E-5
total	5.36870E-4	6.13156E-4	7.41709E-6	1.61604E-4	7.3052E-5	1.56545E-4	4.40575E-6

Var=0.001567

Variance in Reader Studies: iMRMC, DBM

- <http://js.cx/~xin/mrmc.html>

AUC1=0.603 AUC2=0.748 AUC1-AUC2=-0.145 10 Readers, 58 Normal cases, 46 Disease cases.

Statistical Analysis: $\sqrt{\text{total var}}=0.001567$ tStat= 3.65 df(Hillis 2008)= 131.61 p-Value= 0.0004 Conf. Int.=(-0.22, -0.07)

BDG**		BCK**		DBM**		OR**		MS**	

Variance in Reader Studies: iMRMC, OR & mm-ANOVA

- <http://js.cx/~xin/mrmc.html>

AUC1=0.603 AUC2=0.748 AUC1-AUC2=-0.145 10 Readers, 58 Normal cases, 46 Disease cases.

Statistical Analysis: $\sqrt{\text{total var}}=0.001567$ tStat= 3.65 df(Hillis 2008)= 131.61 p-Value= 0.0004 Conf. Int.=(-0.22, -0.07)

BDG** BCK** DBM** **OR**** MS**

	R	TR	COV1	COV2	COV3	ERROR
component	7.75679E-4	0.08018E-4	9.41837E-4	1.32594E-3	7.47220E-4	2.76184E-3
coeff	0.00000E0	0.00000E-1	-2.00000E-1	1.80000E0	-1.80000E0	2.00000E-1
total	0.00000E0	6.1604E-4	-1.88367E-4	2.38669E-3	-1.34500E-3	5.52368E-4

Var=0.001567

Time = 16:15

- Pause
- Time=9:00, Total=22:00

Variance Representations

Methodology Evaluation Tool

- Roe and Metz (1997)
ROC simulation model
 - Multiple modalities (fixed effect)
 - Multiple readers
 - Multiple cases
 - TRUTH!

Except for truth looks like
3-way ANOVA

$$\begin{aligned} X_{ijkt} = & \mu_t + \tau_{it} + R_{jt} + C_{kt} \\ & + (\tau R)_{ijt} + (\tau C)_{ikt} + (RC)_{jkt} \\ & + (\tau RC)_{ijkt} + E_{ijkt} \end{aligned}$$

Variance Representations Size a Trial

- Two Modalities

$$\text{var}(\widehat{\text{AUC}}_1 - \widehat{\text{AUC}}_2) = \frac{\sigma_0^2}{N_0} + \frac{\sigma_1^2}{N_1} + \frac{\sigma_{01}^2}{N_0 N_1} + \frac{\sigma_R^2}{N_R} + \frac{\sigma_{0R}^2}{N_0 N_R} + \frac{\sigma_{1R}^2}{N_0 N_R} + \frac{\sigma_{01R}^2}{N_0 N_1 N_R}$$

Non-diseased cases

Diseased cases

Interaction

Pick N_0 , N_1 , N_R , see the variance.

C.I. & Hypothesis test:
-Gaussian model
-d.o.f. from Hillis

Variance in Reader Studies: Size a Trial

- <http://js.cx/~xin/mrmc.html>

Significant level Effect Size #Reader #Normal #Diseased

Sizing Results: $\sqrt{\text{Var}}=0.039589$ Delta=14.36 DDF=131.61 CVF=3.91 Power(Hillis 2011)=0.96 Power(Z test)=0.97

Significant level Effect Size #Reader #Normal #Diseased

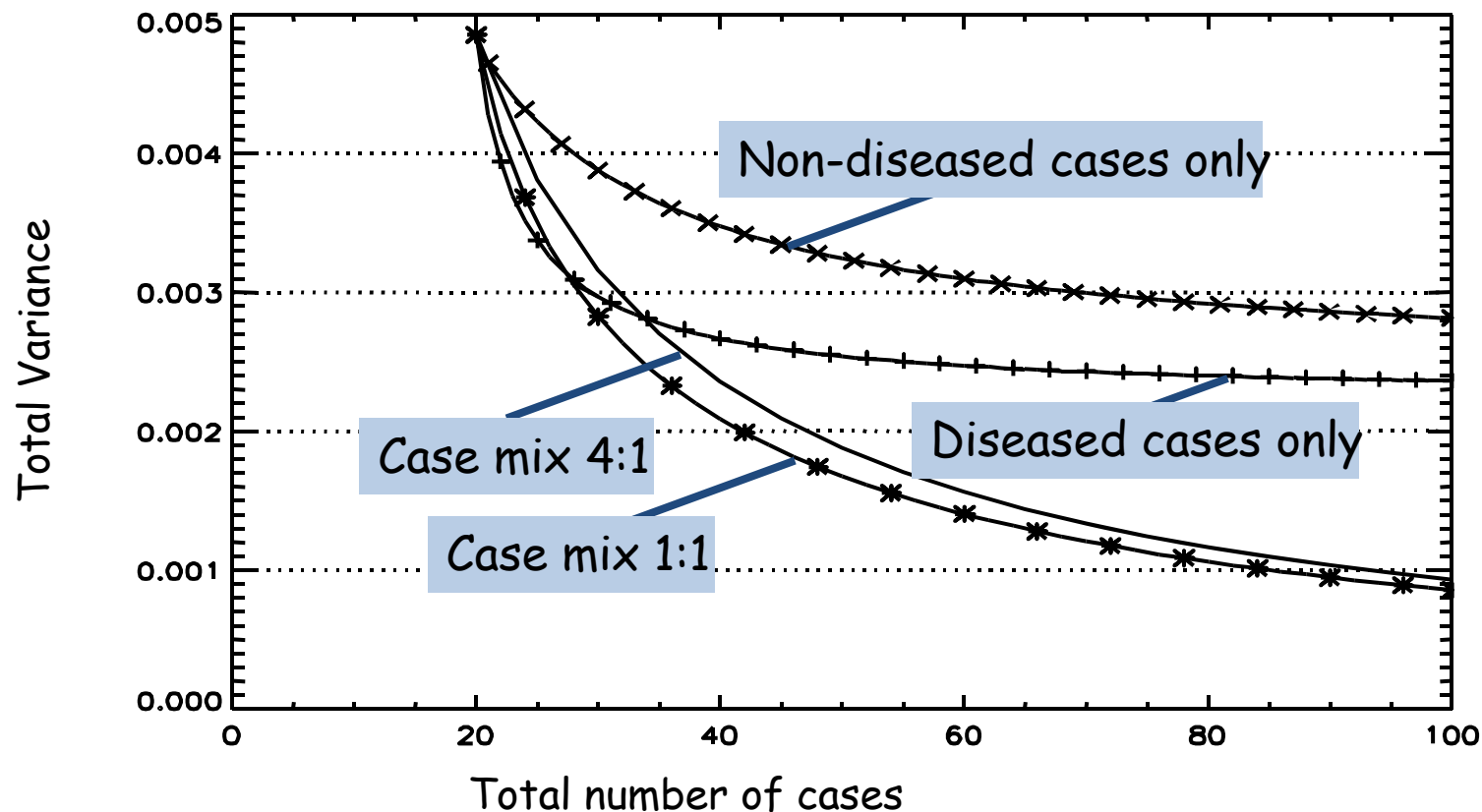
Sizing Results: $\sqrt{\text{Var}}=0.039589$ Delta=1.60 DDF=131.61 CVF=3.91 Power(Hillis 2011)=0.24 Power(Z test)=0.24

Variance in Reader Studies: Size a Trial

- NIH/ASCCP sub-study of ALTS [2-3]
 - Atypical Squamous Cells of Undetermined Significance (ASCUS) Low-Grade Squamous Intraepithelial Lesion (LSIL) Triage Study
 - Colposcopy
- 1,000 women enrolled; 939 with evaluable Cervigrams™
- 21 colposcopists
- 20 patients (16 normal and 4 diseased) had Cervigrams™ read by every reader (420 readings)
- Overall diagnosis for patient

4:1 sampling
→ 25% study prevalence

Variance in Reader Studies: Size a Trial



Reduce variance by 50%.
1:1 sampling: add 15 cases.
4:1 sampling: add 20 cases

Plot courtesy of Hsu, NCI.

Variance in Reader Studies: Size a Trial

- Which components of variance should I use?
 - Pilot study
 - Find data from a completed study that is
 - Relevant to imaging modality
 - Relevant to viewing conditions
 - Relevant to task/disease
- iMRMC: working on annotated database

Time = 21:44

- Pause
- Time=5:30, Total=27:30

Study Designs

- Fully-crossed study
 - All readers read all cases
 - Readers and cases are paired across modalities

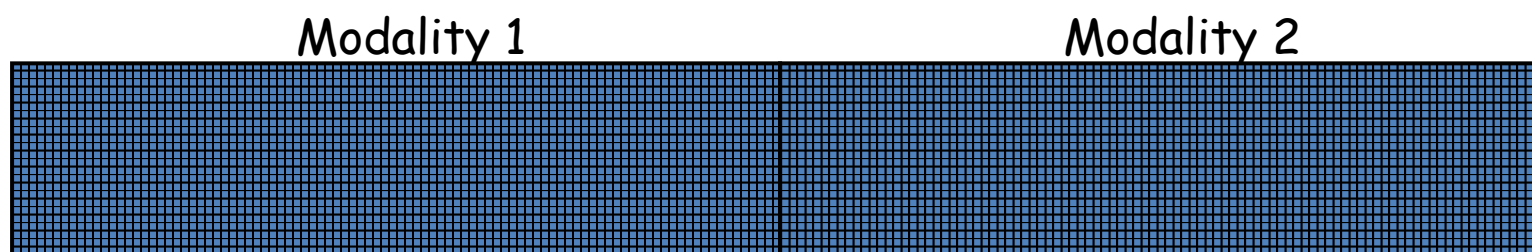
Data Array:
Rows = readers
Cols = cases



Study Designs

- Fully-crossed study
 - All readers read all cases
 - Readers and cases are paired across modalities

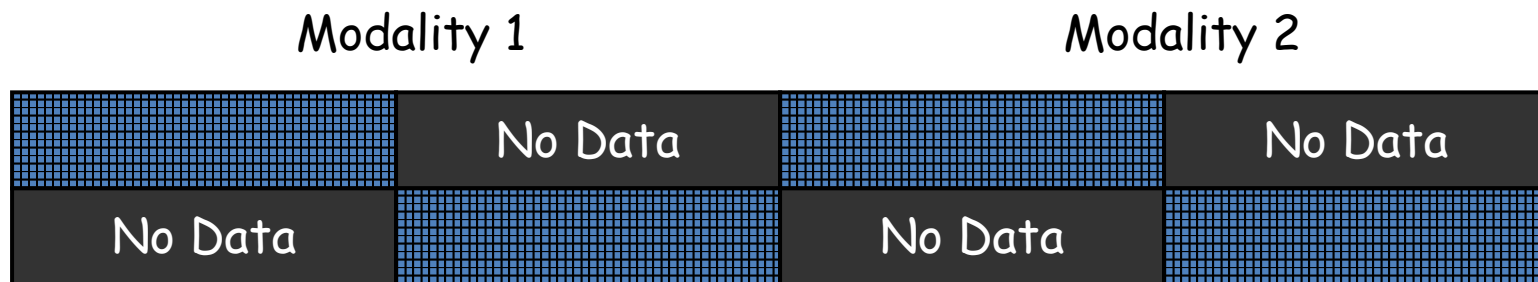
Remove truth labels to unclutter study design concepts.
Diseased and non-diseased cases need to be treated separately.



Data Array:
Rows = readers
Cols = cases

Study Designs

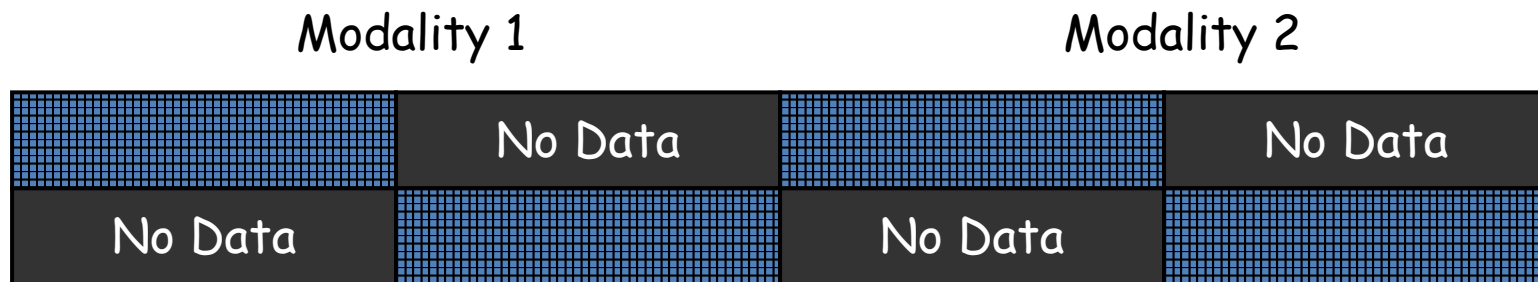
- Fully-crossed study is burdensome
 - All readers read all cases
 - Readers and cases are paired across modalities
- Split-plot study
 - Readers and cases split into 2 groups
 - Data is fully-crossed within a group



Data Array:
Rows = readers
Cols = cases

Study Designs

- Fully-crossed is burdensome
 - A lot of reads per reader
 - A lot of reads total
- Split-plot study may save time (and money)
 - Half the reads per reader
 - Half the reads total



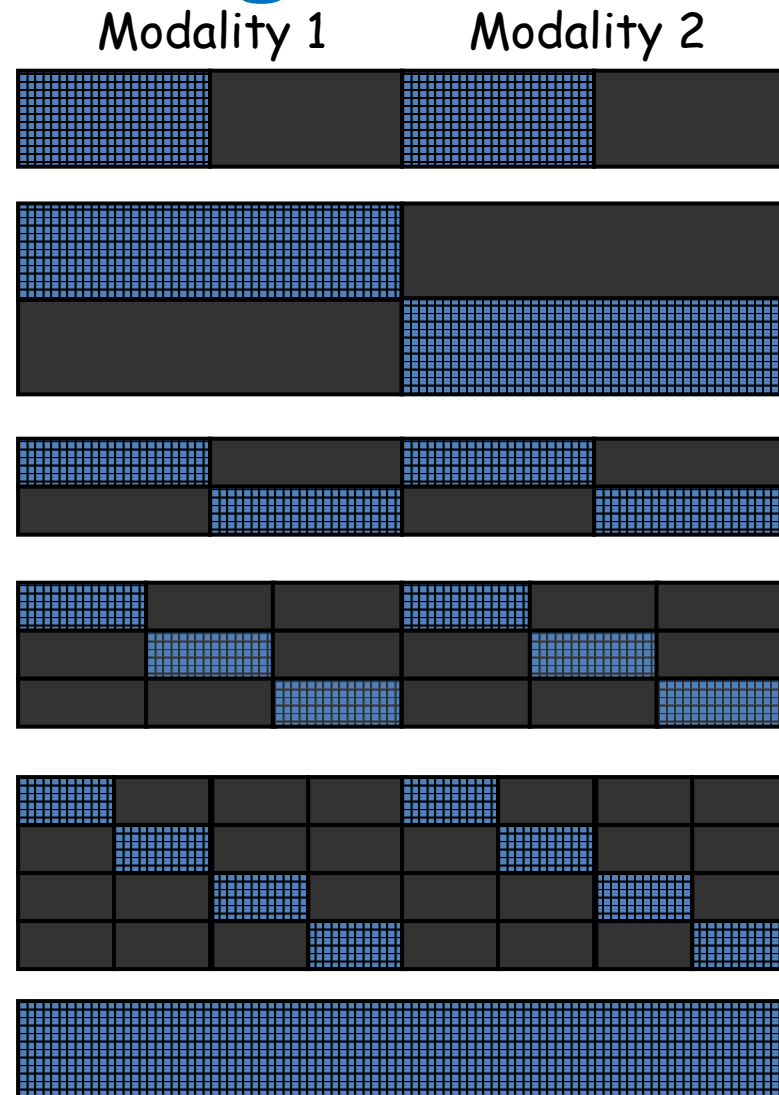
Data Array:

Rows = readers

Cols = cases

Study Designs

- Fully-Crossed A
- Readers Unpaired Across Modalities
- 2-Groups
- 3-Groups
- 4-Groups
- Fully-Crossed B



Study Designs

Efficiency

- “U-statistic” approach that decouples variance components from study design
 - *Gallas and Brown (2008)*
- Roe and Metz simulation
 - given description of scores, know the components of variance (numerical integration)
- Model parameters ($\Delta\mu = 1.53$)
 - | | | | | | |
|------------------------------|------------------------------|---------------------------------|---------------------------------|---------------------------------|----------------------------------|
| $\frac{\text{Var}_r}{0.011}$ | $\frac{\text{Var}_c}{0.100}$ | $\frac{\text{Var}_{rc}}{0.200}$ | $\frac{\text{Var}_{tr}}{0.030}$ | $\frac{\text{Var}_{tc}}{0.100}$ | $\frac{\text{Var}_{trc}}{0.200}$ |
|------------------------------|------------------------------|---------------------------------|---------------------------------|---------------------------------|----------------------------------|

Study Designs: Efficiency

Study Design	Groups	Readers		Cases		Reads		Statistical Efficiency
	G	$\frac{J}{G}$	J	$\frac{N_1}{G} + \frac{N_0}{G}$	N_{Total} $N_0 + N_1$	per reader	total	
Full-A	1	6	6	30+30	60	120	720	0.83
Unpaired Readers	1	6	12*	60+60	120	120	1440	0.90
2-groups	2	3	6	30+30	120	120	720	1.00
3-groups	3	3	9	20+20	120	80	720	1.20
4-groups	4	3	12	15+15	120	60	720	1.33
Full-B	1	6	6	60+60	120	240	1440	1.16

Resources: Tried to control

- total # reads
- total # cases
- # reads per reader

Study Designs: Efficiency

Study Design	Groups	Readers		Cases		Scores		Statistical Efficiency
	G	$\frac{J}{G}$	J	$\frac{N_1}{G} + \frac{N_0}{G}$	N_{Total} $N_0 + N_1$	per reader	total	
Full-A	1	6	6	30+30	60	120	720	0.83
Unpaired Readers	1	6	12*	60+60	120	120	1440	0.90
2-groups	2	3	6	30+30	120	120	720	1.00
3-groups	3	3	9	20+20	120	80	720	1.20
4-groups	4	3	12	15+15	120	60	720	1.33
Full-B	1	6	6	60+60	120	240	1440	1.16

Take-away 1. It is possible (and fairly easy) to compare study designs.

Study Designs: Efficiency

Study Design	Groups	Readers		Cases		Scores		Statistical Efficiency
	G	$\frac{J}{G}$	J	$\frac{N_1}{G} + \frac{N_0}{G}$	N_{Total} $N_0 + N_1$	per reader	total	
Full-A	1	6	6	30+30	60	120	720	0.83
Unpaired Readers	1	6	12*	60+60	120	120	1440	0.90
2-groups	2	3	6	30+30	120	120	720	1.00
3-groups	3	3	9	20+20	120	80	720	1.20
4-groups	4	3	12	15+15	120	60	720	1.33
Full-B	1	6	6	60+60	120	240	1440	1.16

Take-away 2. Pay a price when you don't pair readers across modalities.

Study Designs: Efficiency

Study Design	Groups G	Readers		Cases		Scores		Statistical Efficiency $\frac{\text{var}(2\text{-groups})}{\text{var}(\text{alt. design})}$
		$\frac{J}{G}$	J	$\frac{N_1}{G} + \frac{N_0}{G}$	N_{Total} $N_0 + N_1$	per reader	total	
Full-A	1	6	6	30+30	60	120	720	0.83
Unpaired Readers	1	6	12*	60+60	120	120	1440	0.90
2-groups	2	3	6	30+30	120	120	720	1.00
3-groups	3	3	9	20+20	120	80	720	1.20
4-groups	4	3	12	15+15	120	60	720	1.33
Full-B	1	6	6	60+60	120	240	1440	1.16

Take-away 3. There is a moderate hit to efficiency when you split the experiment into two groups.

Study Designs: Efficiency

Study Design	Groups	Readers		Cases		Scores		Statistical Efficiency
	G	$\frac{J}{G}$	J	$\frac{N_1}{G} + \frac{N_0}{G}$	N_{Total} $N_0 + N_1$	per reader	total	
Full-A	1	6	6	30+30	60	120	720	0.83
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3-groups	3	3	9	20+20	120	80	720	1.20
4-groups	4	3	12	15+15	120	60	720	1.33
Full-B	1	6	6	60+60	120	240	1440	1.16

Take-away 4. You can be more efficient by splitting more. (need more readers, should avoid splitting below 25 cases per truth per reader)

Time = 25:50

- Time=3:45, Total=31:15

Conclusions

- Diagnostic Performance
 - Area under ROC curve
- Variance representations
- Sizing a study
 - Using Components of Variance
 - Investigating Study designs
 - Practical vs. Statistical Efficiency

Future Work

- Include arbitrary study design in iMRMC
- Generalize methods to concordance

Variance in Reader Studies: Methods & Software

- General Regression, Tosteson and Begg (1988)
- The jackknife/ANOVA, Dorfman, Berbaum and Metz (1992)
 - <http://metz-roc.uchicago.edu/MetzROC>
- ANOVA and correlation model, Obuchowski (1995)
 - <http://www.bio.ri.ccf.org/html/rocanalysis.html>
- Ordinal Regression, Toledano and Gatsonis (1995)
- Bootstrap, Beiden, Wagner, and Campbell (2000)
- U-statistics, Gallas
 - <http://js.cx/~xin/index>

Radiologist Variability Example

Beam et al., Arch Intern Med 1996

- 108 US Radiologists
- 79 mammograms:
 - 34 normal/benign
 - 45 breast cancer
- Fully-crossed data
 - Every radiologist read every case

Radiologist Variability Example

Beam et al., Arch Intern Med 1996

- Measurement Scale

BIRADS: Breast Imaging-Reporting and Data System
(Ordinal)

- 1, negative
- 2, no evidence of malignancy
- 3, probably benign findings; short-interval follow-up
- 4, suspicious abnormality; biopsy should be considered
- 5, high probability of cancer; biopsy recommended

Radiologist Variability Example

Beam et al., Arch Intern Med 1996

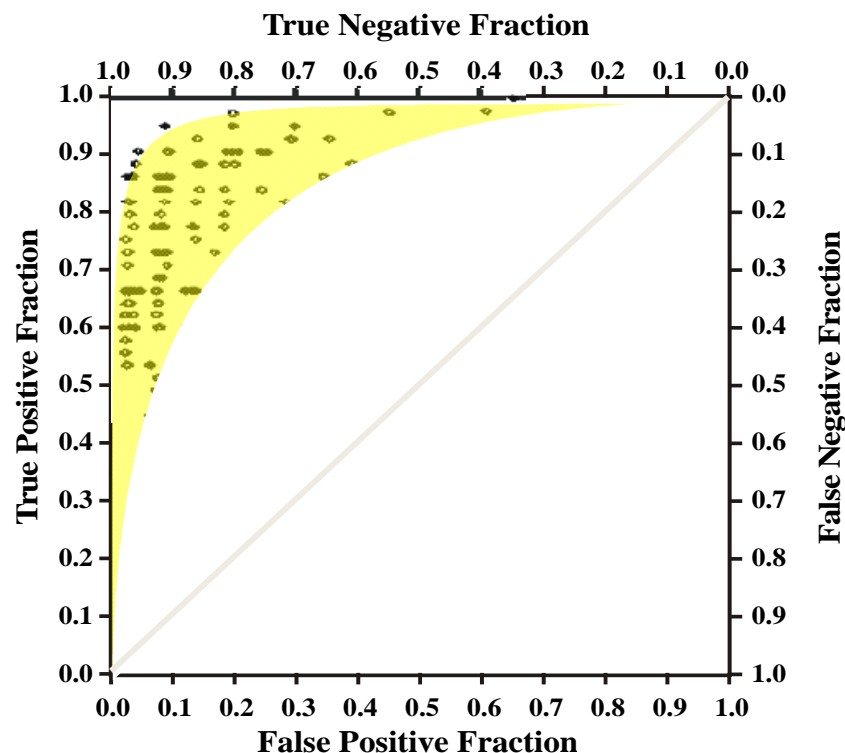
- Measurement Scale
BIRADS (Ordinal)

- 1, negative
- 2, no evidence of malignancy
- 3, probably benign findings
short-interval follow-up

Threshold

- 4, suspicious abnormality
biopsy should be considered
- 5, high probability of cancer
biopsy recommended

Beam et al., Arch Intern Med 1996



Radiologist Variability Example

Beam et al., Arch Intern Med 1996

	Mean	(Min, Max) Range	Variance Confidence Interval
Sensitivity N=45	80%	(47,100) 53	?
Specificity N=34	90%	(35,99) 63	?
AUC N _{normal} =34 N _{cancer} =45	85%	(74,94) 21	?