Rapid Pre-screening: A Better Quality Assessment Tool in Gynecologic Cytology

Andrew A. Renshaw
Baptist Hospital
Miami FL
Conflict of Interest

• None
Outline

- Current standard: 10% review of negative slides
- Rapid and pre-screening
- What people have done with it
- What else people can do with it
Where I want to go:

- **Review of 10% of negatives**
- Correct a handful of errors
- Manage by feel, not numbers

- **Rapid pre-screening**
- Real quality assessment tool (manage by numbers)
- Improves performance - more pts win
- Not every lab wins - more pts win
- Meets CLIA QA and slide limit standards
- Measures sensitivity of lab
- Measures sensitivity of individuals
- Measures impact of life events
- Measures impact of work load
- Measures impact of experience
- Allows evaluation of ASC/SIL and bx rate
- Measures the value of automated screening devices
- Measures impact of HPV+ rate
Accuracy today

- Accuracy rate in non gyn cytology: 95 - 99%

- Cytologists who are 99% accurate think those who are 95% accurate are not competent

- Accuracy (Sensitivity) in gyn cytology for all abnormalities (ASCUS+) 75-85% (3 large clinical trials)
What does this mean?

• A second review in non-gyn is still highly accurate

• A second review in gyn cytology is not:
  – Sensitivity ASCUS and above 30%
  – Sensitivity LSIL and above 0%
  – 1/1,000,000 reviews at a well known laboratory

• When the results change, they can not be interpreted
Non-blinded review of negative smears

• Does not work: doesn’t find enough errors
• Does not improve overall performance
• Every laboratory has a sensitivity >99% (not quantitative)
• Every lab “wins”; patients lose
• Not really quality assurance
Rapid pre-screening

- A two step method
- Each steps contributes something different
Rapid: more effective

- Sensitivity 30-50% for ASCUS, LSIL, HSIL+
- 6-12 x faster than routine review
- Much more effective way to detect missed cases
- Confirmed in multiple studies, no contradictory studies
Pre-screening

• Don’t need to:
  – remove the dots
  – change the labels
  – Select controls/seeds

• Do need to:
  – Hide the pre-screen diagnosis
  – Do some math
Pre-screening

• What do you get for this?
  – Blinded non biased review
  – True seeding of routine screening

• What is the result?
  – Highly accurate measure of sensitivity
Math for pre-screening

• \# of errors found = \# of true errors

Sensitivity of prescreening

• Explained in detail in the papers

• Bottom line: if anyone is willing to do this method, I will do your calculations for you
Rapid + Pre-screening

- Take a group of unscreened slides
- Review each for 30-60 seconds
- Make no dots
- Record abnormal or normal in a separate file
- Return for routine screening
Rapid + Pre-screening

- Only when a final diagnosis has been made, check the records for the pre-screen
- If the pre-screen was abnormal and the final is negative, re-screen the slide again and reach a final diagnosis
- Record the results for both the pre-screening and the final before correlation
Rapid pre-screening: how much effort?

• According to Tavares et al:

  • rapid pre-screening 50% = 10% nl review

  • 1 in 2-3 cases re-screened cases will have an error (specificity 30-50%) (compare that to 1 in 1,000,000)
What rapid pre-screening does:
1. Measures sensitivity of lab

- Sensitivity

- Djemli 2006  88%
- Deschenes 2008  82%
- Tavares 2008  65%
2. Improves sensitivity of lab (significant error reduction)

- Sensitivity

- Djemli 2006 88%----93%
- Deschenes 2008 82%----90%
- Tavares 2008* 65%----87%

- *10% and high risk review – no change
3. Performs better than any laboratory doing routine QA

- Sensitivity from clinical trials 75-85%
- Even a clinic in a small city in Brazil with a not very impressive primary screener beat that
4. Measures the sensitivity of the individual

- Individual screeners vary widely:
  - Djemli 2006 87%----100%
  - Deschenes 2008 51%----99%
  - Tavares 2008 65%
5. Measures change in sensitivity over time

- Individual screening sensitivity varies over time and correlates with life events

  - 90%---51%
  - 100%---51%

- Both techs had difficult personal issues during the second study
6. Sensitivity does not vary with work loads

- No correlation with work loads between 26---38 slides per day
- Studies with higher work loads remain to be performed
7. Sensitivity does not correlate with experience

- No correlation between sensitivity and experience between 7 and 30 years
- Most screeners, like most pathologists, are born not made
8. Allows evaluation of ASC/SIL ratio

- ASC/SIL ratio used to measure performance of cytopathologists
- Surrogate marker for uncertainty level and specificity
- Not widely used to evaluate cytotechnologists
8. Allows evaluation of ASC/SIL ratio:
cytotechnologists

<table>
<thead>
<tr>
<th>ASC/SIL ratio</th>
<th>&lt;1.5</th>
<th>1.5-3</th>
<th>&gt;3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>67</td>
<td>85</td>
<td>95</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.5</td>
<td>98.1</td>
<td>98.0</td>
</tr>
</tbody>
</table>
8. What do these numbers mean?  
1000 cases, 28 abnormals

- ASC/SIL ratio <1.5  
  1.5-3  
  >3

- Abnormals  
  19  
  24  
  27  
  found

- Negatives  
  5  
  18  
  19  
  sent for review

<1.5 is a mixed group – how do you tell them apart?
What else can this test do for me?
9. Validate automated screening devices

- Rapidly pre-screen slides before putting them on the device
- Analyze routinely
- Allows ongoing confirmation that the device is achieving a desired sensitivity
- Allows documentation that individual cytotechnologist’s performance with these devices actually improves (FDA data doesn’t)
10. Makes sense of HPV+ rate

- HPV + rate can go up for two reasons
  - 1. More specific
  - 2. Less sensitive
- By itself you can’t tell these two apart
10. Makes sense of HPV+ rate

• Use rapid prescreening to determine sensitivity
• Compare HPV positive rate in conjunction with sensitivity to determine if improved specificity is affecting sensitivity (just like the ASC/SIL ratio)
If rapid-pre-screening is so great, why isn’t it the standard?

• Rapid is a bad word in cytology

• More math than most cytologists want to do

• CLIA ‘88
CLIA ‘88

• “Review 10% of negative cases before release of report”
  – Letter
  – Spirit
  – Does it save lives?
CLIA ‘88

- 100 slides a day
  - Screen 60
  - Pre-screen 30
There is a reason this data comes from outside the US

- Cytologists are conservative by nature

- Should the ASC (and other organizations) make a statement about rapid pre-screening?
Conclusion
Quality assurance in gyn cytology is lousy

- Lousy quality assurance tools
- Rapid pre-screening can change all that
How can you **not** use rapid pre-screening?

- Performance varies significantly between:
  - Labs
  - Different cytotechnologists
  - Same cytotechnologists at different times

- Without pre-screening you can not know what is happening, so you can not manage it
As a director, how do you want to manage your lab?

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  - Measures impact of experience
  - Evaluate ASC/ISI ratio and bx fu
  - Measures the value of automated screening devices
  - Measures impact of HPV+ rate
  - Improves performance even more when used as a secondary screening method
As a patient, which lab would you want to review your slide?

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