Region of interest tuberculosis screening

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Outline

• Background on Tuberculosis
• Options for screening
• Proposed x-ray system
• Medical study objective
• Materials and Methods
• Results
• Conclusion
Background on Tuberculosis

• 1.4 million died in 2011 as a result of TB
• 60% of TB cases were in S-E Asia and W Pacific, 25% in Africa
• <2% of TB-related deaths were in the Americas
• TB is treatable but must be determined preferably at an early stage

TB diagnostics options

• Symptom questionnaires
• Cartridge-based DNA tests – NAAT (Xpert MTB/RIF)
• Sputum/smear microscopy (LED Fluorescence Microscopy)
• Digital chest x-ray (CXR) (Recommended by World Health Organization, StopTB Partnership)\(^1\)

TB diagnostics options

Relative Costs of TB Diagnostics

Normalized Cost

<table>
<thead>
<tr>
<th>Diagnostic Option</th>
<th>Cost Per Unit</th>
<th>Cost Per Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xpert MTB, NAAT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LED Fluorescence Microscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest X-ray</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FINDDiagnostics.org “LED fluorescence” and “Xpert MTB/RIF”
TB diagnostics options

Sensitivity of TB Diagnostics

- Xpert MTB, NAAT
- LED Fluorescence Microscopy
- Chest X-ray

FINDDiagnostics.org “LED fluorescence” and “Xpert MTB/RIF”
TB diagnostics options

Time to Results for TB Diagnostics

- **Xpert MTB, NAAT**: 90 minutes
- **LED Fluorescence Microscopy**: 0 minutes
- **Chest X-ray**: 10 minutes

FINDDiagnostics.org “LED fluorescence” and “Xpert MTB/RIF”
TB diagnostics options

- CXR alone is more sensitive to TB than symptom surveys alone\(^1,2\)
- 60% of culture confirmed cases are undetected by LED FM (smear negative)\(^2\)
- Digital CXR has value added: tele-radiology, Computer Aided Diagnosis\(^2\)


Digital x-ray system

- Flat Panel X-ray Detector
- Patient
- X-ray Source
- X-ray Trigger
- Desktop Computer & Monitor
- Data
- Detector-Source Sync
Detector size cost reduction

• Using a small-area detector reduces cost
• Relevant for pediatric imaging or single lung instead of full chest radiography
• Can radiologists accurately diagnose tuberculosis given two separate lung images rather than a full chest x-ray?
Medical study objective

• To determine whether a smaller-area x-ray detector could be used for screening tuberculosis

• Hypothesis: there is no difference in diagnostic accuracy of two single-lung images compared to a full chest x-ray.

• This study is not intended to examine correct screening procedures, but to compare two types of images as apples to apples.
Materials

• 570 DR and CR chest x-ray images were collected retrospectively from Aga Khan University Hospital in Karachi, Pakistan
  – 370 of confirmed TB patients
  – 200 of TB-free patients (“non-TB”)
• Used in an online survey of TB-expert radiologists
Image cropping

• Full chest x-rays were each cropped into two 5” x 9” separate lung images
Images were randomly selected from the collection to be used in an online survey.

Each radiologist saw half of the cases in the survey as a full chest x-ray, and half as cropped, split-lung x-rays.

Two versions of the survey were created (as below):

<table>
<thead>
<tr>
<th>Cases</th>
<th>Survey version A</th>
<th>Survey version B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases 1-10 (½ TB, ½ none)</td>
<td>Full chest x-rays</td>
<td>Split-lung, cropped x-rays</td>
</tr>
<tr>
<td>Cases 11-20 (½TB, ½ none)</td>
<td>Split-lung, cropped x-rays</td>
<td>Full chest x-rays</td>
</tr>
</tbody>
</table>
Web survey

- Radiologists were asked if there were any signs of TB in the images.
Measurements

• Two different measurements were made with 1480 data points across 21 survey sessions:
  – Sensitivity (correct TB diagnosis)
  – Specificity (correct non-TB diagnosis)

• These were based on the gold standard diagnosis for each case
## Results: overall

Overall sensitivity and specificity results for tuberculosis with full chest x-ray and split-lung, cropped x-ray

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full x-ray sensitivity</td>
<td>209/356 = 58.7%</td>
<td>354/384 = 92.2%</td>
</tr>
<tr>
<td>Full x-ray specificity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Split-lung, cropped x-ray sensitivity</td>
<td>219/359 = 61.0%</td>
<td>335/381 = 87.9%</td>
</tr>
<tr>
<td>Split-lung, cropped x-ray specificity</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results: sensitivity

- For each radiologist/session, full chest x-ray sensitivity is compared with split-lung, cropped x-ray sensitivity.
- The black line represents equal sensitivity in either type of image.
- Spread out, but overall centred around the “equal accuracy” line.
Results: specificity

- For each radiologist/session, full chest x-ray specificity is compared with split-lung, cropped x-ray specificity.
- The black line represents equal specificity in either type of image.
- Three major outliers out of 21 raters skew the results.
Results: specificity outliers

- Three radiologists performed significantly worse at correctly diagnosing TB-free x-rays compared to the others.
- They incorrectly diagnosed many non-TB cases that no other radiologist incorrectly diagnosed.
- One of the three performed poorly, but since their specificity results were equal for both split-lung and full x-ray cases, hypothesis was not affected.
Results: specificity outliers

<table>
<thead>
<tr>
<th>Rater/Session</th>
<th>Full Specificity</th>
<th>Split-lung Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58%</td>
<td>36%</td>
</tr>
<tr>
<td>2</td>
<td>57%</td>
<td>57%</td>
</tr>
<tr>
<td>3</td>
<td>81%</td>
<td>50%</td>
</tr>
<tr>
<td>4</td>
<td>79%</td>
<td>86%</td>
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<tr>
<td>5</td>
<td>93%</td>
<td>86%</td>
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<tr>
<td>6</td>
<td>93%</td>
<td>89%</td>
</tr>
<tr>
<td>7</td>
<td>93%</td>
<td>92%</td>
</tr>
<tr>
<td>8</td>
<td>93%</td>
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<tr>
<td>9</td>
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<td>93%</td>
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<tr>
<td>10</td>
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<tr>
<td>11</td>
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<tr>
<td>12</td>
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<tr>
<td>19</td>
<td>96%</td>
<td>93%</td>
</tr>
<tr>
<td>20</td>
<td>96%</td>
<td>100%</td>
</tr>
<tr>
<td>21</td>
<td>96%</td>
<td>100%</td>
</tr>
</tbody>
</table>

0%  10%  20%  30%  40%  50%  60%

Percentage of non-TB cases

Full Specificity
Split-lung Specificity
Statistical results

- The data were fit to a generalized linear model.
- A standard Wald test was performed to determine if there was any difference in diagnostic accuracy depending on image type.
- For sensitivity, the p-value was 0.58.
- For specificity, the p-value was 0.037, or 0.41 when the two outliers were removed.
- This shows that there is no difference in diagnostic accuracy between the image types.
Results: rater experience

• Radiologists were asked for their estimation of the task’s relative difficulty
• Scale from 1 ("not difficult") to 5 ("very difficult")
• Radiologists agreed the task was easier than they first imagined before completing the survey

<table>
<thead>
<tr>
<th></th>
<th>Pre-survey</th>
<th>Post-survey</th>
<th>Change from pre-to post-survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Difficulty</td>
<td>2.923</td>
<td>1.462</td>
<td>-1.462</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>1.037</td>
<td>0.660</td>
<td>1.050</td>
</tr>
</tbody>
</table>
Conclusion

• There is no noticeable difference in sensitivity between a full chest x-ray (58.7%) and a split-lung, cropped x-ray (61.0%) for screening for tuberculosis.

• There is some evidence (2 very atypical points) that suggests that specificity is worse for split-lung, cropped x-rays (87.9%) than for full chest x-rays (92.2%), but the majority of radiologists performed well in both cases.
Summary and Future

• Examine the possibility of using pulmonary sized (two-lung) digital X-ray detectors in place of traditional chest sized devices
  – Less user acceptance issues
  – Can still achieve significant cost reductions to make digital technology accessible to lower volume underserved populations

• Variation in radiologist diagnostic capabilities suggests examining the use of teleradiology and/or CAD
  – Teleradiology can send cases to a TB expert populated radiology call center to improve sensitivity and specificity
  – CAD, as a decision support system, could aid a physician or radiologist make a better diagnosis
Thank you

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