TB Tester

Providing healthcare in remote locations

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Market Research

- Market segmentation based on clinic services
- Product development initially as quality control device then eventually point of care

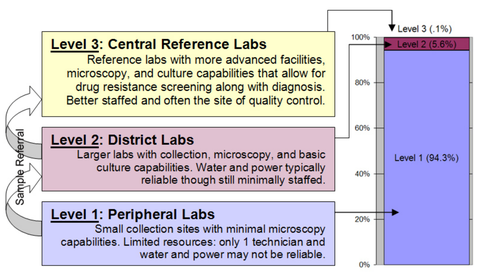


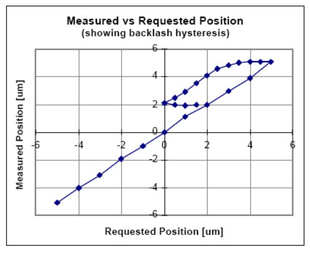
Figure 4: Market segmentation based on clinic resources and service shown with the relative distribution of labs within a country. Numbers based on Columbia's Earth Institute data for India.

Optics Assembly

- 60X objective
- Monochrome, USB 2.0 controlled digital camera

Staging

- Linear-actuator driven X, Y, and Z axis
- Allows for focusing and reading of multiple fields



Figures 5 and 6: A lead screw driven linear actuator from Zaber Corp., and a graph showing the issues of backlash in the linear actuators [Zaber Tech Sheets].

Illumination

- USB 2.0 controlled monochrome LEDs
- Optimized for Ziehl-Neelsen stain

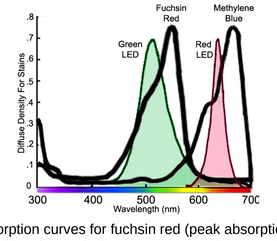


Figure 7: Absorption curves for fuchsin red (peak absorption at 540nm) and methylene blue (665nm) shown with the peak spectral power for the chosen red and green Luxeon LEDs.

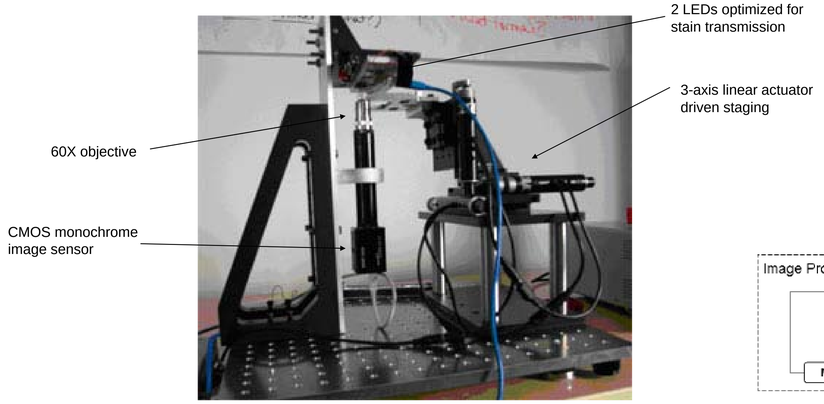


Figure 1: Image of actual TB Tester Prototype (3/16/06)

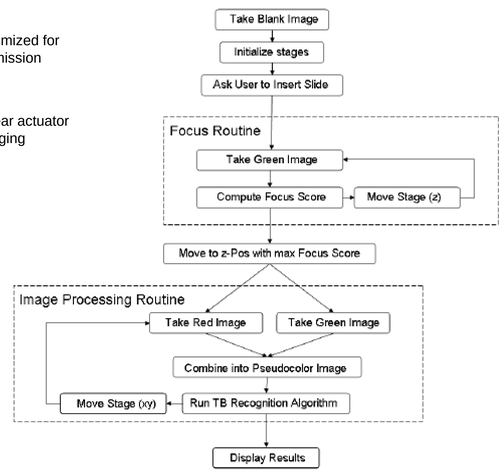


Figure 2: Flowchart of TB Tester system functionality

Objective: The goals of this project are to develop a prototype of an automated device that identifies tuberculosis on Ziehl-Neelsen stained sputum slides and to identify market needs and future sources of funding for eventual production and distribution.

Tuberculosis is the second most deadly disease in the world. The disease kills 2 million individuals annually, and a disproportionate number of cases and deaths occur in regions with poor social and economic conditions.[1] In 1993, the World Health Organization (WHO) declared tuberculosis a global emergency and launched the STOP TB initiative to address this growing epidemic.

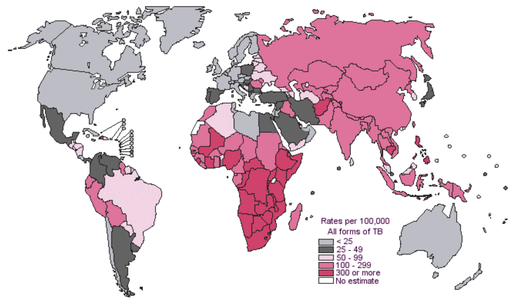


Figure 3. Rates of incidence for Tuberculosis in 2002. From this data, it is evident that economic and social conditions may be a factor in the spread and control of tuberculosis.[1]

Detection and treatment are the primary focus in the control of tuberculosis worldwide. A patient infected with active pulmonary tuberculosis may infect 10-15 people a year if left untreated, making it imperative that tuberculosis is diagnosed and treated as soon as possible.[4] The WHO sponsored DOTS program (Direct Observation Treatment Strategy) identifies an estimated 53% of new sputum microscopy positive TB cases [5]. In a 2003 report, Mark Perkins of the Foundation for Innovative New Diagnostics (FIND) identified the need for a "dedicated point of care device" that requires "minimal skill requirements" for the rapid detection of TB.[2]

Sputum smear microscopy, the current method of diagnostic, produces a high rate of false negative results. This high frequency of false negatives is largely because identifying bacilli on stained slides with light microscopy is a highly subjective process, based on the experience of the technician, technician fatigue after a day of continual reading, the rarity of the bacteria, the presence of stained objects that are not TB, inconsistencies in staining, and the quality of the sputum sample.[3]

"This [device] would be an important step forward and immediately applicable."

- Dr. Don Enarson of the International Union Against Tuberculosis and Lung Disease,

Focusing

- Utilizes an autocorrelation based function to obtain a focus score
- Course and fine focus returns the z-axis position with the highest focus score

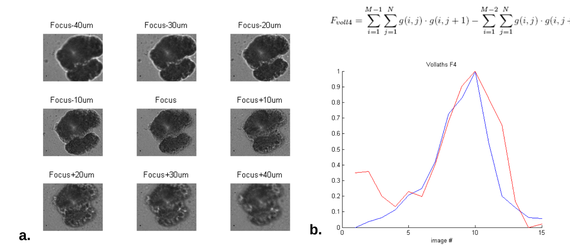
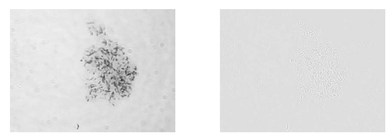


Figure 8: Focusing process. (a) series of images taken during focusing, (b) focus curve generated using a Voll4 algorithm

Image Processing

- Relies heavily on color segmentation
- Uses morphological opening to remove misidentified pixels
- Size and shape analysis may need to be implemented



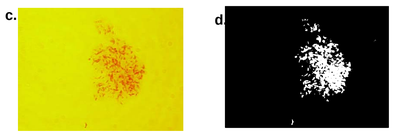


Figure 9. Identification of *M. Tuberculosis* bacilli**.**
(a) Green LED image, (b) Red LED image,
(c) Pseudocolor image, and (d) Color segmentation

Performance Analysis

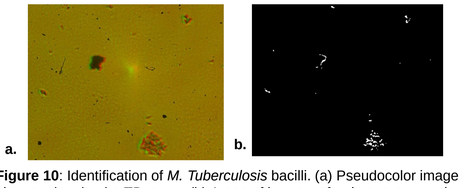


Figure 10: Identification of *M. Tuberculosis* bacilli. (a) Pseudocolor image of a picture taken by the TB tester, (b) Areas of interest after image processing

Major issues that still exist in the prototype:

- Misalignment of LEDs
- Image processing not specific enough (false positives)
- Resolution is insufficient to identify a single bacilli

Selected Bibliography

[1] WHO Report 2005, Global Tuberculosis Control

[2] Perkins, Mark, MD. Diagnostics Working Group Presentation. 29 October 2004.

[3] Toman, K, "What Are the Main Causes of False-positive and False-negative Sputum Smears?", Tuberculosis: Case Detection, Treatment, and Monitoring, 2nd Edition, p.23

[4] Advanced Course on AFB Microscopy: Diagnosis of Pulmonary Tuberculosis. 2003.

[5] "Tuberculosis Fact Sheet". WHO. March, 2006.