Design and Validation of a Low-Cost Microscope for Diagnostics in the Developing World

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Introduction

Many infectious diseases prevalent in the developing world, including malaria and tuberculosis, are difficult to diagnose on the basis of symptoms alone but can be accurately detected using microscope examination. Currently the expense, size, and fragility of optical microscopes impede their widespread use in resource-limited settings. Addressing these obstacles facing microscopy in the developing world is a pressing need; over 800,000 people, primarily children in Africa, die annually of malaria, and more than 1,500,000 people die annually of tuberculosis [1][2]. The aim of this study is to design and validate a microscope for use in the developing world that combines high-resolution imaging, extreme affordability, and long-term durability.

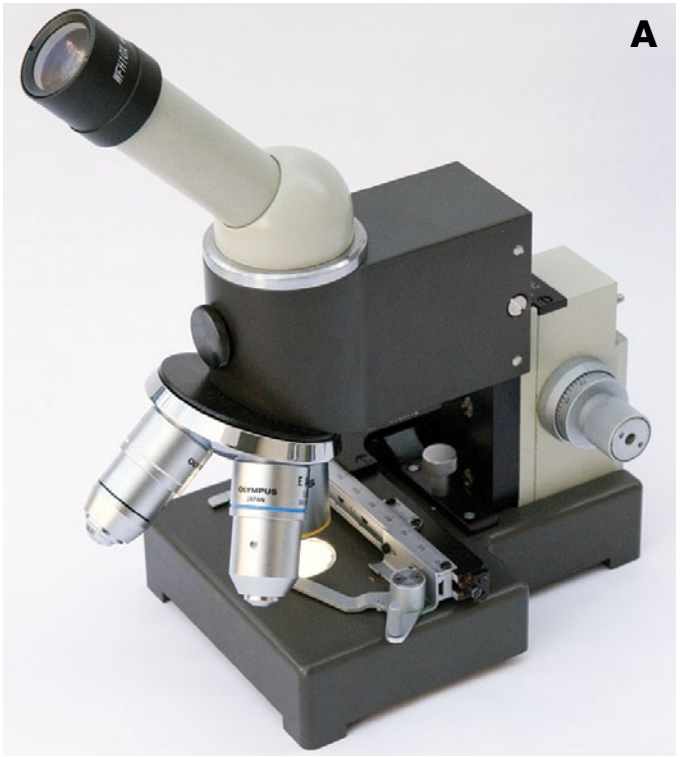
Methods

An optical microscope with bright-field and epi-fluorescence capabilities was designed with a 10x ocular and 10x, 40x, and 100x (oil immersion) objectives (Figure 1). For bright-field imaging, light emitting diodes (LEDs) and high-dispersion holographic diffuser film were used to produce 1.4 numerical aperture Köhler-equivalent illumination. For epi-fluorescence imaging, a 460-nm blue LED, matched with dichroic and colored glass filters, is located in the black horizontal component to which the nosepiece and monocular are attached. The eyepieces and objectives are interchangeable with others that meet the DIN standard, and a binocular head is now available. Components for the initial 25 prototypes were designed by D-Rev and custom machined in California. Leaders of the project are now seeking a manufacturer for volume production.

Three pathologists and two microbiologists evaluated the performance of the scope in the diagnosis of six unknown slides containing Wright-Giemsa stained peripheral blood smears for bright-field detection of *plasmodium* (malarial parasites), Kinyoun stained sputum smears for bright-field detection of *mycobacterium tuberculosis*, and auramine O stained sputum smears for fluorescent detection of *mycobacterium tuberculosis* (Figure 2).

Results

All five pathologists and microbiologists made the correct diagnosis on all six unknown slides used for initial validation



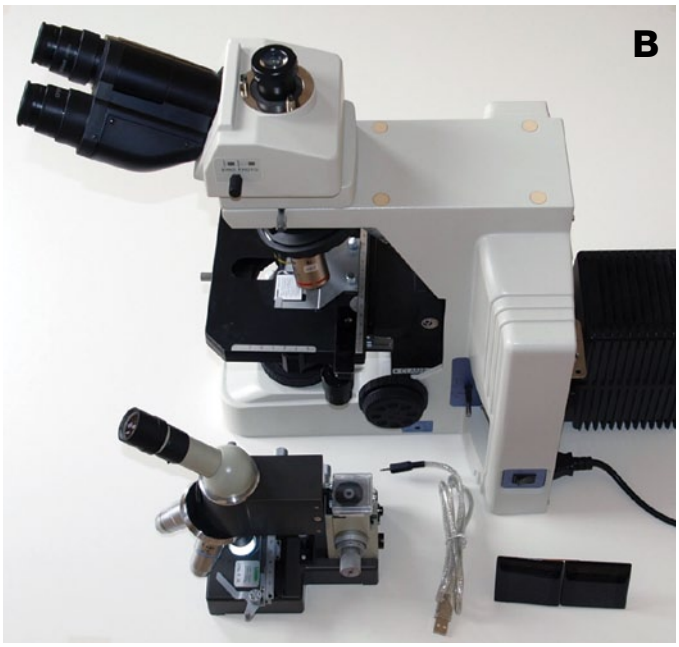


Figure 1: (A) Prototype of the compact, low-cost microscope with both bright-field and epi-fluorescence illumination. (B) Prototype microscope next to Nikon Eclipse E-600.

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of the microscope (100% concordance). By eliminating the precision-aligned optical glass elements used in traditional optical microscopes, the cost of the brightfield illumination system is reduced to less than $5. The total estimated cost of production is under $150 for brightfield illumination and under $200 with epi-fluorescence illumination. Inexpensive stains are available for imaging of tuberculosis and malaria under bright-field (Ziehl-Neelsen and Giemsa respectively) and under fluorescence (auramine O and acridine orange, respectively). The estimated cost per smear is $0.07 (comprised of $0.05 for each glass slide and $0.02 for staining chemicals).

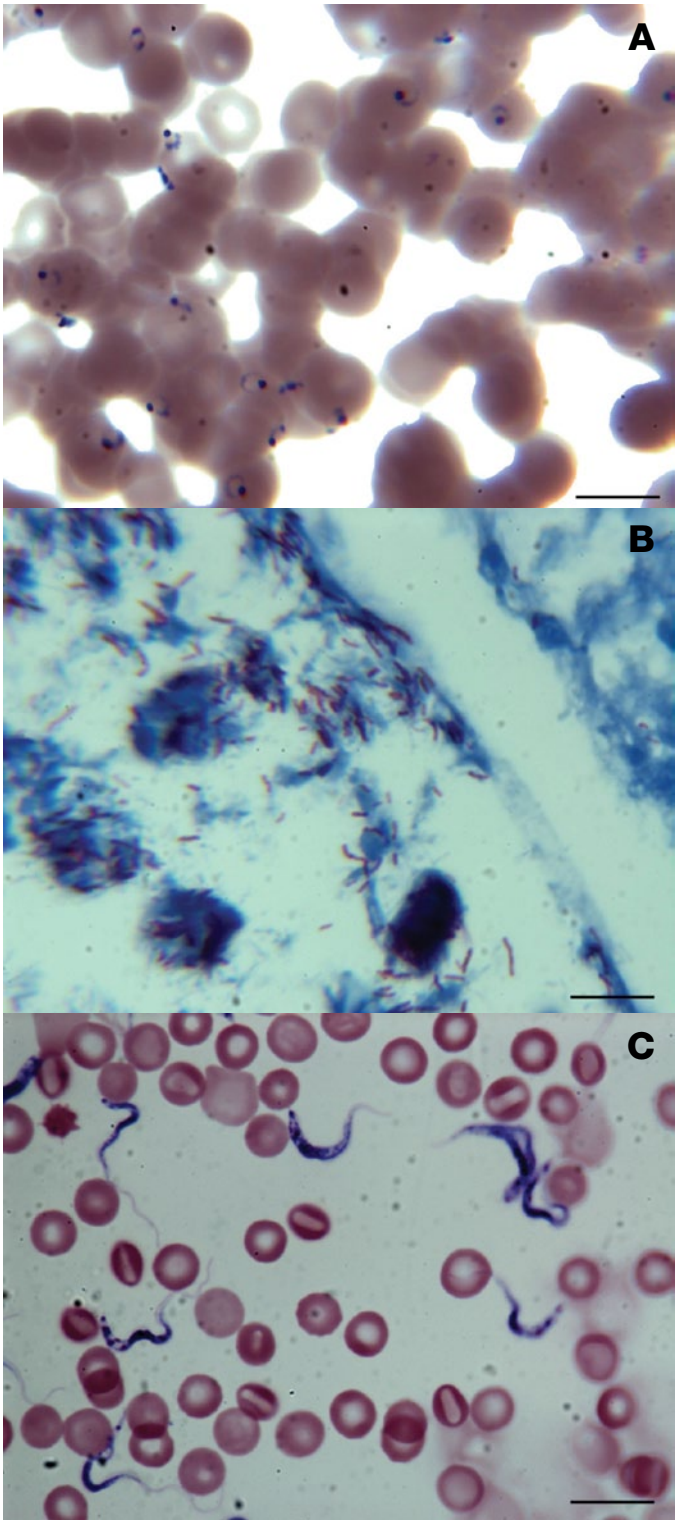

Figure 2: Micrographs taken with the prototype low-cost microscope. (A) Plasmodium falciparum (malarial parasites) in a peripheral blood smear. (B) Mycobacterium tuberculosis in a sputum smear. (C) Trypanosoma brucei gambiense (West African sleeping sickness parasites) in a peripheral blood smear. Scale bar = 10 μm.

The microscope has been designed for resource-limited settings. Operation in clinics lacking consistent access to electricity is aided by the fact that the scope can be charged by a small solar module as well as a wall outlet. Additionally, LED illumination enables low-power consumption: less than 1 W for bright-field imaging and for epi-fluorescence imaging. LEDs also provide far greater lifetime than conventional illumination sources. In conventional fluorescence imaging, the need for frequent replacement of mercury or xenon arc lamps incurs a substantial cost (estimated at $1,500 to $3,000 per year) and requires ready availability of replacement bulbs [3]. In contrast, the new scope's LED illumination has a lifetime of over ten thousand hours, and the amortized cost of replacement is expected to be less than $2 per year. Additionally, no alignment of condenser elements is required in the scope's bright-field illumination system, an important advantage in the developing world where there is often limited technical support for microscopy. For portability, the microscope is compact (6" by 7" by 9") and lightweight at 6 lbs.

Enabling fluorescence imaging provides several benefits, especially for the diagnosis of tuberculosis. A review of studies comparing fluorescence and bright-field screening of tuberculosis found that use of fluorescence increased sensitivity by an average of 10% [4]. Fluorescence imagining enables use of lower magnification, which reduces screening times [4]. This is particularly significant for overburdened clinics in the developing world, where technicians frequently spend less time than recommended examining a slide before declaring it negative, resulting in a high rate of false negatives [5].

Conclusions

A compact, high-resolution microscope with bright-field and epi-fluorescence capabilities can be built for less than $200. Preliminary testing suggests that the microscope enables accurate and inexpensive diagnosis of tuberculosis and malaria. Field validation of the microscope, along with testing of the diagnosis of other tropical diseases, will be conducted in conjunction with partner organizations in the developing world. MT

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