Affordable Rapid Diagnostic Tests for Malaria

Christopher DeFrancesco, Christopher Lacko, Matthew Ondeck, Keshav Raghavan, Marianna Sofman
Dr. James Antaki, Dr. Alberto Gandini

BIOMEDICAL ENGINEERING
Carnegie Mellon University

Tropical Health Systems

Executive Summary

- Malaria constitutes a major global health problem that is endemic in 100 countries globally
- This tropical disease places a heavy financial burden, not only in third-world countries of Africa but also on the United States
- Rapid Diagnostic Tests (RDTs) are currently used because they are accurate and require little training to administer
  - However, they are unable to detect parasite levels when below 100 per µL of blood, at early stages of malaria
- Our microfluidic device takes advantage of the unique magnetic properties of parasitic cells to concentrate malarial cells for better diagnostic capabilities
  - Higher sensitivity than traditional RDTs
  - Yields a rapid diagnostic result within minutes
  - Bypasses necessity of skilled technicians or a central laboratory
  - Inexpensive and effective method of detection suitable for global distribution
  - Allows for possibility of distinguishing malarial infection, particularly *Plasmodium Falciparum*

Problem and Clinical Need

- Malaria is one of the greatest global health problems
  - Tropical disease, predominantly common in children
- Africa contains 44 out of the 100 malaria-endemic countries
  - Accounts for the majority of global malaria cases (86%) and deaths (91%) [1]
  - 300-500 million cases of malaria occur per year globally, with 900,000 deaths
  - A child dies of malaria every 45 seconds in Africa
- Problem:
  - Lack of affordable devices that can diagnose malaria at its early stages
  - Poor availability and processing time of microscopy labs
  - Low parasite sensitivity in early stages

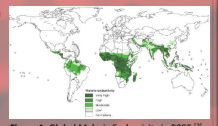


Figure 1: Global Malaria Endemicity in 2005 [2]

Description of Market

- Market in Africa:
  - Accounts for approximately 40% of public health expenditures
  - Annual cost of $12 billion, 1.3% of the continents GDP
- Market in United States:
  - President's Emergency Plan for AIDS Relief (PEPFAR) was launched in 2003, including malaria in its mandate
    - Goal of reducing malaria-related deaths by 50% in 15 focus countries
    - $1.2 Billion in funding for 2006-2010
    - $5 Billion authorized in 2008 for fiscal years 2009-2013

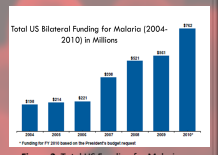


Figure 2: Total US Funding for Malaria

Description of Design

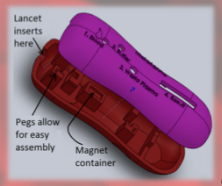


Figure 3: SolidWork file of casing for device

Figure 4: Working prototype of microchannel incorporating nickel grid and antigen strip

Casing Design: (Figure 3)

- Casing designed using SolidWorks
- Prototype constructed via Rapid 3D Prototyping

Microchannel Design: (Figure 4)

- Micro channel laser etched into Poly Lactic Co-Glycolic Acid PLGA
- Etched PLGA plate, with nickel grid, saturation pad, and antigen strip, is heat-bonded to a Polyethylene Terephthalate (PETG) top cover

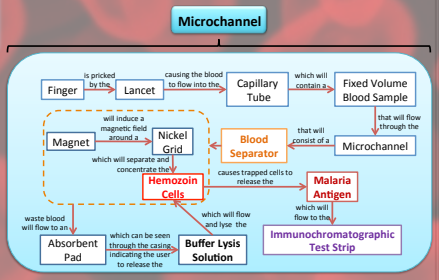
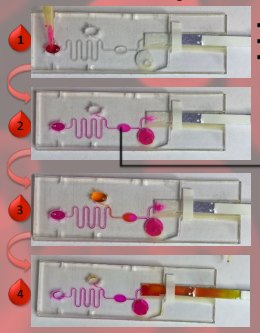


Figure 5: Flow diagram describing overall design incorporating casing and microchannel prototypes

Still Frames of Working Device



- **Frame 1**: Blood enters reservoir and migrates through microchannel via capillary action
- **Frame 2**: Fiberglass becomes saturated with waste blood
- **Frame 3**: Buffer solution is released lysing concentrated parasitic cells
- **Frame 4**: Released antigen flows to immunochromatographic strip

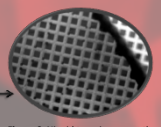


Figure 6: Ni grid trapping magnetic nanoparticles

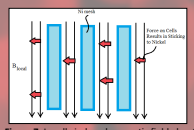


Figure 7: Locally induced magnetic field about the Ni grid formed by permanent magnet

- Malarial parasite digests the hemoglobin of red blood cells
  - Fe^{2+} of remaining heme group becomes oxidized to form Fe^{3+} of paramagnetic hemozoin
  - Resulting parasitic cells have greater magnetic susceptibility
- Permanent magnet and nickel grid form a magnetic field resulting in the magnetic attraction of hemozoin (simulated in Figure 6)
- Antigen is released upon lysis of parasitic cell by buffer solution

What is Novel About the Device?

- Incorporates the known magnetic properties of malarial red blood cells in order to concentrate parasites in a way that has not been done before
  - Earlier diagnosis of malaria over traditional RDTs
  - Minimal blood contacting components provides for a safer handling of devices
  - Cost effective, easily mass produced, and robust for global distribution
  - Improved ergonomics for ease of use
- Combines several systems into one unique all-inclusive diagnostic device:
  - Lancet- facilitates the withdrawal of an appropriate amount of blood
  - Microfluidics- blood flows through device via capillary action
  - Nickel grid- concentrates malarial blood
  - Fiberglass- absorbs waste blood to concentrate antigen
  - Buffer Release- lyses concentrated antigens
  - Immunochromatographic Test Strip-detects malarial antigen with greater sensitivity

Estimation of Product Costs

- Costs are extremely important in developing medical devices for third-world countries and developing nations
- Key Material Costs: PETG and PLGA Plastics, Nickel Grid, Lancets, External Casing Plastic, Plastic Vacuum Bagging, Cardboard for Packaging, Magnet, Buffer Solution, Fiberglass
- Key Manufacturing Costs: Heavy Duty Laser Etcher, Molding Tools for External Casing, Packaging Machines, Heat Press
- Miscellaneous Costs: Electricity, Shipping Costs, Employee Costs
- Early estimates for main raw materials suggest cost feasibility:
  - PETG Plastic per device: $0.10
  - PLGA Plastic per device: $0.10
  - Lancet per device: $0.08
  - External Casing Plastic: $0.25
  - Ni Grid: $0.28
  - Permanent Magnet: $0.10
  - Immunochromatographic test strip: $ 1.20
- Areas to save costs and optimize design: External Casing with enclosed magnet that acts as a semi-permanent piece; Lowering area of nickel grid, packaging efficiency, potentially will be able to use less antibodies in the test strip due to concentration (the greatest cost of the device).

Anticipated Regulatory Pathway

- Focus on the fastest method to move product to market while still proving safety and effectiveness of device
- Class II Medical Device (non-critical, diagnostic)
- 510(k) Submission Due to Parts of Previous FDA Regulated Devices
- Regulatory Division of Immunology and Hematology Devices
- Office of In-Vitro Diagnostic Device Evaluation and Safety
- Center for Devices and Radiological Health
- Planned post market analysis and surveillance