American Research Journal of Biomedical Engineering

Volume 3, Issue 1, 1-5 Pages
Research Article | Open Access

AMERICAN RESEARCH JOURNALS
An Academic Publishing House

Proposed Non Invasive Detection of Malaria by Spectral Analysis of Light of Varied Wavelengths through the Blood

Adegbenro Sunday Ajani[a]* , Olusoji Amos Ogunbode[b], Godwin Babatunde Egbeyale[a], Olaoluwa Peter Oyero[a], Adebayo Segun Adewumi[b] , Oluwatayo Sandra Ajani[c], Abdullahi Nasir Galadima[a], Paulina Funmi Yirenkyi[c]

[a]Kwara State University, Department of Physics and Material Sciences, Malete, Ilorin, Nigeria.
[b]*Ladoke Akintola University of Technology, Department of Pure and Applied Physics, P.M.B 4000 Ogbomoso.
[c]Ladoke Akintola University of Technology Teaching Hospital, Ogbomoso, Nigeria.

ABSTRACT

Malaria is a significant public health problem in many parts of the world. Accurate diagnosis and control currently relies on the invasive detection of parasitemias in the blood samples. This technique is invasive, increases risk of blood-borne disease transmission, and is uncomfortable for the patient. This research summarizes the diagnostic techniques that have been used to detect malaria in blood samples and their limitations. It is important to understand that noninvasive testing of malaria can provide adequate check and control high malaria rate by promoting early detection and treatment from mild to moderate to serve cases and noninvasive detection will never be achieved without good calibration approach. At this point, we are far away from reaching the aim of noninvasive detection of malaria through blood in the body, with many technical problems yet to be resolved. This research provides information that may be useful for future development of highly efficient non-invasive malaria detection methods.

KEYWORDS: *Noninvasive; Plasmodium spp; Malarial.*

INTRODUCTION

Malaria is preventable and treatable yet the disease continues to claim nearly half a million lives a year because of inadequate clinically available tools to test for malaria at one convince. According to the latest data from WHO, there were an estimated 216 million cases of malaria worldwide in 2016, marking a return to 2012 levels [1]. Non invasive testing of malaria can provide adequate check and control high malaria rate by promoting early detection and treatment from mild to moderate to serve cases. Encouraging investments in the development and deployment of a new generation of malaria tools is key to achieving the 2030 global malaria targets. Urgent action is required to get the global fight against malaria back on track[16]. On World Malaria Day 2018, WHO is calling for expanded coverage of proven tools that we know to work – tools that have already dramatically lowered the global burden of malaria, investments in the research and development of new tools to accelerate the pace of progress, to reduce the serve effect of malaria like deaths. The African Region continues to bear 90% of malaria cases and 91% of malaria deaths worldwide [12] Consequently, new techniques have been employed to develop a noninvasive device for blood testing of malaria, and the effort to give a better life to patients by developing their comfort for easy testing of malaria through with non invasive technology, with little fears of medical problem and dying related to this disease. For these reasons, at present the noninvasive technology is the most needed and demanding research topic in biomedical science engineering and its related areas [13, 14, and 15]

VARIOUS DIAGNOSTIC TECHNIQUES FOR IDENTIFICATION OF MALARIA

Recent developments in diagnostic techniques for detection of malaria, give the following list of diagnostic techniques to detect the malaria.

Manual Diagnosis

Manual diagnosis

This remains the most merit way to diagnose malaria. However, the technique is requiring considerable time consuming and need skilled expertise. The two long establishment techniques for manual diagnosis which are clinical diagnosis and microscopic diagnosis

Clinical diagnosis

This is the least expensive and widely used method. It is based on physical findings at examination derived from patient's signs and symptoms. There are certain clinical algorithms

to be followed for diagnosis but the method requires only a minimally trained examiner[17]. However the method shows very low specificity and can lead to over diagnosis due to the non-specific nature of signs and symptoms. Even though the clinical diagnosis often shows around 100% success rate, the overlapping of malaria symptoms with other tropical diseases impair the diagnostic specificity and hence the accuracy can be reduced. Therefore it is always advisable to combine this method of diagnosis with some kind of laboratory diagnostic measurements [14]

Microscopy

This is standard for visualization of parasitemiamiamias in blood smears with an analytical sensitivity under normal circumstances approximately tenfold inferior than that of molecular testing [5]. Microscope has been popularly used as a diagnostic tool in peripheral health centres for several reasons, including availability [6]. However, the quality of such diagnosis depends on the availability and skills of trained microscopists, which might not always be available in the poorer areas, where malaria is endemic. Microscopic examination of malaria is conducted on stained blood films using Giemsa, Wrights or Field stains, out of which microscopic detection and identification of the parasitemia on Giemsa stained thick or thin blood films is considered to be the gold standard for laboratory diagnosis [8]. Microscopic malaria diagnosis is by far considered to be the most effective diagnostic method, but it is highly time-consuming, labor intensive and requires special training. The effectiveness can be affected by poor skills maintenance, slide preparation, quality of the laboratory facilities are required for the effective condition of the microscope. Furthermore, the accuracy of the system solely depends on the expertise of the microscopist [9, 24 and 27].

Molecular Diagnosis

Molecular diagnosis is performed through the use of Polymerase Chain Reaction (PCR) which is a confirmatory test for malaria. The method is used to identify the presence of parasitemias and for species recognition by extracting the genomic DNA of *Plasmodium Spp* and amplify them. The procedure undertakes two-step nested PCR by first amplifying the DNA with genus specific primers followed by species specific primers for species identification [18, 25,27 and 28]. Molecular diagnosis is more sensitive than microscopic examination for low level and mixed infections. Although, the procedure is expensive, including access to reagents and cost of labor and hence the implementation is difficult in laboratories located in areas where there is lacking sufficient money to live at a standard considered comfortable and where malaria is endemic [10, 29, 30, 32]

Rapid Diagnostic Tests

Rapid diagnostic tests (RDT) are immunochromatographic (separation of antigens or antibodies) methods based on detection of malarial antigens, where particular antibodies are used to confirm the present of antigens in peripheral blood. Both asexual and sexual form of *plasmodium Spp* produces parasitemia lactase dehydrogenase (pLDH) antigen which is identified during the tests. The procedure is useful for discriminating *P.falciparum* from other species but cannot recognize others specifically [19, 33,34 and 35]. These tests are mainly used for research studies and even though they produce results faster than microscopic examination, the recognition rate is impaired for low level infection and hence is not very reliable. Several factors including manufacturing process and laboratory and other environmental conditions may affect the performance of the tests. It is usually suggested in situations such as outbreaks or occupational exposure where microscopic examinational capabilities exceed [22].

Automated Diagnosis Using Digital Slide Analysis

This diagnosis technique is the latest addition to the several detection techniques for malaria. The method works on the principle of digitizing the whole microscopic examination process with little of human interference. This emulates all the methods and techniques of manual microscopy and incorporating it into a machine-vision platform. The diagnostic system consists of hardware and software components [36]. The hardware requires imaging equipments such as a slide scanner, digital microscope that has provisions for auto-focusing, automated or semi-automated field selection, slide movements and processing devices such as a computer, mobile phone or tablet. The software requires robust image processing algorithms for pre-processing and final diagnosis of the infection. Apart from the initial set-up cost, the automated system needs only basic training and possesses consistent timing with accuracy reaching up to that of manual diagnosis [38]. These algorithms need to achieve diagnostic accuracy approaching that of an experienced pathologist yet be incorporated into a platform used by technicians with only basic training. In addition, the time taken should not be longer than that taken using manual methods. The methods can be used to for quantitative analysis, research, peripheral blood screening, post treatment diagnosis as well as an alternative or secondary option for manual microscopy [21].

DRAWBACK OF APPLICATION OF INVASIVE TECHNIQUE AND NON-INVASIVE AS POSSIBLE SOLUTION

The diagnostic technique technologies and limitations for invasive detection of malaria are discussed. These barriers include: pain associated with finger pricking, fear of contracting blood-borne diseases, proper disposal of used needles, physical damage and environmental, susceptibility with RDT test strips need for supervision with RDTs to ensure correct interpretation of results and adherence to hygiene practices and high cost. Unfortunately none of these technologies have produced a commercially available

clinically reliable device without involving the introduction of instruments or other objects into the body to extract blood for the test (invasive detection of malaria). Non-invasive approaches to test malaria through blood will help to overcome these problems. Accurate, effective, cheap and non invasive diagnosis is the first step to further pursue efforts to eliminate and reduce the global burden of malaria by 90% in 2030[23, 28 and 29]. The benefits of non invasive detection of Malaria are: no need to draw blood from patients (safety), less expensive, quick and reliable diagnosis, can be performed in absence of medical professionals, and ability to be shared among affected populations.

Good Calibrations approaches and its stability for various conditions is an important factor to accomplish clinical desired aim of a successful noninvasive detection of plasmodium spp causing malaria.

The fault-finding parameters are stated below:

i) To measure and record good quality of output signals with low interference (Signal to noise ratios)

ii) Vigorous calibration procedures for the experimental technique

iii) Filtering to prevent unwanted components or features from signal bearing the parasitemias

iv) Ability to produce repeatable and consistent output results

PRINCIPLE OF MEASUREMENT

The Lambert-Beer law explains for the intensity change on the light path by a specific wave number of the wavelength. Where the absorption is represented as A and the wave number is given as (v), The expression is represented as follows;

$$A(v) = -\log I(v) / Io(v) \qquad (1)$$

Where (I_0) represents the intensity of incident light of the medium, (I) denotes the intensity of the light after it has passed through the sample at specific wave number (v) [7].

PROPOSED METHODOLOGY

Figure 1.From the sketch of a proposed noninvasive testing of malaria in the blood device. The light source unit (Multi-Modal Light emitting diodes) provides light in the Infra red, visible light and near UV region. It is being focused on the arm. The output transmitted bio-signal is received by the Multi-Modal Photodetectors (sensors). Amplification is incorporated to magnify the feeble bio-signal. Filtering is introduced to prevent unwanted signals or features from the feeble bio-signal. Alpha Numeric keypad uses to send message to the signal processing unit .The Signal Processing Unit helps in quantifying the plasmodium spp related information and after suitable signal processing and conditioning the desired plasmodium parasitemia displayed on the Liquid Crystal Display.

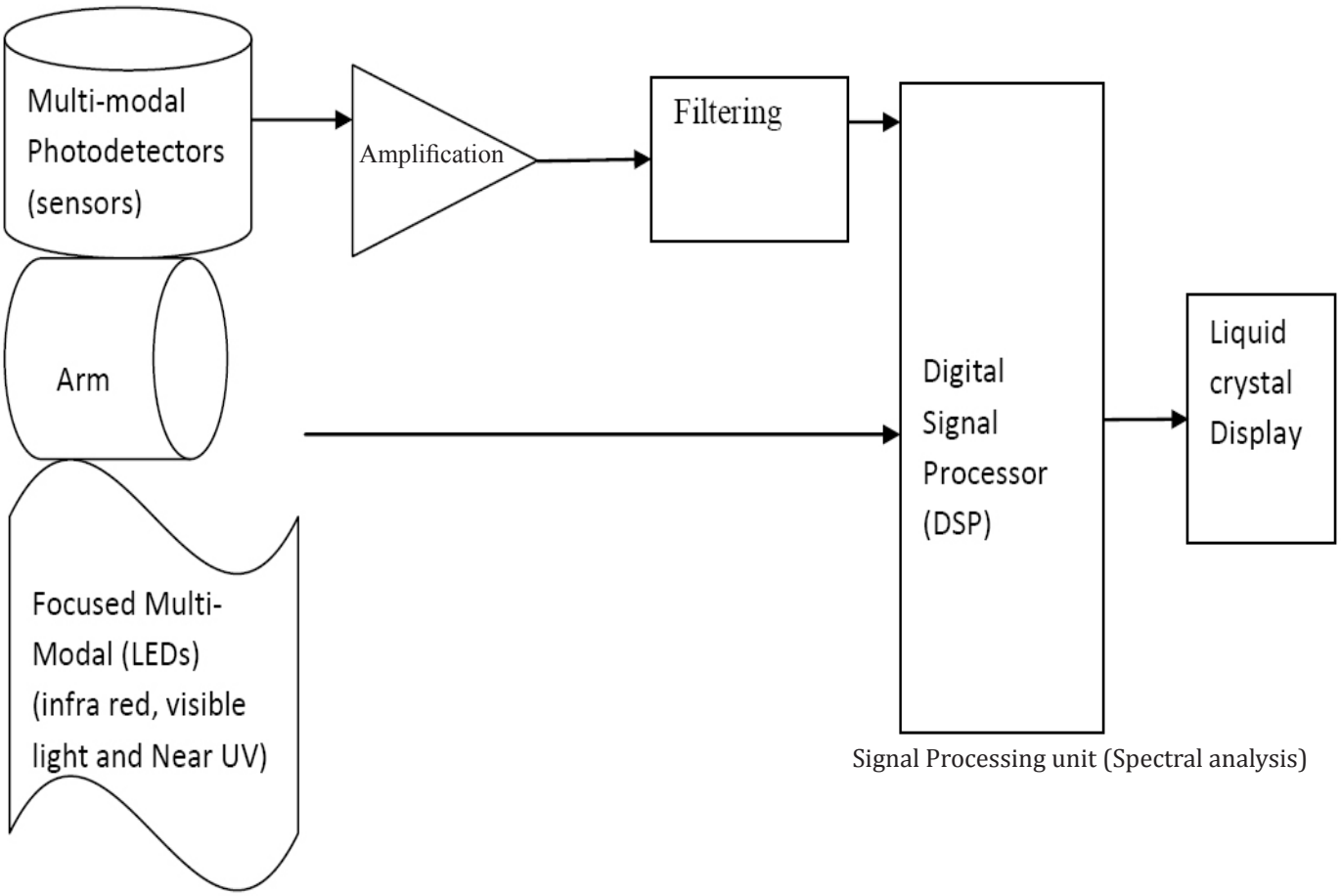

Figure1: Block diagram of the proposed non-invasive device for testing of malaria

CONCLUSION

Expensive and painful ways associated with invasive technique of diagnosis malaria demand urgent development of new devices that could challenge and have better improvement in term of less-expensive, effective and painless method of detection of malaria from patients' blood. Designing and development of noninvasive Malaria detection technology will yield a novel edge for continuous prevention of malaria in order to detect accurate plasmodium spp status in patients, promoting and increasing patient compliance, securing blood testing for malaria, and reduces work load over hospital workers, with easy test control regimen. It can provide adequate check and control high malaria rate by promoting early detection and treatment from mild to moderate to serve cases

RECOMMENDATION

The authors would like to recommend the light source unit to provide light in the Infra red, visible light and near UV, multi-modal Photodetectors (or suitable sensors) should be used and incorporation of suitable filtration and amplification circuits in design and development of non-invasive method of malaria detection system, in order to achieve clinical output result.

ACKNOWLEDGMENT

The authors wish to acknowledge the contribution of the following people: Professor Adebayo Olaniyi Aina, Mr T. Oladosu and Mrs Jimoh Taiwo Faidat for their contributions

REFERENCES

1. WHO, World Malaria Day 2018 www.who.int/campaigns/malaria-day/2018/en/
2. A. Tura, A. Maran and G.Pacini, "Non-invasive glucose monitoring: Assessment of Technologies and devices according to quantitative criteria", Diabetes Research and Clinical Practice, Vol.77, 2007, pp.16-40.
3. O.S.Khalil, Non-invasive glucose measurement technologies: an update from 1999 to the dawn of the new millennium, Diabetes Technol. Ther.6 (2004), 660-697.
4. R.W. Waynant, V.M. Chenault, Overview of non-invasive fluid glucose measurement using optical techniques to maintain glucose control in diabetes mellitus. (http://www.ieee.org/ organizations/pubs/newsletters/leos/apr98/overview.htm.
5. Hofmann N, Mwingira F, Shekalaghe S, Robinson LJ, Mueller I, Felger I. Ultra-sensitive detection of *Plasmodium falciparum* by amplification of multi-copy subtelomeric targets. PLoS Med. 2015;12:e1001788.
6. WHO. New perspectives malaria diagnosis. Geneva: World Health Organization; 2000.
7. S. Radel. M. Brandstetter, B.Lendl, 'Obrservation of particles manipulated by ultrasound in close proximity to a cone-shaped infrared analysis probe', Ultrasonic 50(2010), pp.240-246
8. Noppadon Tangpukdee, Chatnapa Duangdee, Polrat Wilairatana, and Srivicha Krudsood,"Malaria Diagnosis: A Brief Review", Korean Journal for Parasitology; Pages: 93–102.Published online 2009 May 26. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2688806/, June 2009
9. Chansuda Wongsrichanalai, Mazie J. Barcus, Sinuon Muth, Awalludin Sutamihardja, and Walther H. Wernsdorfer," A Review of Malaria Diagnostic Tools: Microscopy and Rapid Diagnostic Test (RDT)", Defining and Defeating the Intolerable Burden of Malaria III: Progress and Perspectives: Supplement to Volume 77(6) of American Journal of Tropical Medicine and Hygiene. Northbrook (IL): American Society of Tropical Medicine and Hygiene, December 2007.
10. Stephanie P. Johnston, Norman J. Pieniazek, Maniphet V. Xayavong, Susan B. Slemenda, Patricia P. Wilkins, and Alexandre J. da Silva ,"PCR as a Confirmatory Technique for Laboratory Diagnosis of Malaria", Journal of Clinical Microbiology, 44(3): 1087–1089. PMCID: PMC1393165, March 2006;
11. Saumya Kareem Reni, Automated Low-Cost Malaria Detection System in Thin Blood Slide Images Using Mobile Phones, University of Westminster Faculty of Science and Technology 2014
12. Snounou G, Viriyakosol S, Zhu XP, Jarra W, Pinheiro L, do Rosario VE, et al. High sensitivity of detection of human malaria parasitemias by the use of nested polymerase chain reaction. Mol Biochem Parasitol. 1993;61:315–20.
13. Perandin F, Manca N, Calderaro A, Piccolo G, Galati L, Ricci L, et al. Development of a real-time PCR assay for detection of Plasmodium falciparum, Plasmodium vivax, and Plasmodium ovale for routine clinical diagnosis. J Clin Microbiol. 2004;42:1214–9.
14. Beadle C, Long GW, McElroy PD, Hofman SL, Long GW, Weiss WR, et al. Diagnosis of malaria by detection of Plasmodium falciparum HRP-2 antigen with a rapid dipstick antigen-capture assay. Lancet. 1994;343:564–8.
15. Britton S, Cheng Q, McCarthy JS. Novel molecular diagnostic tools for malaria elimination: a review of options from the point of view of high-throughput and applicability in resource limited settings. Malar J. 2016;15:88.
16. Okell LC, Ghani AC, Lyons E, Drakeley CJ. Submicroscopic infection in Plasmodium falciparum—endemic populations: a systematic review and metaanalysis. J Infect Dis. 2009;200:1509–17.
17. Singh B, Bobogare A, Cox-Singh J, Snounou G, Abdullah MS, Rahman HA. A genus- and species-specifc nested polymerase chain reaction malaria detection assay for epidemiologic studies. Am J Trop Med Hyg. 1999;60:687–92.

18. WHO. Malaria policy advisory committee meeting: meeting report, Octo ber 2017. Geneva: World Health Organization; 2017. https://apps.who.int/ iris/ handle/10665/255044. Accessed 12 June 2019.

19. Lloyd YM, Esemu LF, Antallan J, Thomas B, Tassi Yunga S, Obase B, et al. PCR-based detection of Plasmodium falciparum in saliva using mitochon drial cox3 and varATS primers. Trop Med Health. 2018;46:22.

20. Buppan P, Putaporntip C, Pattanawong U, Seethamchai S, Jongwutiwes S. Comparative detection of Plasmodium vivax and Plasmodium falciparum DNA in saliva and urine samples from symptomatic malaria patients in a low endemic area. Malar J. 2010;9:72.

21. Al-Shehri H, Power BJ, Archer J, Cousins A, Atuhaire A, Adriko M, et al. Non-invasive surveillance of Plasmodium infection by real-time PCR analysis of ethanol preserved faeces from Ugandan school children with intestinal schistosomiasis. Malar J. 2019;18:109.

22. Oriero EC, Jacobs J, van Geertruyden JP, Nwakanma D, D'alessandro U. Molecular-based isothermal tests for feld diagnosis of malaria and their potential contribution to malaria elimination. J Antimicrob Chemother. 2015;70:2–13.

23. Moody A. Rapid diagnostic tests for malaria parasitemias. Clin Microbiol Rev. 2002;15:66–78.

24. Wilson ML. Malaria rapid diagnostic tests. Clin Infect Dis. 2012;54:1637–41.

25. Fagbamigbe AF. On the discriminatory and predictive accuracy of the RDT against the microscopy in the diagnosis of malaria among under-fve children in Nigeria. Malar J. 2019;18:46.

26. Cook J, Xu W, Msellem M, Vonk M, Bergström B, Gosling R, et al. Mass screening and treatment on the basis of results of a Plasmodium falciparum-specifc rapid diagnostic test did not reduce malaria incidence in Zanzibar. J Infect Dis. 2015;211:1476–83.

27. Tao D, McGill B, Hamerly T, Kobayashi T, Khare P, Dziedzic A, et al. A salivabased rapid test to quantify the infectious subclinical malaria parasitemia reservoir. Sci Transl Med. 2019;11:eaan4479.

28. Sikulu-Lord MT, Maia MF, Milali MP, Henry M, Mkandawile G, Kho EA, et al. Rapid and non-destructive detection and identifcation of two strains of Wolbachia in Aedes aegypti by near-infrared analysis. PLoS Negl Trop Dis. 2016;10:e0004759.

29. Fernandes JN, dos Santos LMB, Chouin-Carneiro T, Pavan MG, Garcia GA, David MR, et al. Rapid, noninvasive detection of Zika virus in Aedes aegypti mosquitoes by near-infrared analysis. Sci Adv. 2018;4:eaat0496.

30. Esperança PM, Blagborough AM, Da DF, Dowell FE, Churcher TS. Detec tion of Plasmodium berghei infected Anopheles stephensi using nearinfrared analysis. Parasit Vectors. 2018;11:377.

31. Ferreira Maia M, Kapulu M, Muthui M, Wagah M, Ferguson H, Dowell F, et al. Detection of malaria in insectary-reared Anopheles gambiae using near-infrared analysis. Malar J. 2019;18:85.

32. Mayagaya VS, Michel K, Benedict MQ, Killeen GF, Wirtz RA, Ferguson HM, et al. Non-destructive determination of age and species of Anopheles gambiae s.l. using near-infrared analysis. Am J Trop Med Hyg. 2009;81:622–30.

33. Lambert B, Sikulu-Lord MT, Mayagaya VS, Devine G, Dowell F, Churcher TS. Monitoring the age of mosquito populations using near-infrared analysis. Sci Rep. 2018;8:5274.

34. Sikulu-Lord MT, Devine GJ, Hugo LE, Dowell FE. First report on the application of near-infrared analysis to predict the age of Aedes albopictus Skuse. Sci Rep. 2018;8:9590.

35. Krajacich BJ, Meyers JI, Alout H, Dabiré RK, Dowell FE, Foy BD. Analysis of near infrared spectra for age-grading of wild populations of Anopheles gambiae. Parasit Vectors. 2017;10:552.

36. Ntamatungiro AJ, Mayagaya VS, Rieben S, Moore SJ, Dowell FE, Maia MF. The infuence of physiological status on age prediction of Anopheles arabiensis using near infra-red analysis. Parasit Vectors. 2013;6:298.

37. Milali MP, Sikulu-Lord MT, Kiware SS, Dowell FE, Corliss GF, Povinelli RJ. Age grading An. gambiae and An. arabiensis using near infrared spectra and artifcial neural networks. PLoS ONE. 2019;14(8):e0209451.

38. Gonzalez-Jimenez M, Babayan SA, Khazaeli P, Doyle M, Walton F, Reedy E, et al. Prediction of malaria mosquito species and population age struc ture using mid-infrared analysis and supervised machine learning. Wellcome Open Res. 2019;4:76.

Citation: Adegbenro Sunday Ajani, Olusoji Amos Ogunbode, et al., "Proposed Non Invasive Detection of Malaria by Spectral Analysis of Light of Varied Wavelengths through the Blood", American Research Journal of Biomedical Engineering, Vol 3, no. 1, 2021, pp. 1-5.