

Performance Evaluation of AiDx assist in the diagnosis of Lymphatic Filariasis (LF) in field settings

A field study conducted by the INSPIRED NWO Project - Dec.2021

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Performance Evaluation of AiDX Assist Device

A field study conducted by the INSPIRED NWO Project - Dec.2021





STUDY GOAL

Assessing efficiency and usability of a developed point-of-care diagnostic device for the detection of parasites.

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SUMMARY

The field study was designed to evaluate the performance of AiDX assist device for the quick screening of microfilaria in blood samples. Urine samples were also screened for the presence of schistosoma ova. 550 blood samples and 97 urine samples were independently examined by expert microscopy. Results obtained will be analyzed and compared with results of the AiDX Assist device on the same sample set. Results will be discussed and published accordingly.

Background of Project partnership

The INSPiRED Project:

INclusive diagno**ST**ics for **P**overty **RE**lated parasitic **D**iseases (INSPiRED) is a research project for development and validation of inclusive, smart, easy to use, cost effective and efficient optical devices for the diagnosis of poverty related parasitic diseases in Nigeria and Gabon. For effective implementation, the INSPiRED project is subdivided into different work packages (WP). While the WP 1 focuses on the development of optical techniques integrated with the data-driven algorithm for the quick screening and detection of parasites in human biological samples particularly in resource-poor settings. The WP 2 & 3 focuses on co-creation of product specifications for the development, adoption and use by the relevant stakeholders. Testing, validation and performance evaluation of new devices is tested and compared with other World Health Organization (WHO) approved reference standard. INSPiRED project is NWO/WOTRO funded and the collaboration thereof includes scientific researchers from the following institutions: Delft University of Technology, Leiden University Medical Centrum, University of Ibadan, CERMEL (Gabon) and University of Lagos.

AiDX Medical BV

AiDx Medical BV (<https://www.aidx-medical.com/>) is a MedTech spin-off start-up founded in early 2019 and is based in Rijswijk. The company focuses on bringing an affordable alternative to standard microscopic examination by optimally addressing all components of the diagnostic cycle. To achieve this, Aidx Medical develops low-cost automated diagnostic microscopes with reliable and fast AI-assisted detection. In 2019, AiDx Medical was selected as one of the winners of the EIT Health Headstart Fund Belgium-Netherlands and received €50,000 in funding. This money was used for the development of an application for malaria diagnostics in low- and middle-income countries, and a minimal viable product was brought to Gabon to be tested in local research laboratories in 2020 and pre-market launch is expected in 2021. AiDx Medical is now looking to expand their market and develop diagnostic microscopes for different indications which could benefit from automated, fast, and reliable diagnosis

Summary of Project partnership

Since AiDX Medical BV is a spin-off startup of the Delft University of Technology, it is part of the INSPiRED project goals to validate the performance and assess the efficiency and usability of the developed point-of-need AiDX Assist device developed for the quick screening of microfilariae in Giemsa-stained human blood samples. The quick screening and detection of Neglected Tropical Diseases are of primary interest

In this project because of their disruptive impact on human and economical productivity particularly in Low-Medium Income Countries.

Application: The future application of the developed AiDX NTDx device aims at the following:

1. Quick screening of group of diseases such as lymphatic filariasis (LF), or elephantitis, Schistosomiasis (both urine and stool), Onchocerciasis, Guinea worm diseases as well as more than a dozen of other diseases currently screened by manual microscopy.
2. Strengthening of the healthcare system: The healthcare system is grossly understaffed particularly in the rural and remote areas. It is part of the goal to provide AiDx diagnostic

assist to areas and locations where technical expertise is relatively scarce as well as the standard laboratories in the urban areas for high diagnostic throughput.

3. Disease mapping for the control and elimination programs: The current global drive for the control and elimination of the NTD's in resource-poor settings is grossly impeded by the lack of accurate data which would help the allocation of the human, material, medical and financial resources to disease endemic areas and communities.
4. Impact assessment: Diverse mass drug administration programs are currently ongoing in Nigeria particularly. Accurate assessment of the impact of treatment on the target population will help to estimate progress or limitations of the treatment plan and protocol. AiDX diagnostic assist aim to complement and contribute to the impact assessment programs by making rapid NTD disease screening available for all.
5. Task shifting: Since the AiDX assist provides expert-independent analysis of blood, urine and stool samples, we envisage that the device at its optimal performance could strengthen task shifting programs such that non-experts such as community health care workers could be easily trained and empowered to perform quick sample screening for NTDs at community and primary health care level.

The AiDX Diagnostic Assist system and specifications

The AiDx NTDx Assist machine is an automated digital microscope that has the capabilities of rapidly screening prepared blood samples for the detection of blood parasites like microfilaria worms, and it can also be used for the detection of Schistosoma eggs in urine samples. Thus, it is an automated microscope designed for the quick detection of parasitic worms in thick and thin blood samples with evidence of detecting other NTDs in urine samples during laboratory testing.

It has the following specifications:

- Technology: Artificial Neural Network
- Supported stains: Wright – Giemsa
- Slide scan: Automatic scanning of user definable areas of a slide (Typical fields of view = 64-120)
- Automated scanning in the x-y and z direction
- Automated focusing
- Body fluid: Blood
- Turnaround time (scanning and data processing) = 10 minutes/ sample
- Fast and easy access to data
- Result is presented to medical expert for conclusive diagnosis.

Research questions

- What is the performance capacity of AiDx Assist device for the quick screening of blood and urine samples for Lymphatic filariasis, Schistosomiasis as compared to microscopy?
- What is the user-related capacity to conduct sample preparation, testing and diagnosis using the AiDx Assist device?
- What are the context-related factors that can improve the acceptability of the AiDx Assist device?
- What factors can contribute to the acceptability and adoption of the AiDx Assist device by end-users?
- To what extent can the AiDX device enhance task shifting such that quick diagnosis of prevalent NTD's can be shifted to non-expert health care workers at the community level?
-

Study Objective

The overall aim of the study is to assess the Performance, Usability and Acceptability of the AiDx Assist device for the detection of parasites.

The specific objectives are to:

1. Test and validate the AiDx Assist device for detecting Lymphatic filariasis and Schistosomiasis in the Nigerian context.
2. Compare the diagnostic performance of AiDx Assist device to standard microscopy. Performance metrics to be measured will include, sensitivity, specificity, negative predictive value, time efficiency.
3. Assess the usability of the AiDx Assist device in respect to sample preparation, testing and diagnosis.
4. Assess the acceptability of the AiDx Assist device in respect to sample preparation, testing and diagnosis
5. Identify potential factors that could improve the usability and acceptability of the AiDx Assist device.
6. Apply the results obtained to propose modifications to optimize the design of the device and process of the AiDx Assist device.

Planned Sample collection sites and protocol

Due to the current insecurity of the region the sample collection was restricted to the Ward 7 of the Oluyole Local Government Area. Site was recommended by the State NTD officer who worked closely with Prof. Oladimeji Oladepo of the Public Health and promotion department at the University College Hospital Ibadan. Sample collection was restricted to the Ajoofeebo community. The area has a lot of water bodies and the location was known to have significant prevalence of urinary schistosomiasis according to the data obtained from the state.

Current intervention

It was also stated that the area is an active intervention program and treatment ongoing in the area. Treatment has been active for the past 3 – 4 years. The intervention program allows us to also evaluate the impact of the ongoing intervention to a very limited extent. Although this is not part of our study goal, we could gain some insights into the efficacy of the intervention program based on the results of microscopy as compared to AiDX devices on the collected urine samples.

Ethical approval

The appropriate ethical approval was obtained from the University College Hospital by Prof. Oladimeji Oladepo.

Approval from Ministry of Education

Due to recent experiences of teachers revolting and accusing the government of allowing religious medical outreach in the schools, collecting samples from school has become more difficult. A letter of approval from the commissioner of Education was required in addition to the ethical approval before parental consent forms were given to the students. This new law would have terminated our project but for Prof who used his connection to the permanent secretary to quickly secure the required approval. Interested readers could access the approvals at the appendix.

Protocol

A very clear protocol drafted by a team led by PhD candidate Adeola Onasanya was used for this study. The protocol can also be accessed at the appendix.

Team composition on the field

The team consist of primary health care workers at the Ajoofeebo Primary health care facilities, NTD officer of the state, two medical doctors (community medicine specialisation), three high-profile laboratory scientist, 3 public health scientist, 2 community mobilizers and 1 PhD candidate from Tudelft and a technical expert from AiDX Medical Bv. The team members are listed below:

S/No	Name	Responsibility
1	Prof. Oladimeji Oladepo	Principal Investigator UI
2	Adeola Onasanya	Lead – Usability testing and central team lead
3	Dr. Opeyemi Oladunni	Lead - Community mobilization and interactions
4	Dr. Omolade Falade	Lead – Sample collection, storage and documentation
5	Dr. Ekene Igwegbe	Sample collection and adherence to protocol
6	Mr Iyiola Olaoshun	Expert Lab. Scientist -Department of Microbiology,UCH
7	Mr. Olawale Animasahun	Expert Lab Scientist – Ajoofeebo Primary Health Care
8	Mr. Austin Adugbe	IT support, Public Health Expert
9	Mrs. Modupe Akanmu	Expert Lab Scientist – Ajoofeebo Primary Health Care
	Mrs.F.O.Oluwatuase	Oluyole LGA NTD officer
10	Dr. Temitope Agbana	AiDX Medical

Team composition in the Netherlands

The management team in the Netherlands planned and organized the project, supervised the development of the protocol, accessed the budget, provided the funding for the implementation of the field study and ultimately monitored and provided support for the field.

S/No	Name	Responsibility
1	Dr. Jan Carel Diehl	Principal Investigator of the field study - TUD
2	Dr. Lisette van Lieshout	Principal Investigator - INSPiRED project
3	Dr. Michel Bengtson	Project management and administration
4	Adeola Onasanya	PhD candidate- Industrial Design
5	Brice Meulah	PhD candidate – (Filaria sample databank
6	Prof. Akim Adegnika	Principal Investigator - CERMEL
6	Dr. Temitope Agbana	CEO AiDX Medical BV

Materials and devices.

Technical devices.

- Three AiDX Assist devices were purchased from the AiDX Medical BV and brought along to Ibadan for the project implementation.
- Monitor screen: Three monitors for use with the device purchased in Lagos (by Austin Adugbe) and Abuja (Tope Agbana) were brought to Ibadan for use with the AiDX device. An uninterrupted power supply (2kVA) unit was also purchased to provide stable power to the device. Also, a standard extension unit was purchased accordingly.

Diagnostic materials.

- All relevant diagnostics materials needed for the field study were purchased and brought in by the Ibadan team led by Prof. Oladimeji.

Sample analysis and processing.

1. For this operational research, 650 blood samples of microfilariae prepared on standard glass slides between Feb-March 2020 and stored in standard slide box were taken to Nigeria for microscopy analysis. Sample set would be screened by the AiDX assist and results would be compared with microscopy result to estimate the sensitivity, specificity, positive and negative predictive value and other performance metrics that may be defined for publication.
2. 97 urine samples were collected and processed. The samples were examined by standard microscopy and results will also be compared with the outcomes of the AiDX device. The amount of collected samples is short of three when compared to the target 100 samples which is in the designed protocol. The shortage was due to the unexpected demand for approval from the ministry of Education. This unexpected mandatory request caused the delay in sample collection.
3. 38 skin snip were collected instead of the planned 100 samples.

Kick-off Meeting for the project

The kickoff meeting for this project was organized on the 16th of November 2021 at the Department of Public Health and promotions, University College Hospital Ibadan.

Goal of the kick-off meeting: To provide clear direction for the team on ground, clarify all doubts, answer all questions, align all participants with project goals. Also, demonstrate the AiDX device and provide training for all participating project team member.

Attendance

The project kick-off meeting was well attended by every member of the team listed in in Table 1.

Conclusions and resolutions from the kick of meeting by all:

Definition of the aim of the study: Based on the input from the project team members, it was resolved that the study should focus on the performance of the devices as relevant to quick disease or case identification to enhance quick and rapid treatment. Therefore, the research can be referred to as an – **Operational research**.

Based on the resolutions above, the following points were further clarified and established:

1. This implies that the AiDx assist should be designed to identify the number of parasites in one high power field. Which means the measurement should stop as soon as a parasite, egg, or worm is identified in one high power field. In the case of negative patient sample, it therefore means that the measurement should not stop until a parasite is identified in one high powered field. That means that the system can continue running until the end if the sample or specimen tis negative.
2. The identified patients will be treated ASAP so infection load is not needed for this as treatment would be done as soon as the parasite is identified.
3. In the case of efficacy or drug administration and treatment, infection load estimation can be done with specific samples of interest. And as such the entire slide would be scanned and screened by the device. This is also applicable to research-based study, and this means that a different protocol would be developed for research purposes and urine samples would be collected at specific time intervals such as 2 hours before or after midday.
4. There is a standard high powered field estimates based on WHO regulations. Therefore, the AIDX device should be scaled to compare with the WHO standard definition for manual brightfield microscopy.

Conclusion and Resolutions: Concluded that the study would focus on clinical analysis and treatment and not on research study.

For clinical analysis: The medical expert is not interested in the infection load but in the state of the sample. He or she wants to know if the patient is positive or negative and as such one target parasite in one high power field is already sufficient to commence treatment. So, the focus is on evaluating the performance of the device as based on confirmatory test.

Community mobilization and Sample collection

Community Urine sample collection started on the 17th Nov.2021. It was decided that since the Skin nip is painful and uncomfortable the non-invasive urine sample collection process should commence first. The team agreed that getting the urine sample would help the villagers relax and feel comfortable and this will help sample collection throughout the project. But to start with the skin snip may cause them to avoid supplying other samples.

Sample processing and storage.

Collected urine samples: The collected urine samples were centrifuged, and the sediments were smeared on a standard glass slide for microscopy analysis. Corresponding sample analysis was conducted on the 30% of the samples and the results were stored accordingly. The familiar urine filtration was not used in this study.

Microfilaria samples from Gabon: A total of about 500 samples (data still being processed) were analyzed by two expert microscopists. The results were manually stored and presented to PhD candidate Adeola who is digitally processing and storing the results for comparison with the results obtained from AiDX.

AiDX devices has so far registered and processed over 400 samples. The results obtained were digitally documented and shared with PhD candidate Adeola Onasanya. She is the independent result collation officer.

Plan of the analysis

- We propose to use the result of the analysis of the blood filaria sample for the performance evaluation of the AiDX device because the AiDX device has been developed and optimized for filaria detection.
- Then we can also use the sample from the field for impact assessment of the efficacy of the drug treatment administered for Schisto in the area.
- For the skin snip, the AiDX device is not trained for the tissue analysis. Manual analysis with AiDX works well. Skin tissues were visible, and the experts were impressed but the automation, autofocusing algorithm is not designed for such so samples would be stored and brought back to Holland for analysis once algorithm is fully developed if we get some specific samples.

Usability testing

To test the usability of the device, a usability test was conducted by PhD candidate Adeola. Designed questionnaires can be obtained online at:

AiDX observation and post observation questionnaire:

https://tudelft.fra1.qualtrics.com/jfe/form/SV_8kAxxKWkXUuzT70:

AiDX usability testing questionnaire:

https://tudelft.fra1.qualtrics.com/jfe/form/SV_bvzUWaOfcy2GAD4

- Ten laboratory experts were examined. The laboratory experts were selected from Tertiary laboratories, private laboratories, non-governmental laboratories, and primary health care laboratories. They were first trained to use the AiDX assist by Temitope Agbana. A senior lab scientist (Mr. Animashaeun) who worked on the project also gave them some training on his personal experience with the use of the device. He was trained during the kick-off meeting. An AiDX assist device was dedicated for usability testing and feedback data were already gathered. The usability test was successful, and PhD Adeola commenced immediate processing of the data. All participants were also given stipends for their participation. Participation was unbiased, clear, and done in a very professional manner.
- Ten Students: Ten 2nd year students undergoing the community health extension workers (CHEW) training were also selected for the usability testing. The students were trained and then asked to use the systems to measure and access the usability testing accordingly. The training and usability testing was very successful. The questionnaire was administered personally by PhD Candidate Adeola and Dr. Ope with Adeola supervising. Students were interested and participated actively.

New Idea

During their training, PhD candidate Adeola discussed an idea of a gathering data which could help analyze the impact of task shifting. We eventually defined a study goal to gather data to examine the possibility of shifting the task of performing diagnostic screening to the community health care worker level at the community level. Testing the expert independency of the AiDX assist device.

Protocol

- The protocol selected a few students out of the visiting Community health care 2nd year participants and provided some samples for them which they measured with the Aidx device. They were challenged to individually make conclusive diagnosis with the help of the AiDX device. Their results will be compared with the expert microscopist to ascertain their accuracy. This will help us validate the possibility of shifting task from experts to community health care workers at rural level in the diagnostic of NTDs.
- The set of students returned four hours after their first training and this measurement was done with data collected for potential analysis and a subsequent publication.

The usability testing was well done and organized, and all participants were interviewed afterwards. Also, participants were duly appreciated by providing some reward. It is also important

to note that aside the treatment provided for participants, students were also given exercise books as a reward after the submission of their urine samples.

Technical feedback on the performance of the AiDX Assist device.

The AiDX assist device, is an integrated automated microscopy. This NTDx diagnostic device was optimized for the detection of filaria in blood samples using developed Artificial Intelligence software.

Robustness: At the set-up of the AiDx devices it was observed that only 1 system worked optimally. The labelled system 1 was sometimes erratic in operations. The error was that the sample scanning system was unstable in operations. They system could continue running without any purposeful activity. At this state, the sample holder is pulled in, but no activity except the continuous activity of the control systems is observed.

Solution: The system returns to standard operations after a hard reset.

The two other systems were misaligned and with some remote supports with AiDX technical team, the systems were realigned accordingly, and they worked well. The challenge of misalignment has been communicated to the technical team and the design will be optimized.

Software challenge

- After the training of the Community Health Care worker which was done towards the end of sample analysis and processing with the AiDX device, all the systems suddenly log off and it was impossible to gain access to the system despite the remote support from AiDX in the Netherlands. This is obviously a challenge that would be fixed accordingly.
- It is also observed that the software interface has some unnecessary technical information such as the determination of the grid size, the autofocus in the x and y directions which is not necessary for the users. This observation has been duly communicated to AiDX technical team.
- The final presentation of the annotated detected filaria worms should be mapped to the corresponding registered image for easy, quick and direct image observation and validation.

Additional features

- The private laboratories also solicited for extra features such as the total blood count and differential blood count functionalities for multipurpose use in the laboratory.
- Complete blood smear analysis and data processing with AI currently takes 10 minutes. This is 5 minutes slower than expert microscopist as observed by Mr. Olaoshun. AiDX Medical should also aim at optimizing the device for faster data analysis.

Meeting with stakeholders – NGO

Although this is not part of this study, planned meetings with two non-governmental organizations active in the NTD control and elimination space were realized.

- Meeting with Sight Savers: in attendance were Dr. Tope, Prof. Oladimeji (UI), Martin (SS) and Omosefe(SS). The goal of the meeting was to explore collaboration possibilities. The sight saver senior research staff also tested the AiDX device and observe the operations. However, the focus is to integrate the Schistoscope into their surveillance program in Nigeria. To further explore the collaboration possibilities, we agreed to jointly explore the COR-NTD funding of 500k with INSPiRED, UI, SS, AiDX and Federal Ministry of Health as project partners. A meeting for further discussion and planning is scheduled for next week. The meeting plans to feature the INSPiRED team and the SS team both at the global level and the local level. I planned and proposed INSPiRED to play the active role in leading this research. Furthermore, we also want to explore the possibility of joint collaboration on the field implementation of the NTD award proposal. This would be further discussed as well.
- Meeting with END FUND: In attendance were Dr. Tope Agbana, Dr. Louise (Director of NTD Programs - NTD), and Chief Amen. The meeting was conducted in Abuja Nigeria and the goal was to explore the potential of using the AiDX device for impact assesment in specific areas where treatment is being planned. A new planned treatment site is Oyo state Nigeria. It is intended that AiDX device will do pre, post and assesment after second treatment to evaluate the impact of treatment accordingly. This is the overall goal. It was agreed that the project partners should include Amen foundation (local NGO, partners providing treatment in Oyo State Nigeria), University of Ibadan, INSPiRED and AiDX. I plan and propose AiDX to play the active role of leading this research. Subsequent meeting is being planned for the coming week. A proposal will be drafted and shared with the END Fund partners accordingly.

Plan for Data analysis and result

Together with Adeola we propose the following data analysis plan.

1. First conclusive diagnosis of the remaining 100 microscopy-analyzed sample would be done with AiDX next week. **Action point** – Temitope Agbana
2. Cleaning, sorting, and organizing the data of the microscopy result for the 500 samples and corresponding alignment with data of the AiDX result for the 400 samples. Results of the analysis of the remaining samples will be shared with Adeola by the end of next week at most. **Action Point** – Adeola & Temitope
3. Final comparative data analysis and computation of the performance metrics e.g: sensitivity, specificity, positive predictive value, and negative predictive value. The AiDX algorithm would be compared with the standard microscopy and the result of the digital microscopy would also be compared with standard microscopy. All necessary plots would be computed, and results will be presented to the group and documented for paper writing. **Action point** – AiDX technical team, Adeola (result of the microscopy analysis in Nigeria) & Brice (result of the reference data in Gabon).

Publication plan

We expect 3 manuscripts from the data collected. The papers will focus on the following:

- a) Performance evaluation of the novel automated AiDX NTDx for screening of NTD – Lead: Data analysis (AiDX), paper writing (Brice).
- b) The extent to which co-creation with local stakeholders influences the design, usability, and adoptability of a diagnostic device - Lead: Adeola
- c) The possibilities of task-shifting in the quick screening of NTD's at community level – Lead: Adeola

Goal: Our goal is to jointly work on the paper and submit all three before the beginning of March 2022.

Propose future plan:

- Impressed with the innovation and the performance of the AiDx assist device, the participating laboratory scientist suggested the collation of samples to build a data bank for future easy access to samples. Mr. Animashaeun, the team lead of the Ajoofeebo primary health care center who is also the secretary of the Association of Medical Laboratory Scientist of Nigeria already sent out a message to all the primary health care centers in Oyo state Nigeria to prepare extra samples and store them for future use. If this is an interesting proposal to consider then we will need to probably commit to this proposal and plan a structure around it somehow so that we can make the. Most of it. We can plan a future meeting to this effect and invite the scientist to share his plans and thought on this.
- For the proposed NTD innovation field study, it was recommended to start early planning with all stakeholders such as the lab scientist, the NGO, UI and the INSPiRED team etc. So that all relevant approvals can also be obtained to maximise time efficiency.

Field study project closure

- The field study was officially rounded up on the 1st of December with Prof. Oladimeji, Dr. Tope, Mr. Animashaun and Mr Olaoshun in attendance. Adeola joined online and the goal of the final meeting was to review the process, discuss, clarify, and reconcile results of the microscopy analysis as stored by PhD candidate Adeola.

Field Test Performance Result (Nigeria, Nov 2021)

Introduction

512 microfilaria samples obtained from Gabon were screened using the AiDx device and reference standard microscopy. Samples were collected by the CERMEL team in Gabon in 2020. 10 microliter of blood was used to prepare a semi-thick smear on standard blood slides. The prepared samples were air-dried and stained with a fluorescent dye (Hoechst stains) but not stained with Giemsa before storage. Samples were however stained with Giemsa dye in October 2021 (About 18 months later). And screened to evaluate the performance of the AiDx device as compared to reference standard microscopy.

Microscopy analysis

The expert microscopy analysis team was led by Mr. Olaoshun, head of the Microscopy Laboratory in the University College Hospital Laboratory he was seconded by Mr. Animashaun (the head lab scientist in charge of Ajofeebo primary health care center). Samples were independently analyzed, and recorded data were managed by Dr. Adeola, Onansanya.

AiDx assist device

The AiDX assist device was designed to automatically screen the samples, process, and analyze the registered images for filaria worms. The mosaic of the analyzed data is presented as an output for a human operator to validate and confirm the presence of microfilaria worms accordingly. Conclusive results are therefore dependent on the decisions made by the human operator. The AiDX assist was operated by Dr. Ope and data recorded were independently shared with Dr. Adeola.

The performance metrics

The performance metrics analyzed in this report are, True positive (TP), True negative (TN), False positive (FP), False negative (FN), Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV).

1. **True positive (TP):** It says a diagnostic test result is positive given a person is actually diseased.
2. **True negative (TN):** It says a diagnostic test result is negative given a person is actually healthy or not diseased.
3. **False positive (FP):** It says a diagnostic test result is positive given a person is healthy or not diseased. This depicts that a diagnostic test is unable to identify a normal person and give a false positive diagnosis.
4. **False negative (FN):** It says a diagnostic test result is negative given a person is diseased. This depicts that a diagnostic test is unable to identify a diseased patient and gave a false negative diagnosis.

Sensitivity = true positive fraction (TPF): Sensitivity is the ratio of TP to the actual number of positives/diseased. It refers to the probability of a positive test result for patients with disease i.e., conditional probability of correctly identifying the diseased subjects by a diagnostic test. Sensitivity is used to determine whether the test is sufficiently sensitive to pick up the disease.

$$\text{Sensitivity (TPF)} = \frac{\#TP}{\#actual\ positives}$$

Specificity = True negative fraction (TNF): It is the ratio of the number of TN to the actual number of negatives/healthy persons. It refers to the conditional probability of correctly identifying non-diseased subjects by test i.e., represents the proportion of people without disease who have a negative test result.

$$\text{Specificity (TNF)} = \frac{\#TN}{\#actual\ negatives}$$

Positive predictive value (PPV): It is defined as the probability of disease for positive test results i.e., the ratio of number of TP to the actual number of predicted positives.

$$\text{Positive predictive value (PPV)} = \frac{\#TP}{\#predicted\ positives}$$

Negative predictive value (NPV): It is defined as the probability of being healthy for negative test results i.e., the ratio of number of TN to the actual number of predicted negatives.

$$\text{Positive predictive value (PPV)} = \frac{\#TP}{\#predicted\ positives}$$

Results

Using results from field-microscopy as ground truth (512 samples in total)

The obtained data is processed in two folds. First the performance metrics are evaluated based on conclusive diagnosis and AI - only diagnosis as shown below.

Conclusive diagnosis (AiDx Assist + operator) vs field-microscopy

In this analysis, the conclusive diagnosis refers to the validation of the output of the AiDx algorithm by a human operator. Note: This is the original system design and configuration for the AiDx assist device.

>	Number of samples with without infection:	32 480
>	TP TN:	30 477
>	FP FN:	3 2
>	Sensitivity:	93.750 %
>	Specificity:	99.375 %
>	PPV:	90.9091 %
>	NPV:	99.5825 %

AiDx Assist vs field-microscopy

>	Number of samples with without infection:	32 480
>	TP TN:	31 364
>	FP FN:	116 1
>	Sensitivity:	96.8750 %
>	Specificity:	75.8333 %
>	PPV:	21.0884 %
>	NPV:	99.7260 %

Discussion and recommendations

The AiDx (Assist + operator), demonstrated superior performance as compared to AiDx Assist AI alone. The increased false positive of 116 as compared to 3 In (Assist + operator) was attributed to the staining. Since the samples were stained with Giemsa about 18 months later after they were prepared and air dried. The dried edges, contours and dried areas of the samples trapped some Giemsa dye which are like the shape of filaria worms.

Further analysis of the result presented will be performed by Brice Meulah and published in an appropriate peer-review journal.

Recommendations

To increase the performance of the AI on the field, the Lab scientist recommended, it is recommended that fresh sample should be prepared, fixed, and stained within 24 hours with Giemsa. By so doing, the number of false positives will be significantly reduced accordingly thereby increasing the accuracy of the AiDx + AI performance.

This is however unnecessary for AiDx + operator as it is easy for operators to distinguish between worms and false positives of filaria samples.

Technically, AiDx team is working on improving the Positive predictive value of the Algorithm.

The result analysis for the CHEW students is given below.

The students are first given a quick one-hour training on how to distinguish filaria worms from artifacts generated by the AI in the final output mosaic of the result of the automated screening. The CHEW students were then presented with calibrated samples with specific bias to samples that provided more false positives so that their ability to distinguish between false positives and real positives can be measured. The result of the analysis is listed below. Analysis of the result will be performed by Dr. Adeola Onasanya and published in an appropriate peer-review journal.

CHEW student's vs AiDx

Total samples: 64

CHEW students vs Mr Animashaun

- > Number of samples with | without infection: 7 | 57
- > TP | TN: 6 | 47
- > FP | FN: 10 | 1
- > Sensitivity: 85.7143 %
- > Specificity: 82.4561 %
- > PPV: 37.50 %
- > NPV: 97.9167 %

There are two columns for AiDx result!

AiDx result (AiDx machine) vs Mr. Animashaun

- > Number of samples with | without infection: 7 | 57
- > TP | TN: 7 | 24
- > FP | FN: 33 | 0
- > Sensitivity: 100.0 %
- > Specificity: 42.1053 %
- > PPV: 17.50 %
- > NPV: 100.0 %

AiDx result (AiDx machine used by Lab scientist) vs Mr. Animashaun

- > Number of samples with | without infection: 7 | 57
- > TP | TN: 7 | 33
- > FP | FN: 24 | 0
- > Sensitivity: 100.0 %
- > Specificity: 57.8947 %
- > PPV: 22.5806 %
- > NPV: 100.0 %

CONCLUSION



From the result analysis, the AiDx device performed optimally when used according to the intended design. The AiDx integrated AI model detects all targets perceived as worms and the output result is presented as a mosaic for the operator to make a diagnostic conclusion. By so doing, the final diagnostic decision is made by a human operator who looks through the displayed mosaic. In this optimal case, the AiDx device has demonstrated 94% sensitivity and 99% specificity. The other performance metrics are also indicated in the result section of this report accordingly. This results shows that the AiDX_NTDx device is a potential diagnostic tool in the control and elimination of Neglected Tropical Diseases.

The project was well organized in my opinion. The composition of the team is also very impressive. Professional interaction and delegation of task was quite enjoyable. Experts on board allows for clarity and good understanding of the project.

I think the target sample proposal was overstated: An attempt to collect a total of 200 samples and conduct expert microscopy analyses of 650 blood Gabon samples in 12 working days and with two active expert microscopist and one back-up is a bit too much. We can further improve this in the planning for future field studies.

I will suggest an online meeting with the entire team, lab scientists, Primary health care worker etc to help them already start thinking ahead and along way before the commencement of the field study.

Conclusively, Prof. Oladimeji assembled a good team and gave his full time and attention to the supervision and coordination of the work. He was regularly on the field with the team and in the lab with the team.

Prof Oladimeji and I were the first to arrive the faculty building every morning sometimes before 7 am and we were the last to leave the building during the project. His attitude to work is very pleasant and enjoyable for me.

PERFORMANCE EVALUATION OF AIDX ASSIST DEVICE

Appendix





AiDx system setup and training of expert Laboratory scientist who performed the examination



Urine sample collection process at the schools located in Ajoofeebo community. A patient with one of the NTD diseases. Lymphatic Filariasis or Oncho is suspected.



CHEW 2nd year students performing task shifting measurement on the AiDX system and the leg of a patient from which skin snip sample was collected.



OYO STATE OF NIGERIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
DEPARTMENT..... **SCHOOLS**.....



Your Ref: No.....
All correspondence should be addressed to
the Honorable Commissioner quoting

EDU / FLHE / 22A VOL. 2

26th November, 2021

Our Ref: No.....

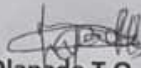
20.....

**Department of Health Promotion and Education,
Faculty of Public Health,
College of Medicine,
University of Ibadan,
Ibadan, Nigeria.**

RE: Request for permission to conduct a Pilot Study on: Assessing Efficiency And Usability of a Developed Point – of – Care Diagnostic Device for the Detection of Parasites.

I am directed to acknowledge the receipt of your letter and inform you that the Honourable Commissioner has graciously granted approval to your request to conduct a pilot study on the above subject in selected Schools within Akinyele and Oluyole Local Government Areas.

2. I am directed again to inform you that extra precautions should be taken by the group of researchers before embarking on the project by informing the communities and parents / guardian of wards that will be tested for the research work.
3. I thank you for contributing to the general well being of our students and the communities.


Olapade T.O

For: Honourable Commissioner.

INSTITUTE FOR ADVANCED MEDICAL RESEARCH AND TRAINING (IAMRAT)

College of Medicine, University of Ibadan



Director: **Prof. IkeOluwapo O. Ajayi**,
MBBS (Ib), M.Cl.Sc., MPH, Ph.D, MD, FMCGP, FWACP
Tel: 08023268431
E-mail: ikeajayi2003@yahoo.com



UI/UCH EC Registration Number: NHREC/05/01/2008a

NOTICE OF FULL APPROVAL AFTER FULL COMMITTEE REVIEW

Re: Assessing efficiency and usability of a developed point-of-care diagnostic device for the detection of parasites

UI/UCH Ethics Committee assigned number: UI/EC/21/0641

Name of Principal Investigator: **Professor O. Oladepo**
Address of Principal Investigator: Department of Health Promotion & Education
College of Medicine
University of Ibadan, Ibadan

Date of receipt of valid application: 25/10/2021

Date of meeting when final determination on ethical approval was made: N/A

This is to inform you that the research described in the submitted protocol, the consent forms, and other participant information materials have been reviewed and *given full approval by the UI/UCH Ethics Committee.*

This approval dates from **03/11/2021 to 02/11/2022**. If there is delay in starting the research, please inform the UI/UCH Ethics Committee so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related to this research may be conducted outside of these dates. *All informed consent forms used in this study must carry the UI/UCH EC assigned number and duration of UI/UCH EC approval of the study.* It is expected that you submit your annual report as well as an annual request for the project renewal to the UI/UCH EC at least four weeks before the expiration of this approval in order to avoid disruption of your research.

The National Code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations and with the tenets of the Code including ensuring that all adverse events are reported promptly to the UI/UCH EC. No changes are permitted in the research without prior approval by the UI/UCH EC except in circumstances outlined in the Code. The UI/UCH EC reserves the right to conduct compliance visit to your research site without previous notification.



03/11/2021

Professor IkeOluwapo O. Ajayi
Director, IAMRAT
Chairperson, UI/UCH Research Ethics Committee
E-mail: uiuchec@gmail.com