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DETECTION OF IRON DEFICIENCY ANAEMIA BY MAGNETOMETER- A REPORT

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ABSTRACT

Background: In maternal and child health arena iron deficiency anaemia has been recognized as a major health issue for developing countries. This has a huge impact on maternal morbidity, childhood morbidity, and child development. There is a critical need for low cost, diagnostic capability to guide iron supplementation. There is currently a crisis in diagnosis and associated treatment guidelines, as health workers lack the tools to make immediate decisions for treatment of distressed mothers and children. **Proposal:** We propose development of a non-invasive device to measure body iron and also the presence of malaria non-invasively. However the World Health Organization has recently called a halt to iron supplementation in malaria endemic regions, but this stalemate will be unacceptable in the long term. **Methodology:** The above mentioned goals will be accomplished by a measurement of the paramagnetic properties of iron in the liver as well as in Plasmodium hemazoin. While operating, the device is simply held near the liver for a body iron measurement. It can be held near the extremities for a malaria screening. No blood or body part touching is needed for the functioning of the instrument. **Results:** The initial screening validates the non-invasive magnetometer model has 99% Naive Bayes accuracy and above 95% SVM accuracy in identifying iron deficiency anaemia using liver as the medium. **Conclusion:** If AI machine learning techniques are used to support this non-invasive approach to iron detection, it will show to be effective, economical and time-efficient. Before being put into practice, the experiments must be validated on a bigger scale.

KEYWORDS

Anaemia, Non-invasive, Body-iron, Paramagnetic, Artificial intelligence and Machine learning.

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INTRODUCTION

Iron deficiency anaemia (IDA) is a serious public health problem which is characterized by low peripheral blood iron and is measured by haematocrit or haemoglobin. Iron Deficiency anaemia (IDA) is a measure of the whole body iron, traditionally measured with a liver biopsy[1]. Infection or inflammation causes anaemia without necessarily causing IDA. During infection the body withholds iron from the pathogens thus infection is a battle over iron since most microbes require it. So patients presenting with anaemia may have low iron or an infection. The current suspicion is that infected patients, given iron, will suffer a relapse, and some data supports this as well[2].

The rationale for this high risk, high payoff instrument which we are suggesting is a low cost solution to the public health issue. This refers to the WHO recommendation that widespread iron screening be conducted in the developing world[3]. In words, "widespread screening for iron deficiency is unlikely to be practical or affordable in the developing world using current techniques" More accurate measures of iron status require blood collection and laboratory testing, which are more expensive and risky because they involve the handling of blood, and are potentially not feasible because of logistics and cultural taboos[4]. Thus, non-invasive screening methods for Iron Deficiency Anaemia are urgently needed. It is in response to this need that we propose this non - invasive, low cost device for body iron measurement.

This instrument can be used as a non-invasive test for malaria as well although this is not the immediate focus of this article, it is possible that the presence of malaria can be detected non- invasively by this magnetometer. The reason is that, when the parasites destroy the haemoglobin inside the red blood cells, they don't have the metabolic machinery to utilize the iron and since iron is poisonous, they tuck it away in a complex called hemazoin, which has strong magnetic properties[5]. This is not a weak magnetic effect and infected red blood cells have been separated macroscopically by ordinary magnets in the laboratory[6]. This fact has led us to suspect that presence of malaria may be detected by this device.

BACKGROUND LITERATURE REVIEW

For other approaches considered for background diligence on this development, several authors of papers about iron deficiency and a literature search on the medical and physics issues, with analysis of possible alternative approaches to measuring whole body iron has been done. The conclusion put forth is about serum ferritin - In healthy individuals, serum ferritin is a measure of body iron. It is assessed using radio labelling immunochemistry or Elisa in a clinical laboratory. This test presumably can be made portable. Serum ferritin is elevated in infection as well, so absolute dependence on serum ferritin is unreliable for the underprivileged population from developing countries[7,8]. Other biomarkers or other blood tests include transferrin, transferrin receptor, zinc protoporphyrin. These also vary with infection and are not accurate measures of IDA[9]. The third alternative is SQUID susceptometry - a million dollar machine that measures liver iron[10]. MRI liver scan, another million dollar machine also measures iron[11]. In the past as we went back a hundred years in clinical chemistry, no test that measured body iron has been found in the records[12,13]. To summarize, these tests mentioned are not suitable for field screening because they are either not accurate or too expensive.

The previous work, involving SQUID magnetometer or MRI, showed good correlation with liver biopsies for body iron estimation. In an effort to simplify the equipment used for magnetometers[9,10], a group developed at room temperature, much lower cost, magnetometer and achieved comparable sensitivity to SQUID[14,15]. It is our aim to extend that work and arrive at a low cost, hand held version. Our plan of action will be discussed next, as concisely as possible.

METHODOLOGY

Overall system description

The idea of the analytical magnetometer system is first to impose a magnetic field on the liver and measure the responding field with a nanoparticle-based sensor which has fluorescence sensitive to the imposed magnetic field. Parts of this instrument include a rapid-collapsing electromagnet, a time-domain led-phototransistor fluorimeter for sensing the nanoparticles, and electronics for control and amplification. These will be discussed in turn.

Techniques employed to measure the anti-paramagnetic signal include signal processing for pattern recognition of weak signals, chopper stabilization for noise cancellation, time domain fluorimetry and various electrical engineering techniques of signal conditioning. These techniques will be described as well, as much as possible. A complete engineering prototype may be impossible in phase one, but key tests can be done to validate the approach.

With rapid decay electromagnet we want to impose a magnetic field on the liver ferritin and then quickly remove the field before the relaxation time of the ferritin. We want the imposed field out of the way, to enhance the detected signal, which is a million times smaller. The system will energize the electromagnet and then short it out to collapse the field. The circuit to energize may be based on a capacitor similar to a photo-flash circuit, except ours will be triggered by a MOSFET power transistor rather than the external wire a camera flash use. A concern is the electromagnetic pulse associated with rapid changes in magnetic field that will send a voltage spike, destroying the transistor. For this we will put "sentries" around the MOSFET, MOS varistors of the type used to protect computers against line surges. These will remove the spikes. In case the varistors are not adequate, a photoflash tube will be used as a type of thermistor, with its trigger wire connected to one terminal (Figure No.1).

Rationale of SNR and signal processing

The signal-to-noise ratio (SNR) determines the viability of measurement, as we can always amplify a weak signal, but if it is buried in the noise, all is lost. One way to boost SNR is to impose a particular pattern on the signal and then look for that pattern in the detector. This is essentially how a cell phone or radio detects the extremely weak signal from broadcasters, either by listening on a certain frequency or locking onto a particular digital code. This kind of detection has been used in sonar and the odd hobby of bouncing a low power radio signal off the moon and detecting it. A low power radio signal travelling round trip to the moon is many billion times weaker than what we have to detect, but the power of signal processing manages to pull it out of the noise. In our case, the rapid control over our imposing electromagnet allows us to set up a specific time window to look for our signal, thus boosting SNR (Figure No.2).

Chopper Stabilization

This rubric describes the process of sampling the background noise and subtracting that from the measured signal. Variations in the earth's magnetic field or other sources are dynamically tracked and removed. In our case, the magnetic sensor will take readings while the signal is present and after it decays.

The iron quantum Nano-particles will be made, derived and cast into epoxy using simple synthetic methods recorded in the literature. These particles react to magnetic fields by changing the fluorescence of attached fluorescent dyes. There does not seem a final theory of this behaviour, but the following qualitative view may be pertinent. A Nano particle confines an electron into a small cell. As Heisenberg's uncertainty principle arguably says, electrons don't like to remain confined. (The solidity of matter is attributed to this principle, although matter is 99% empty space). The electrons are pushing back to maintain their "free range." In any case, it may be argued that electrons which cause magnetic fields are tunnelling from the iron particle out to the fluorophore, affecting fluorescent output.

Time domain led fluorimeter has the detector that senses the fluorescence of the iron quantum dots in the following way. First the laser diode emits a pulse of ultraviolet rays, after it shuts off, a phototransistor integrates decaying light output. Since the UV source is shut off, a significant source of noise is removed. Again, chopper stabilization allows for subtraction of noise or circuit drift, etc. The laser diode and phototransistor, being solid state, are extremely fast, well within our needs.

The notable feature is the quantum dot magnetic detector is sought after because it is solid state, fast, inexpensive and possibly very sensitive. But should unforeseen difficulties arise in making it work, necessitating more materials development, then the imposing electromagnet itself may be used as a detector in "fluxgate" mode, controlled by switching transistors.

The electronics for control and amplification involves the following: the control of the timing of magnetic pulse and sensing sequences will be done with a low cost microprocessor. ("Imposing a temporal pattern"). In prototyping this system, an Arduino board would be a good choice, since the high speed activities of the circuit are conducted with peripheral electronics. The microprocessor will allow different measurements to be subtracted from each other. ("Chopper stabilization") as well as recording measurements in digital form. Amplification of the weak signals will be done with operational amplifiers in various differential and sample-and-hold configurations controlled by the microprocessor. The laser diode, phototransistor, and pumps are less than 25 cents each in production quantities proving that this is a low cost device. The microprocessor is less than one dollar. There are no circuit items which are costly (Figure No.2).

EVALUATION AND RESULTS

A realistic goal for phase I is to attempt to measure the super paramagnetic effect using a bread boarded circuit and a good oscilloscope. This would be measured on beef liver using a function generator and associated protection circuitry as described above. The hypothesis this tests is that a signal of magnetic susceptometry can be measured by a circuit of this type. We will use a fluxgate coil at first and construct a chopper stabilized amplifier circuit that takes sequential measurements directly after a magnetic field is shut off.

The initial screening of the experiments showed that the model of magnetometer performed appropriately in a small setting of volunteers. AI machine learning tools Naïve Bayes achieving more than 99% accuracy and SVM (Support Vector Machine) achieved over 95% in the lowest accuracy level (Figure No.3).

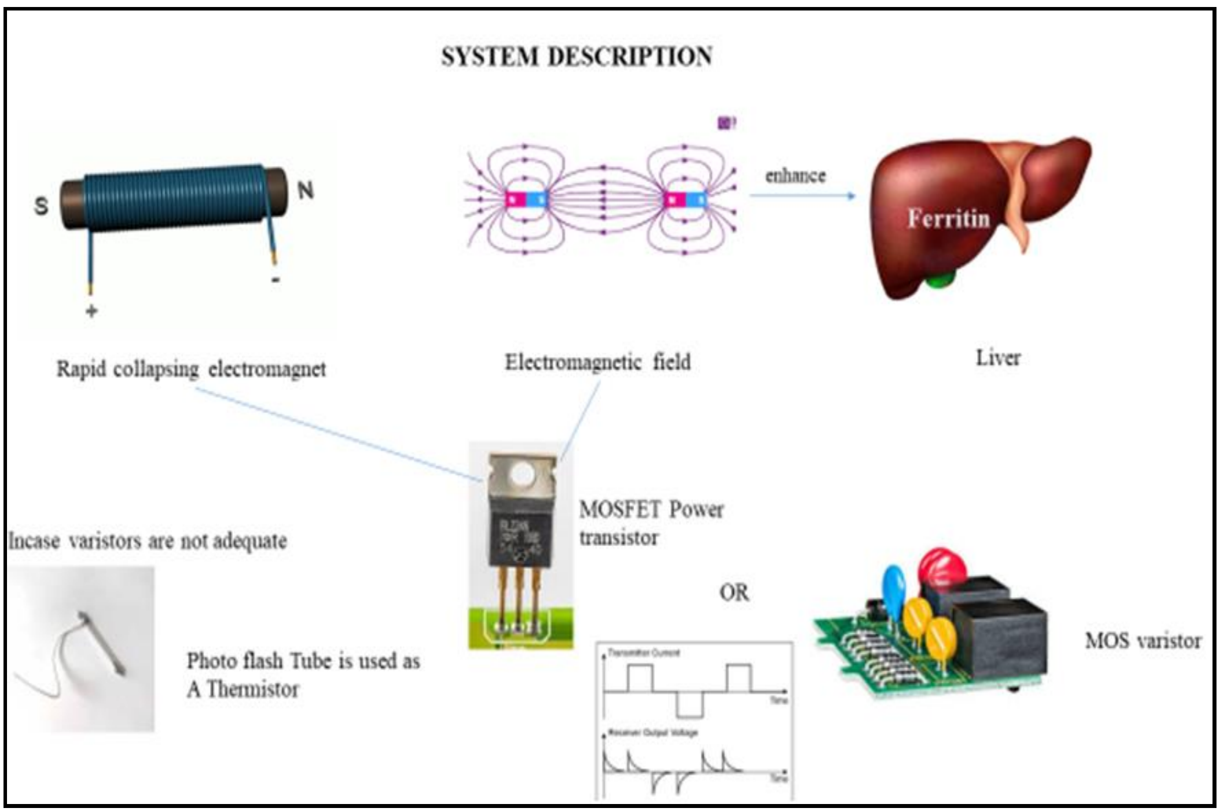

Figure No.1: Overall system description

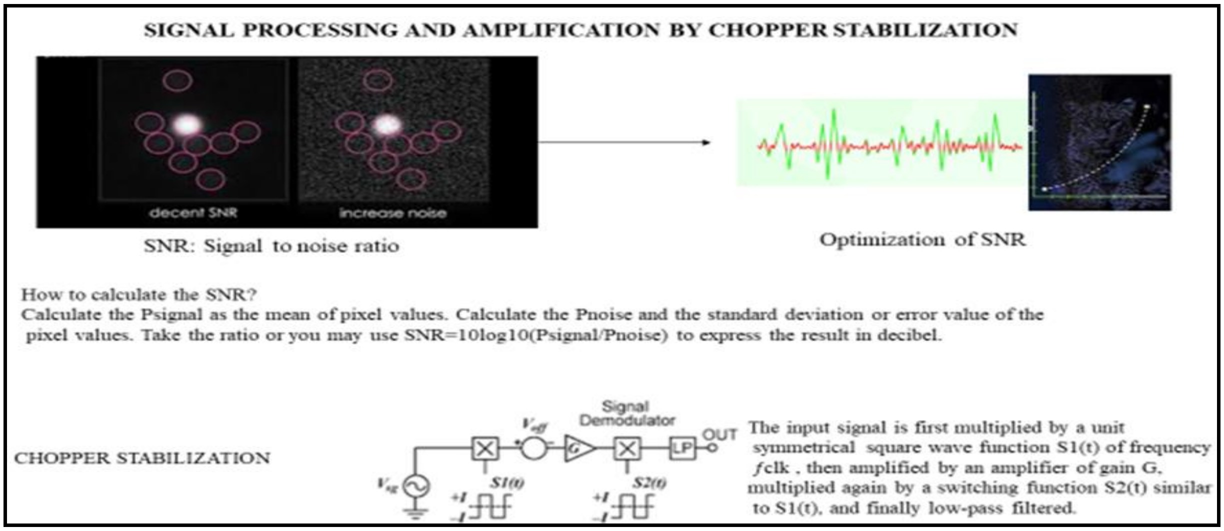

Figure No.2: Signal processing and amplification

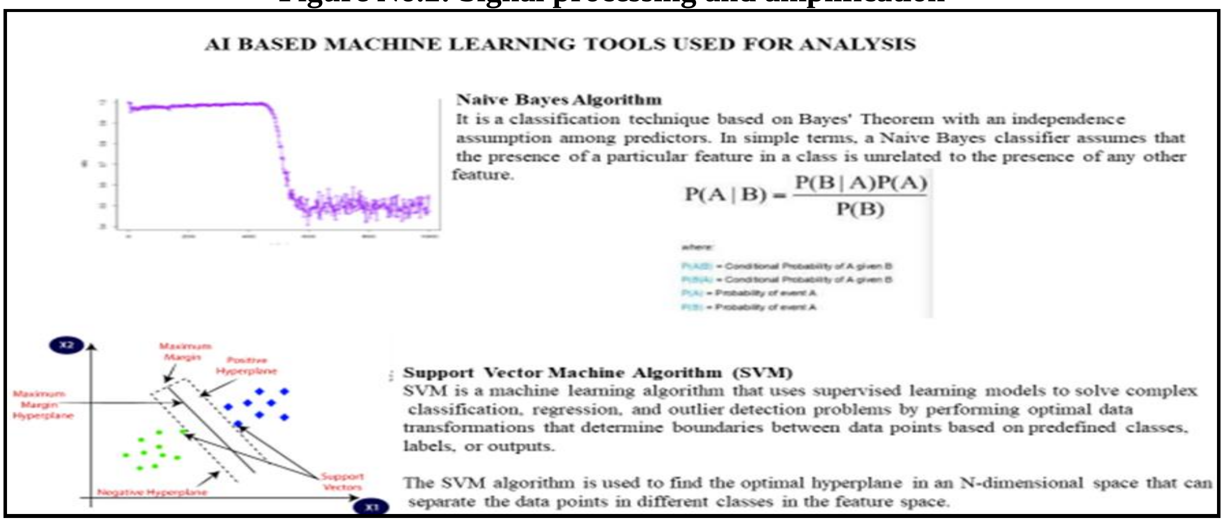

Figure No.3: AI based machine learning tools used for screening of the performance of the magnetometer

CONCLUSION

This non-invasive method of iron detection if supported by AI machine learning algorithms will prove to be efficient, cost effective and less time consuming. The experiments need to get validated on a larger scale before implementation. Due to inadequate funds we had to remain satisfied with the initial screening procedures. But we can conclude from the study that the potency of the magnetometer supported by machine learning algorithm can prove as a low cost non-invasive method in detecting iron deficiency anaemia in developing countries.

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ETHICS APPROVALAND CONSENT TO PARTICIPATE

Not applicable

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CONFLICTS OF INTEREST

There are no conflicts of interest. The initial stages of the work was submitted to The Gates Foundation Grand Challenge, 2015.

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