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SpO2 MONITORING FOR TUMOR HYPOXIA AND PROGNOSIS PREDICTION

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ABSTRACT
Oxygen is essential for maintaining aerobic cell homeostasis. Hypoxia is a condition in which cells do not receive the oxygen they need to function properly. While hypoxia can occur during physiological activities, hypoxia is often associated with pathological diseases. It has been identified as a stressor in the tumor microenvironment and an important mediator of cancer development. Many pathways are activated in hypoxic cells, affecting cell signaling and gene regulation and promoting them by stimulating angiogenesis, changing cell metabolism, slowing their growth, and preventing cell apoptosis in vivo. Hypoxia causes metabolic dysregulation in cancer cells, leading to an aggressive tumor phenotype characterized by rapid growth, resistance to treatment, and poor prognosis. Noninvasive assessment of hypoxia-induced metabolic and tumor changes can reduce the need for invasive biopsy procedures and evaluate tumor response, thus improving the overall therapeutic management of breast cancer (BC) patients. This paper provides an overview of hypoxia-induced changes in cancer tumors, focusing on their use and their advantages and limitations.

Keywords: Hypoxia; Non-Invasive; Tumor; Cancer.

INTRODUCTION
Hypoxia is defined as less oxygen in the tissues following the difference between oxygen consumption and lack of oxygenation of the cells. When the condition is physical and often permanent, tissues can control increased oxygen through other metabolic pathways such as vasodilatation, decreased oxygen consumption, and cellular triggering. However, when the damage continues and the mechanisms in the homeostatic response are not met, hypoxia can become pathological. Therefore, it is associated with the onset and development of certain diseases such as heart disease, chronic kidney disease and diabetic retinopathy, or inflammatory diseases such as rheumatoid arthritis [1-5]. Some efforts have been made to determine a cutoff number for the hypoxic state [6].
Various mechanisms are involved in the production of tumor hypoxia, including perfusion-limited O_2 delivery, diffusion-limited O_2 delivery, and anemic hypoxia. Different mechanisms lead to significant heterogeneity in tumor oxygenation levels [7]. Blood vessels are chaotic and do not have normal blood vessel structure—perfusion-limited O_2 delivery results from major processes and dysfunction in the tumor vasculature. Abnormal blood vessels cause geometric resistance that impedes blood flow [8]. In addition, the walls of blood vessels in the tumor vasculature are more permeable because they lack smooth muscle and often contain disorganized endothelial cells and basement membranes. 3 Abnormal processes in the tumor vasculature can cause ischemic hypoxia. This type of hypoxia is called "acute" hypoxia—diffusion-limited O_2 delivery results from disruption of arterial diffusion geometry. In normal tissues, blood vessels are arranged controlled, and systematically, thus maintaining cell-

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capillary distance to create a constant and uniform oxygen gradient. In cancer cells, blood vessels can form far from the cells, depriving them of oxygen.

Hypoxia is a characteristic of cancer cells and directly affects the properties of cancer cells [9-11]. When cells create a hypoxic environment, they must adjust their metabolism to adapt to this hypoxic microenvironment. Tumors adapt to their environment by activating hypoxia-inducible factor (HIF), which plays an important role in the transition to anaerobic energy production [12].

HIF promotes tumor survival by upregulating the expression of various genes involved in angiogenesis, metabolic regulation, pH balance, and apoptosis. The important role of HIFs in vascular protection and regulating blood and nutrient supply to tumors complicates the treatment of tumors, leading to immunosuppression, chemotherapy (CT), and immunosuppression [12].

Negative effects of hypoxia on the treatment of Cancer Tumors:

The resistance of cancer cells to apoptosis is one of the greatest challenges of cancer treatment [16]. Many people with cancer come back and the tumors come back due to low levels of antibodies [an anti-cancer drug], leading to local recurrence and/or metastasis [17]. Cancer hypoxia occurs due to uncontrolled cell growth, altered metabolism, and decreased oxygen and transport due to abnormal tumor tissue [18]. Hypoxia is one of the key features of cancer and is associated with poor prognosis in cancer patients [19]. Although hypoxia is lethal to many cells, tumor cell subpopulations not only adapt to hypoxic conditions but may also be resistant to chemotherapy and radiation. The role of hypoxia in clinical outcomes has been known for at least 60 years [20, 21].

Hypoxia provides treatment to cancer cells by controlling the following processes: i] triggering cell cycle arrest, which is a state of reduced cell proliferation that protects cells from external stress [22,23], ii] preventing cell apoptosis and aging, iii] regulating autophagy, p53 and mitochondrial activity [20,23]. In addition to the cellular changes affected by hypoxia, reducing tumor oxygenation also has an anti-inflammatory effect by iv] affecting drug delivery and cellular uptake associated with acidity and expression of drug efflux pumps, and v] many chemotherapeutic agents. Lack of oxygen required for cytotoxicity of the drug [24].

How to detect Tumor Hypoxia?

All tumor types, especially malignant tumors, are affected by hypoxia, and oxygenation levels are often found to be lower than the tissue from which they originate [13-15].

Growing tumors use maximum oxygen for their growth which means there is a maximum oxygen level near the tumor. We can detect the Hypoxia on tumor by measuring SpO2 levels.

The early hypoxia will be detected at the growing tumor, which means the SpO2 level will be maximum. And at solid tumors, the SpO2 level will be minimal, which means Hypoxia is there.

To detect the early Hypoxia, we try to make a device that can detect early Hypoxia with a non-invasive method.

Working of Device:

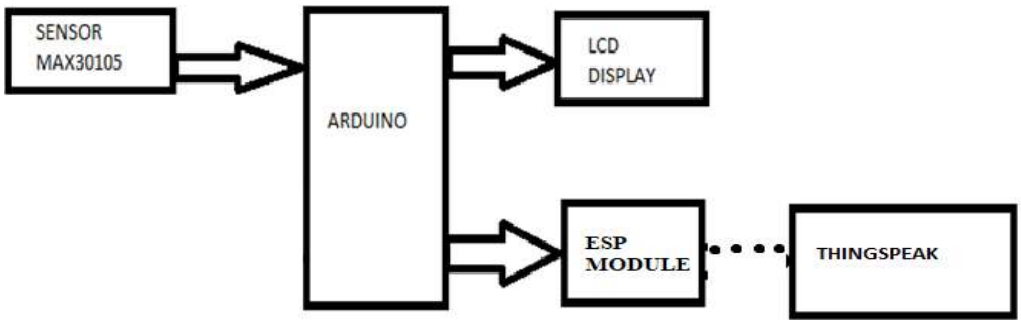

Fig.1 System block diagram

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The above figure shows the system block diagram. As shown in the figure it consists of different components which are, Sensor MAX30105, ARDUINO, LCD Display, and ESP module.
The sensor MAX30105 is the input of the device, it consists of inbuilt Red and IR LED with a photodetector. Place the module where the tumor is , and power it on. The Red and IR LEDs will emit the light, these lights are absorbed by Oxygenated and Deoxygenated blood, and the remaining light will be reflected and absorbed by the photodetector. This photodetector collects the light which is not absorbed and converted into analog form. After this, the analog signal is converted into a digital signal with the help of analog to digital converter.
The other main component of our device is Arduino, the digital data from the MAX30105 module is given to the Arduino, the Arduino will calculate the SpO2 according to the data which is provided by MAX30105. This module enables the microcontroller to connect to Wi-Fi and be used for Internet Of Things [IoT] applications. Here we are using ThingSpeak;ThingSpeak is an open source platform that enables IoT applications. ThingSpeak is associated with MathWorks; This means that Matlab supports the use of various protocols for storing and retrieving data.

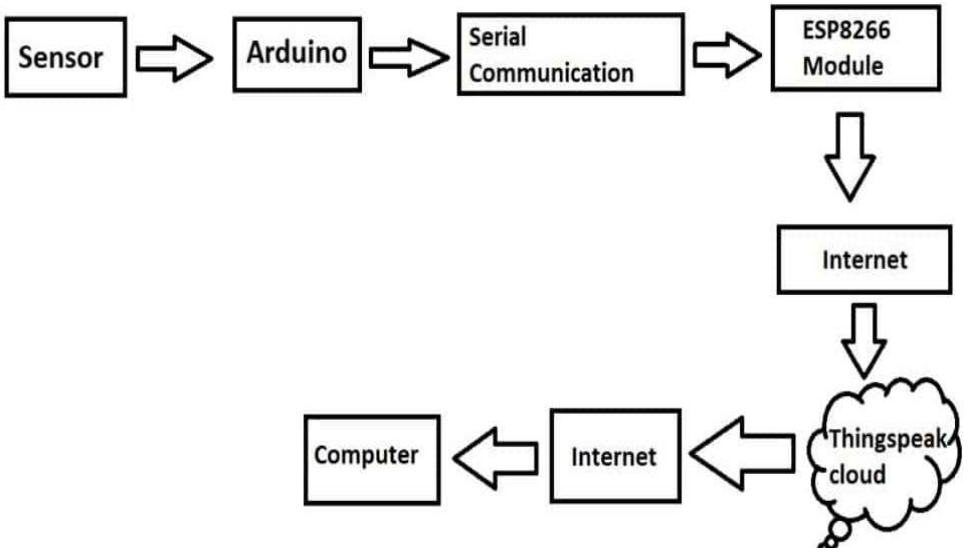

Fig 2. Working principle of ThingSpeak

We try our device on different patients. We measure the SpO2 on the tumor and the index finger and compare both the SpO2's, is there any difference or not? The following graphs show the SpO2 level of the fingertip and on the tumor.

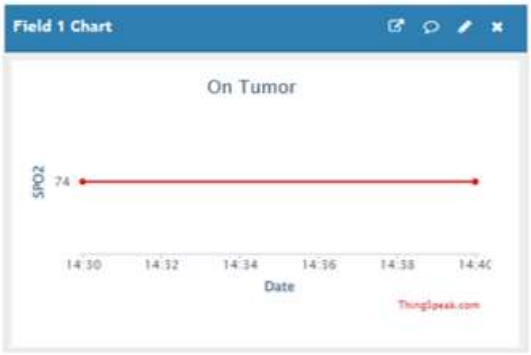

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Fig. 3 Patient 1: SpO2 Graph

Fig. 4 Patient 2: SpO2 Graph

As shown in the above graphs the SpO2 on the fingertip is between 90% to 99% which means it is normal and the second chart shows the SpO2 level on tumor, the SpO2 level is below 90% this stage is called Hypoxia.

Conclusion:

This article highlights important advances in cancer research through the development of continuous monitoring of tumor hypoxia. Integration of hardware and software components provides a comprehensive solution for real-time measurement and prediction. The hardware configuration enables accurate and continuous monitoring, overcoming the limitations of traditional measurements. The software provides a powerful platform for processing and interpreting continuous data using ThingSpeak for data recording and MATLAB for analysis.

Instant prediction of continuous monitoring has the potential to update our understanding of tumor hypoxia dynamics. This system provides information on physiological changes in the tumor microenvironment and forms the basis for more personalized and targeted treatments. Continuous monitoring combined with real-time prediction using SVM algorithms has the potential to improve cancer research and patient outcomes. This work paves the way for further investigation, collaboration, and optimization of continuous monitoring in the context of cancer and personalized medicine.

Measurement Accuracy: Test the accuracy of the MAX30105 SpO2 module by comparing the measured value with the reference standard.

The average difference between the two measurement methods is within the acceptable range indicating that the MAX30105 module provides SpO2 readings. The accuracy of the system can be further improved by calibrating the MAX30105 module and ensuring finger placement and alignment.

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