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Devices and Techniques of Non-invasively Measurement of Haemoglobin - A Review

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ABSTRACT: Non-invasive techniques are one of the leading technologies now a day. Devices using these technologies provide awareness for various medical fields. The present review provides the knowledge for progress made so far in non-invasive techniques for the measurement of blood hemoglobin. In addition to this, it also describes different kinds of methods such as conductance method, digital photometry, multi-wavelength pulse co-oximetry, occlusion spectroscopy, dual wavelength pulse co-oximetry which has been utilized for non-invasive measurement of blood contents like haematocrit, haemoglobin, carboxyhaemoglobin, methaemoglobin. Masimo and OrSense produce devices with the help of leading techniques just as Pulse co-oximetry and occlusion spectroscopy. Masimo series with its improved versions, Radical-7, Rad-57, Rad-87, Pronto-7 are described. In the same way, knowledge of devices of OrSense, NBM-200 and its next version Glasswing is also provided. Purpose of this review article is to figure out the developments made so far for the development of this technology followed by their accuracies and variable laboratory practices. The comparison of devices is also done according to improvements in techniques along with method procedures so far.

KEYWORDS: Non-invasive, Haemoglobin, pulse co-oximetry.

I. INTRODUCTION

Human body contains crucial constituent of blood called as Haemoglobin. The main function of hemoglobin is to transfer oxygen through blood from lungs to tissues. If a required amount of oxygen is not supplied throughout body to the vital organs and tissues in a body, it may cause to sever conditions like kidney damage, improper organ and brain functioning, coma or even a death. Proper supply of oxygen to the cell provides energy to perform their functions optimally. Anemia is also a serious issue which is mostly seen in pregnant women as well as people who are suffering from low level hemoglobin. Therefore, computation of the hemoglobin in blood is essential for health care[1, 2]. Generally, in various medical cures, invasive techniques are used to measure haemoglobin level in which collection of blood sample invasively is required. Existing invasive method requires several steps for final results and hence, process consumes time as well as full of pain for patient. But now days' technology is touching the sky and non-invasive technology for measurement of hemoglobin is one of futuristic innovation. Technology established yield to ease for testing blood without any extraction of blood from the body. Continuous monitoring is useful in critical conditions for emergency department. Detection in changes in haemoglobin values helps for early investigation of treatment[3]. Different sorts of non-invasive methods or techniques are utilized for various prescriptions. This review of distinctive routines of non-invasive methods and devices innovated by using non-invasive technologies can provide the knowledge of enlargement of innovations in Non-invasive field. There are various methods such as Pulse co-oximetry, retinal imaging technique, occlusion spectroscopy is discussed to provide easiness in study of in this technology. Devices developed by Masimo Corporation and Orsense Ltd are leading examples in this field. Both companies introduced their

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own technology for measurement of various parameters. Reducing human efforts and enlargement of possibilities to find out required values are acquired by Masimo and Orsense. Proper replacement of invasive technique with non-invasive technique is still a challenge itself for all techniques.

Here, we are dealing with problems with old techniques and new inclusions for improvising accuracies. Comparison with accuracies of devices gives us knowledge of what we need to improve and what are the drawbacks that we can remove.

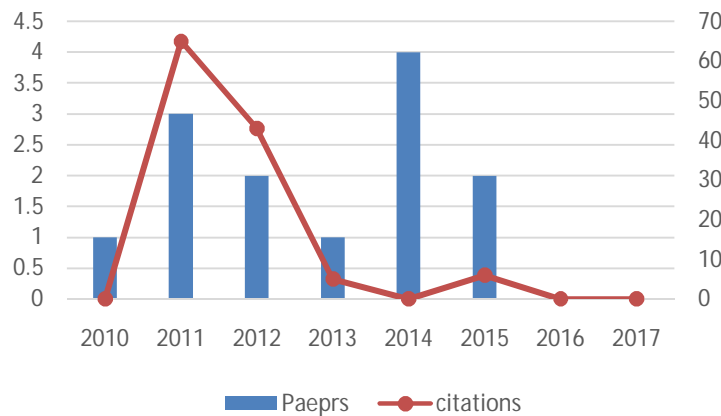


Figure 1: Chart for number of paper and citation regarding topic from 2010 to 2017(Updated on 1 July 2017)

Till the date non-invasive haemoglobin measurement technique related study has been done by many researchers. Graph shows basic idea of papers and their citations according to year describing knowledge of non-invasive haemoglobin measurement.

II. LITERATURE SURVEY

Distinctive techniques and devices

Following study gives introduction to non-invasive haemoglobin measurement methods as well as currently available devices in market along with their advantages and limitations. Methods described below have their own special purpose to find values of parameters.

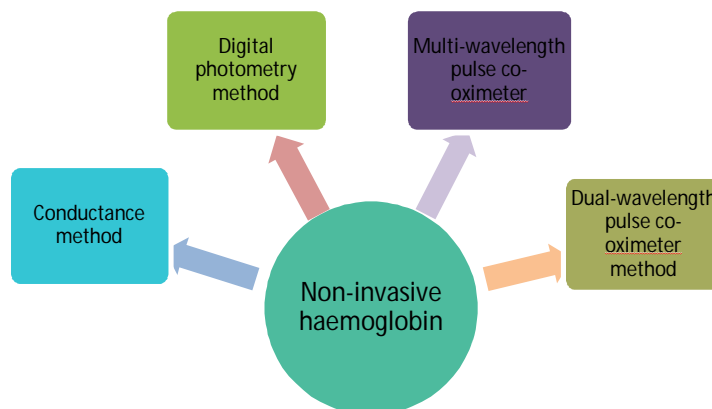


Figure 2: Non-invasive haemoglobin measurement method

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III. CONDUCTANCE METHOD

Conductance method is used for the non-invasive measurement of haematocrit (Hct) which is described by Yamakoshi et al[4]. After this, a new improved technique is introduced in 1989 as 'Electrical admittance cuff'. Further with new attempting they added parameters to calculate Hct i.e. haematocrit. In this respective method, non-invasive measurement of haematocrit, blood pressure and arterial elasticity can be done. According to principal of this technique, segment is placed in the cuff which is mounted by rubber. This particular cuff is fitted in the chamber which consists of electrolyte solution and electrodes are placed in solution to calculate change in admittance of solution. This particular electrolyte solution in chamber has specific resistivity. Here, care has to be taken for the segment. If finger is placed in cuff, as shown in figure 3, then a particular pressure is created by cuff so that variation in blood volume can be recognized.

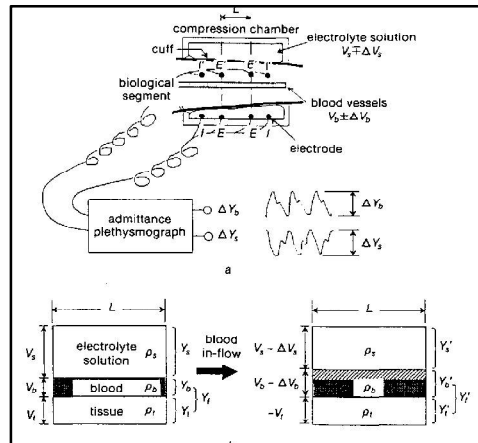


Figure 3: Conductance method for measurement of haematocrit value[4]

Blood flows through the body in systolic and diastolic states which causes variations in blood volume. When current is passed through both electrolyte solution and segment through electrodes, change in the flow of blood in finger causes to change in resistivity and length between pick-up voltages of electrodes. Electrical admittance of finger and solution changes accordingly. With the help of the differences in admittance during pulsation, it is possible to calculate required parameters. Haematocrit is the function of blood resistivity so we can relate haematocrit value with resistivity. With the help of proposed instrument, when 48kHz and 52kHz of 2mA of current passed through solution and finger by electrodes results into signals due to change in pulsations. These changes in signals in the form of admittance are recorded by using AC amplifiers and DC amplifiers[4, 5]. Points taken to be in interest and limitations of this method are given.

- Respective method helpful to calculate continuous measurement of not only Hct but also blood pressure and arterial elasticity. Due to use of improved setup of chamber good results can be obtained.

In study of this technique, it is observed that errors may occur due to difference in pressure on finger by rubber. Also, calibration is required for more accurate results of Haematocrit.

IV. DIGITAL PHOTOGRAPHY TECHNIQUE

In 2007, new method proposed using digital photography for non-invasive measurement of haemoglobin. Worldwide most of people are suffering from anemia which is related to haemoglobin. This can be detected by using digital photography method[6]. Haemoglobin has property to reflect red light and absorbs green light so it changes colour of tissues[7]. Those properties are useful for haemoglobin detection. This method states that measurement of haemoglobin can be done with the help of digital photographs of eyelids. In description, digital photographs of conjunctiva in eyelids are taken. As shown in figure 4, it is instructed to patient or photographer to stretch lower portion of the eye so that image of palpebral conjunctiva can be taken. Conjunctiva is position where we can easily determine anemia[8]. The

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selected area of image is cropped for analysis and observed in red, blue and green colour environment. Conjunctive and constant values for appropriate results are obtained with the help of pixels in the pictures. Pixel properties in the selected areas are utilized to find out relationship between conjunctiva colour and haemoglobin. Evaluation for relations of respective factors is carried out with the help of algorithm proposed. Algorithm explained for prediction of haemoglobin value. Figure 3 shows steps of algorithm to follow, one can find results. Digital photography technology gives strong relation between haemoglobin values and colour of conjunctiva. This method is not a total replacement of invasive technique but one can use this method for daily checkups of patients to take rough idea of haemoglobin.



Figure 4: Way to take images of conjunctiva[8]

Technique consists of some benefits as well as drawbacks which are given below.

- The whole study and results of this method states that there is vigorous relation can be find out between color of conjunctiva and haemoglobin. It can be used in Emergency Departments of hospitals.
- It is not sure that this particular algorithm will work in outdoors. This respective method requires pre-programmed computers for execution which is not practical for the outdoor works or medical camps.

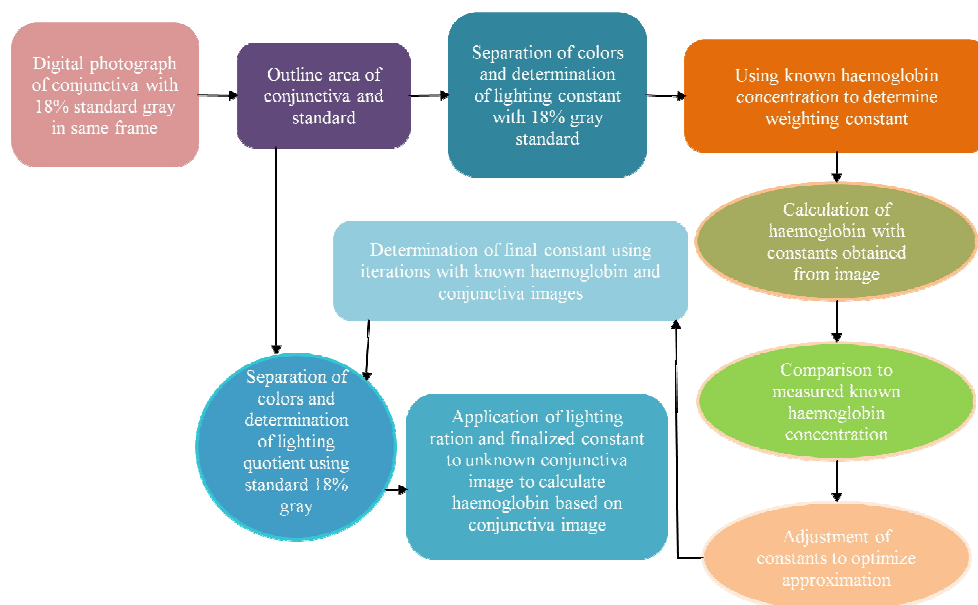


Figure 5: Algorithm for digital photography[2]

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V. MULTI-WAVELENGTH PULSE CO-OXIMETRY TECHNIQUE

Increase in number of wavelengths of light emitting diodes led to more accurate and calibrate values of HB can be obtained. Using principle of pulse oximeter, improved multi-wavelength pulse co-oximetry technique is introduced in which several wavelengths are used. According to principal of pulse oximeter LED light is passed through finger and transmitted signals are received by photo-detector. These signals are correlated with the help of Beer-Lambert law and oxygen saturation can be calculated. In multi-wavelength pulse co-oximetry technique instead of two wavelengths multiple wavelengths are used and algorithm is modified through which different multiple signals are taken simultaneously for calculation of total haemoglobin along with fractional haemoglobin[9]. Profits and impediments are stated as

- Introduced system tends to increase in accuracy as a result increase in safety for patients. It provides more accurate oxygen saturation level and haemoglobin fractions such as methaemoglobin, carboxyhaemoglobin results into immediate treatments. There is 1.5g/dl of biasing between non-invasive pulse co-oximetry results and standard laboratory result when observed in critical spin surgery[10].
- According to this concept algorithm which is to be used is more challenging task due to number of signals. As specified it has multiple wavelengths which may results in more complicated module.

Masimo introduced in their technology that motion to the body may affects the results of systems. According to the research, comparing results of laboratory values and other devices such as space labs and Hewlett-packard have 23% and 13% of lower values[11]. According to Masimo, for accurate results reference signal is required. There are always arterial and no-arterial components during motion which produces pulsatile signals and cannot be separated from arterial signals. So, considering reference signals accurate values can be obtained. Adaptive filter matches the input signal with reference signal and give final results. While increasing number of wavelength with same technique more fine results can be obtained[11].

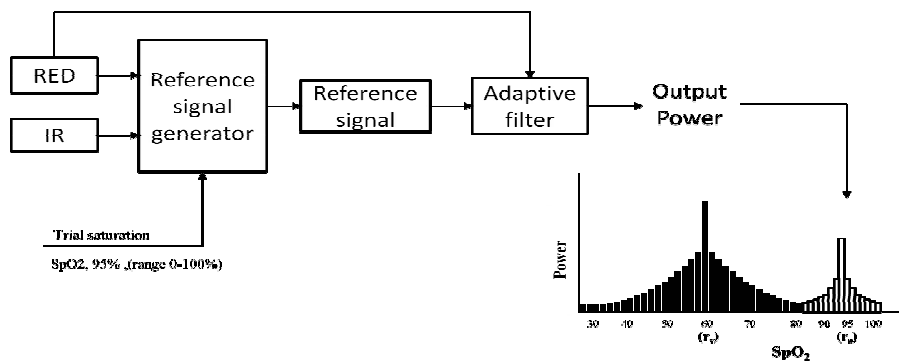


Figure 6: Multi-wavelength pulse co-oximetry method by Masimo[11]

Using this technology few profitable devices are developed by Masimo Corporation. Shows devices described in this paper. Radical-7, RAD-87, Rad-57 and Pronto-7 are recent devices used for various clinical purposes.

Masimo Radical-7

Device introduced by Masimo corporation uses same concept of pulse oximetry i.e. spectrophotometry method to calculate total haemoglobin concentration. Radical-7 can calculate total haemoglobin along with pulse rate and oxygen haemoglobin[12]. Total more than seven wavelengths are used in this device. For calculation of haemoglobin concentration finger is placed between light emitting diode and photodiode. Collected signal get self-calibrated with the help of algorithm for haemoglobin measurement. When we calculate Hb values few patients undergoing cesarean section delivery with the help of Bland Altman analysis using Radical-7, -1.09% of biasing is observed as compared with laboratory values. Factors affecting to accuracy includes thick skin of patient and difference in the blood flow to

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various sides of body[13, 14]. When haemoglobin of patients in operating theater is calculated using Radical-7 then the bias was 0.2g/dl in comparison with lab values[15].



Figure 7: Masimo Radical-7

Masimo Rad-57

This is eight wavelengths pulse co-oximeter launched by Masimo corporation. Two wavelengths are used in pulse oximeter to find out oxyhaemoglobin and deoxyhaemoglobin results into SpO₂ value. If any other light gets interrupted in oximeter then there is a big difference in oxygen saturation values which is observed in various studies. To overcome this factor by using eight wavelengths, Rad-57 pulse co-oximeter is created by Masimo which can give values of methaemoglobin and carboxyhaemoglobin, pulse rate, along with SpO₂ values. Placing sensor to fingertip, electronic signals are collected which are send to pulse co-oximetry device for measuring respective values. While discussing about accuracy of Rad-57, It is noted that mean difference in laboratory values and RAD values of carboxyhaemoglobin is 1.4% when number of subjects are 120 and 95% confidence interval (CI)0.2% to 2.6%. Also in one case when laboratory value of carboxyhaemoglobin is less than 15% while RAD showed greater than 15% for same. In burn center, when carboxyhaemoglobin values of 20 patients are calculated then there is 3.2% of biasing obtained comparing with laboratory values[16, 17].

Masimo Rad-87

A device with upgradable Masimo Rainbow technology is used for continuous measurement of oxygen saturation, pulse rate, carboxyhaemoglobin and methaemoglobin with addition of total haemoglobin and arterial oxygen content. According to Masimo, when observations on adult volunteers is done then it is calculated that accuracy of 2.9% SpO₂. While testing of normal patient laboratory values of SpCO is in between 4% to 10% while Rad-87 values were 7% i. e. +/-3% of difference.

Masimo Pronto-7

Multiple wavelength device pronto-7 given by Masimo Corporation proposes more accuracy in HB measurement comparing to other Masimo devices. This technique follows signals of pulsatile motion of arterial blood by passing light through finger. Sensor consists of LVAD which detects change of flow of blood during systolic and diastolic conditions. Different software's are used consisting of mathematical algorithms to acquire values of haemoglobin values. During measurement of haemoglobin using bland-Altman analysis, 0.14g/dl biasing is observed between SpHb and Hb values. While, in the absence of pulsation it is tough to find out Hb values also in emergency stages, Hb value calculation is critical when HB value is very low[18]. While 474 subjects of different ages, gender as well as different health conditions are taken for observation. In measurement of haemoglobin of all subjects, it is noted that the mean biasing and standard deviation of SpHb was -0.1% and +/-1.1g/dL.

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Figure 8: Masimo Pronto-7

VI. OCCLUSION SPECTROSCOPY TECHNIQUE

For betterment of non-invasive technique in measurement of haemoglobin as well as other blood components occlusion spectroscopy method is used. Using signal to noise ratio and absorption of light in blood required quantities can be calculated. Technique consists of finger probe having ring shaped cuff which is used for application of pressure on finger. When finger is placed in probe then pressure is applied on finger at time systolic flow so that blood flow will occlude temporarily at that point. Passing multi-wavelength light through finger and transmitted signals are gathered. Range for wavelength is kept 600nm to 1500nm[19]. Pressure applied to finger will be near about 200mmHg and up to 15 cycles of blocking-releasing is needed. At every cycle, different lights of different wavelengths are used and data is recorded. These signals are analyzed by specific algorithm to find out oxygen saturation and hematocrit[20]. Cuff using in process should be expansive. The maximum volume of 0.5 to 1cc is sometimes about 0.6c. During the process cuff will expand and occlude according to need. Material using in this structure should be flexible such as rubber. Pressure applied can be maintained during occlusion process so that at that particular portion light can be passed and transmitted light detected by detector[21].

- According to trials with this technique, non-invasive measurement of haemoglobin can be calculated.
- During procedure, pain and anxiety is observed from patients.

Orsense Ltd have most recent device called as NBM-200. Technology used in Glasswing is wireless technology which takes to next level of generation in this field.

OrSenseGlasswing

In 2012 OrSense introduces next generation wireless non-invasive device called as Glasswing. Results obtained in this device are by using occlusion spectroscopy technique. Addition to this portable and wireless data can be taken for measurement of haemoglobin. Advantage of Glasswing is no risk of infection, fast analysis and easy to use for staff and can be used in various clinical purposes like in labor room, blood donation camps and for anemia detection.

OrSense NBM 200

Device by OrSense was introduced in May 30 2014 known as NBM 200. It is used for haemoglobin measurement using occlusion spectroscopy technique. Finger probe as shown in figure gives unique type of signals which are used for haemoglobin measurement. It provides safe, comfortable environment to patient[22]. By comparing with other non-invasive device like Pronto-7 by Masimo, it is less calibrated in non-invasive results and laboratory results[23]. For finding accuracy of this device, test is done on pregnant women. In this case, it is calculated that biasing of NBM 200 with comparison of laboratory value is 0.1g/dl and standard deviation error was 0.86g/dl. Also by bland-Altman analysis, accuracy of NBM 200 compared to coulter devices during 95% limits of agreements is -1.59 to 1.79g/dl[22]. When data is collected of 269 pregnant women from villages with median age of 21 years, Hb levels of subjects by using System XP-100 was ranges between 5.5g/dL to 14.1g/dL with S.D. of 1.28 where as NBM-200 shows results

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between range 9.5g/dL to 14.6g/dL with S.D. of 1.43. While, by using Bland Altman analysis, results showed difference of -1.8g/dL[24].



Figure 9: Orsense NBM-200

VII. DUAL WAVELENGTH PULSE CO-OXIMETER TECHNIQUE

This is proposed technique through which upgradation of system is possible. Recent technique by using two wavelengths follows basic concept of pulse oximeter given by J. Webster[25]. Measurement of haemoglobin concentration is the total measurement of oxygenated haemoglobin, deoxygenated haemoglobin, carboxyhaemoglobin and methaemoglobin concentration mainly. Thus, these functions of haemoglobin plays vital role in total haemoglobin monitoring[26]. RED and IR light emitting diodes of 810nm and 1300nm wavelengths. NIR technology with PPG signals is used for analysis. Wavelengths described in pulse oximeter are 660nm and 940nm. Here, for haemoglobin measurement those values are replaced by 810nm and 1300nm. Reason behind this selection of values is, we can directly relate oxygen saturation value with haemoglobin value. So, isobestic points are selected. Further, procedure of method is same as that of pulse oximeter. Finger is placed in probe type device as shown in which LEDs and photo detector are placed opposite to each other. Light is made to pass through finger and unique signals are collected by detector, which are used to calculate total haemoglobin in blood. Algorithm for calculation of haemoglobin is needs to upgrade. This technique tends sophisticated hardware device with low cost and can be used in emergency units in operation theater as well as for cure of Anemia. Once we obtain signals from wavelength 810nm and 1300nm we can go for the data acquisition by using software[27]. Figure 8 shows block diagram of proposed method in which we are using two LEDs with which will drive by control driver. We have one photo-detector. So, need to do switching of LEDs. For improvement of ranging of current amplification is required. Final step will be the data acquisition and analysis of data.

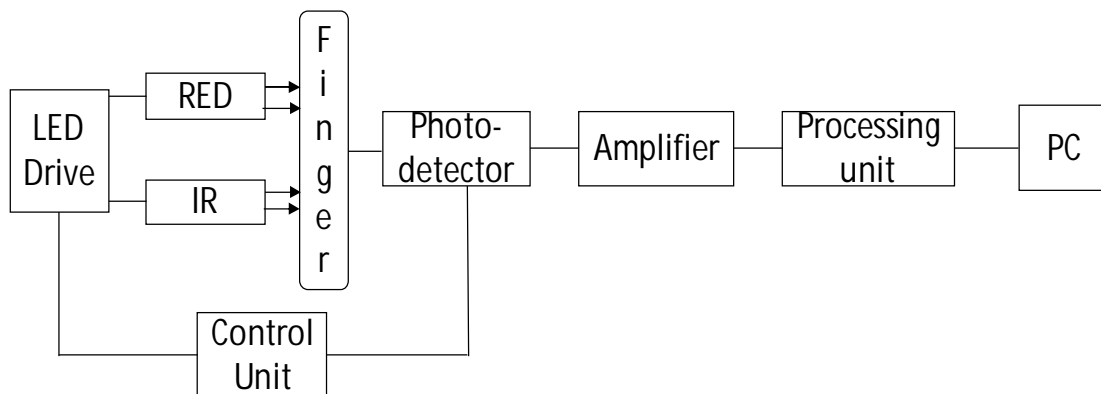


Figure 10: Dual-wavelength pulse co-oximetry method

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Table 1: Name of the devices with their properties and accuracies

Sr. No.	Device name	Technique used	Measurements of	Condition for Calculation of accuracy	Accuracy observed	Comparison with
1.	Masimo Radical-7	Multi-wavelength Pulse co-oximetry	SpHb, Pulse rate spO2	a. Hemoglobin calculation of patients undergoing cesarean section delivery	1.09% of biasing	Laboratory values
				b. SpHb values of patients in operating theater	0.2g/dL of standard deviation	Laboratory values
2.	Masimo Rad-57	Multi-wavelength Pulse co-oximetry	SpMet SpCO Pulse rate SpO2	a. SpCo measurement of 120 subjects	1.4% of biasing	Laboratory values
				b. SpCO measurement of 20 patients in Burn center	3.2% of biasing	Laboratory values
3.	Rad-87	Multi-wavelength Pulse co-oximetry	SpO2 SpCo SpMet, SpHb Pulse rate	a. SpO2 measurement of adult volunteers	2.9% of difference	Standard system
				b. SpCO measurement of subjects	+/-3% of biasing	Laboratory values
4.	Pronto-7	Multi-wavelength Pulse co-oximetry	SpO2 Pulse rate SpHb	a. Measurement of SpHb using Bland-Altman analysis	0.14g/dl of standard deviation	Laboratory values
				b. SpHb measurement of 474 subjects	0.1% of biasing and +/- 1.1g/dL of SD	Laboratory values

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5.	Orsense MBM-200	Occlusion Spectroscopy	SpHb Pulse rate SpO2	a. SpHb measurement of pregnant women	0.1g/dL of biasing and 0.86g/dL of S.D.	Laboratory values
				b. SpHb measurement of pregnant women using Bland-Altman analysis	-1.59g/dL to 1.79g/dL Of biasing	Coulter devices
				c. Measurement of SpHb of 269 pregnant women in villages	2.7g/dL to 4.0g/dL of biasing	XP-100
				d. Measurement of SpHb of 269 pregnant women in villages using Bland-Altman analysis	-1.8% of biasing	Xp-100

The table gives overall idea of all the devices we have discussed above in brief. It's accuracy, model number and all the specifications are given in table 1.

VIII. CONCLUSION

Non-invasive technique is most encouraging technique. Technologies given by Masimo and Orsense are uplifting techniques for haemoglobin measurement. As designated detailed methods support somewhat refinement of precision for technology. Medical practitioner's desire for proper replacement of invasive haemoglobin measurement method but still finding a particular renewal is a task itself. Till the date technology reached to 0.1% of biasing in system but giving continuous same biasing will not be obtained. The reason behind this can be technical faults or physical activities. Lack of proper algorithms put down to final precisions. Perhaps, inappropriate construction of system such as disturbance of surrounding light in original signal, unfitting of finger in finger probe are assignable for biasing in final results. From conductance method to pulse co-oximetry method, accuracies of devices increased. Given all approaches stand in need of effective changes in efficiency. Further, need to concentrate on calibration of recent methods so that non-invasive technique will be most accurate with comparison of laboratory values. Described proposed method i. e. dual-wavelength pulse oximeter technique can upgrade the system and leads to remove some downsides of other methods. This particular technique will help to remove disturbance acquiring by physical activities. By reforming valid way of calibration, it is possible to find out replaceable system for invasive method.

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