



## ***A Study of Peripheral Oxygen Saturation Measured by a Novel Pulse Oximeter under Hypoxic Conditions in Healthy Japanese Volunteers***

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### Abstract

*Pulse oximetry is a non-invasive technology for continuous monitoring of arterial oxygen saturation that has become a standard tool for assessment of oxygenation and respiratory function. Various pulse oximeters have been developed over the years. However, to date not all parts of pulse oximeters are made in Japan, and there are no established methods for pulse oximetry assessment under hypoxia. Therefore, we attempted to create hypoxic conditions via a novel method and measure peripheral oxygen saturation using a new pulse oximeter manufactured in Japan.*

**Keywords:** Hypoxia; Pulse Oximeter; Gas; SpO<sub>2</sub>; Peripheral Oxygen Saturation

### Introduction

Pulse oximetry is a noninvasive technology for continuous monitoring of arterial oxygen saturation and has become a standard tool for assessment of oxygenation and respiratory function in patients [1-3]. Healthcare providers routinely measure oxygen saturation (SpO<sub>2</sub>) by pulse oximetry to obtain accurate oxygen saturation data for the detection of hypoxemia.

The technique of pulse oximetry has been described previously [4]. Using spectrophotometric methodology, pulse oximetry measures SpO<sub>2</sub> by illuminating the skin and measuring changes in light absorption of oxygenated blood (oxyhemoglobin) and deoxygenated blood (reduced hemoglobin) using two light wavelengths: 660 nm (red) and 940 nm (infrared) [4,5]. Pulse oximeters use transmission sensors in which the light emitter and detector are on opposing surfaces of the tissue bed. To date these sensors have been manufactured in other

countries; however, the HOKS Co., Ltd (Oita, Japan) has now built sensors for its new pulse oximeter. Our aim in this study is to evaluate whether this novel Japanese probe can secure measurement accuracy equivalent to the SpO<sub>2</sub> measured by conventional probes under hypoxic conditions of our devising.

The accuracy of SpO<sub>2</sub> depends on two factors: the validity of the calculating formula (the calibration curve) and deviations from the calculating formula. For this reason, JIS T 80601-2-61, the International Standard of pulse oximetry equipment, requires each manufacturer to conduct controlled desaturation studies on human subjects and validate the SpO<sub>2</sub> accuracy in comparison with “gold standard (SpO<sub>2</sub>),” which is intended to include the validation of these two factors. In the JIS T 80601-2-61, the SpO<sub>2</sub> value determined by analyzing arterial blood samples with a hemoximeter is deemed the

reference value, and SpO<sub>2</sub> accuracy of the pulse oximetry equipment is stated in terms of the RMS (root-mean-square) difference between measured value (SpO<sub>2</sub>) and reference value (SpO<sub>2</sub>). We will examine the difference between the SpO<sub>2</sub> measured by a standard device and the SpO<sub>2</sub> measured by the new device made by HOKS. This RMS difference means that two-thirds of the SpO<sub>2</sub> values measured by a pulse oximeter can be expected to fall within the range of RMS. All pulse oximeters and patient monitors with HOKS SpO<sub>2</sub> technology are designed and manufactured to meet the same specifications for SpO<sub>2</sub> accuracy in our simulation.

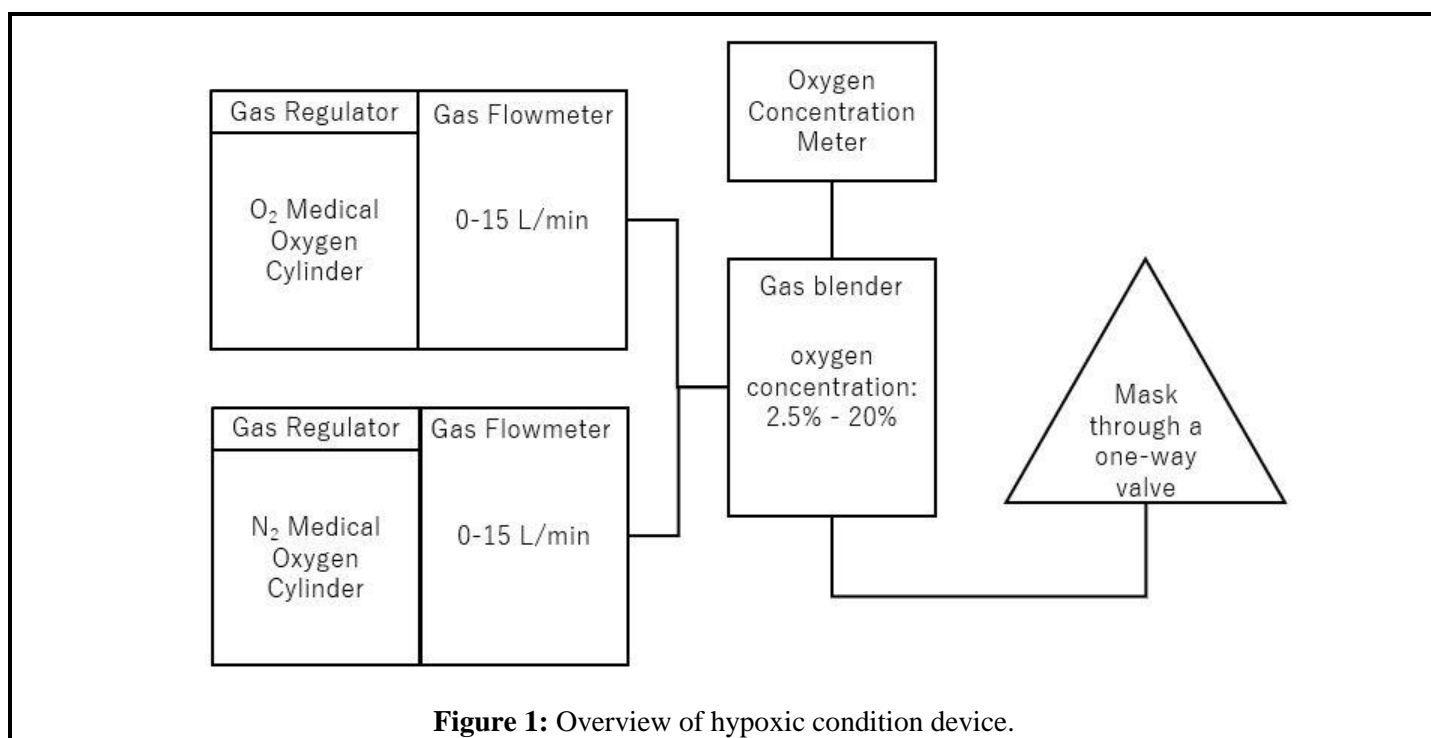
One can create a low-oxygen environment by, for example, climbing to high altitude or breathing a low-oxygen gas. By manufacturing a gas-mixing device, we were able to create a hypoxic condition (oxygen concentration: 2.5% to 10%) under low-oxygen inhalation at bedside. The aims of this study are to obtain approval for the new pulse oximeter and establish a novel method for oximetry assessment under hypoxic conditions.

## Primary Endpoints

The primary endpoints of this study are assessment of the peripheral oxygen saturation measured by a novel pulse oximeter under hypoxic conditions in healthy volunteers, the comparison of the novel device and the standard device, and safety.

## Eligibility Criteria

To participate in the study, the volunteers will be required to fulfill the following criteria: (1) aged 20–45 years, (2) having body mass index (BMI) 18.5–30.0, and (3) having provided written consent to participate in the study. The exclusion criteria are as follows: volunteers (1) with SpO<sub>2</sub> of less than 94% in room air; (2) with chronic obstructive pulmonary disease, asthma, sleep apnea syndrome, methemoglobinemia, or lung cancer; (3) with a history of pneumothorax or any thoracic surgery; (4) deemed unsuitable for measurement, e.g., digital anomalies such as absent index or middle finger; and (5) having abnormal data for any examinations with the goal of treatment.



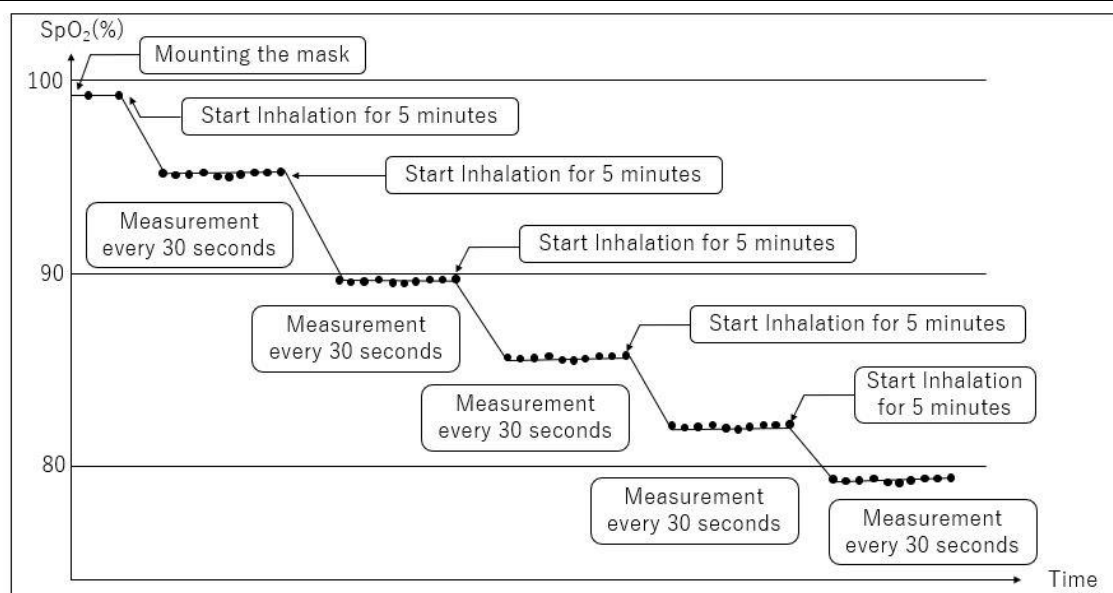
## Treatment Methods

**Study design.** After the acquisition of written consent, the subjects will be screened. The subject mounts a mask, produced by Koken Ltd (Tokyo, Japan), which covers the nose and mouth, and starts to inhale a mixture of O<sub>2</sub> and N<sub>2</sub> through a respiratory gas blender (KOFLOC Corp.)

(Figure 1). The subject undergoes SpO<sub>2</sub> assessment while breathing the O<sub>2</sub>/N<sub>2</sub> mixture (oxygen concentration: 2.5% to 10%) (Figure 2). The subject mounts the standard device on the forefinger of the right hand, and the test device on the middle finger of the right hand and the forefinger and middle finger of the left hand. The

subject inhales the gases and waits 5 minutes. We check that the SpO<sub>2</sub> value of the standard pulse oximeter is at steady state and record it. The value measured by the new pulse oximeter is also recorded in the same manner. The measurements are repeated every 30 seconds for a total

of 10 measurements (Figure 1). If the decline of SpO<sub>2</sub> is less than 2%, we stop the measurement and proceed to the next hypoxic stage. For safety reasons, if the measured the SpO<sub>2</sub> of the standard pulse oximeter is 75% or less, the subsequent experiments are discontinued.



**Figure 2:** Trial flowchart.

**Ethics considerations.** This study was approved by Oita University Faculty of Medicine Institutional Review Board on February 25, 2019 (reference no. B18-008). The study will be conducted in compliance with the Declaration of Helsinki in conjunction with our hospital's Ethical Guidelines for Medical and Health Research Involving Human Subjects. This study was registered in the Clinical Trial Registry (UMIN-CTR) on March 11, 2019 (UMIN000036103). In connection with this study, we have carried liability insurance as a compensation measure for eventual health damage caused to the subjects.

### Statistical Considerations

**Sample size.** The number of registered patients was planned as  $n = 3$ . As the purpose of this study is to assess the accuracy and safety of the novel pulse oximeter for development, and the number of these devices is limited, the number of patients was based on feasibility rather than on testing the statistical hypothesis.

**Statistical analysis.** The number of patients enrolled in the study and who are observed using the investigational device is considered an analysis set. The frequency distribution of the ratings of each evaluation item will be

calculated. The SpO<sub>2</sub> of mean, standard deviation, count, and RMS are provided for each oximeter's bias in the following ranges of SpO<sub>2</sub>: 70%–80% and 80%–100%.

The RMS error is calculated as follows:

$$\text{RMSError} = \sqrt{\frac{\sum (\text{SpO}_2 - \text{SaO}_2)^2}{n}}$$

### Conclusion

For the development of a novel pulse oximeter in Japan, it has become necessary to devise an evaluation method for hypoxia. However, at present very few devices described in previous studies can create hypoxic conditions. The present study aims to develop and obtain approval for a new pulse oximeter using a novel method under hypoxia.

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### Conflict of interest

The authors declare no conflicts of interest.

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