

# Effect of Bispectral Index versus End Tidal Anaesthetic Gas Concentration on Time to Tracheal Extubation for Isoflurane Based General Anaesthesia- A Prospective Observational Study

SHALINI JAIN<sup>1</sup>, RAVINA PANDYA<sup>2</sup>, KISHORE KUMAR ARORA<sup>3</sup>, NEETU GUPTA<sup>4</sup>

## ABSTRACT

**Introduction:** Modalities like Bispectral Index Monitoring (BIS) and End Tidal Anaesthetic Gas (ETAG) concentration guided anaesthesia have been used to study the intraoperative awareness but their efficacy for achieving early tracheal extubation has not been established.

**Aim:** To compare the effect of BIS monitoring and ETAG concentration guided anaesthesia on time to tracheal extubation and haemodynamics for isoflurane based general anaesthesia.

**Materials and Methods:** This prospective observational cohort study was conducted in the Department of Anaesthesiology at Mahatma Gandhi Memorial Government Medical College and MY Hospital, Indore, Madhya Pradesh, India, from June 2020 to June 2021. Total 60 patients with American Society of Anesthesiologists (ASA) grade I and II who received isoflurane based general anaesthesia were included in study. Depending upon the modality being used by the anaesthesiologist to monitor and maintain the depth of anaesthesia, the patients were

allocated in equal numbers into two group. Group B received BIS guided anaesthesia, where BIS value was kept between 40 and 60 and group E received ETAG concentration guided anaesthesia, where Minimum Alveolar Concentration (MAC) was kept between 0.7 to 1.3. Tracheal extubation time was recorded from stopping all anaesthetic agents upto the time of extubation. Unpaired t-test was applied for analysis of data.

**Results:** The mean tracheal extubation time was significantly longer in the BIS group (21.14±2.23 minutes) as compared to ETAG group (15.20±1.27 minutes). All haemodynamic parameters i.e., pulse rate, mean arterial pressure and oxygen saturation remained within normal limits and were comparable between the two groups at all the time intervals.

**Conclusion:** The tracheal extubation time is significantly longer in BIS guided anaesthesia as compared to ETAG guided anaesthesia. The ETAG monitoring promotes earlier extubation of patients as compared to BIS monitoring in isoflurane based general anaesthesia.

**Keywords:** Depth of anaesthesia, Haemodynamic parameters, Minimum alveolar concentration, Recovery time

## INTRODUCTION

In patients undergoing surgical procedures under general anaesthesia, early extubation has always been a desired goal for the anaesthesiologist as well as surgeon [1]. Early extubation not only reduces respiratory complications like pneumonia and atelectasis, and postoperative morbidity, but also reduces Intensive Care Unit (ICU) and hospital stays thereby reducing expenses and helping early mobilisation of patients [2]. It has been observed that application of “fast track” and early extubation protocols by the anaesthesiologists and the surgeons for the patients undergoing cardiac surgeries have important clinical implications for quality improvement and resource utilisation [3,4].

Besides early extubation, maintaining the proper depth of anaesthesia during the surgical procedure is also important. It not only helps in maintaining haemodynamic stability of the patient intraoperatively but also prevents patient's intraoperative awareness. Thus, intraoperative monitoring of the depth of anaesthesia is important for the maintenance of adequate anaesthesia. From all the available devices, the Bispectral Index Monitoring (BIS) and End Tidal Anaesthetic Gas (ETAG) concentration guided monitoring have proven to be effective for this purpose. Numerous studies have been conducted comparing BIS monitoring and ETAG concentration in reducing intraoperative awareness using different inhalational agents under General Anaesthesia (GA) but their efficiency in achieving early tracheal extubation has not been established.

Studying extubation time using these modalities, i.e., BIS guided monitoring and ETAG concentration guided monitoring has been done for halothane and sevoflurane in general surgery procedures [1,5].

However, very few studies have been done using Isoflurane as an inhalational agent of choice to compare the effect of BIS monitoring and ETAG monitoring on tracheal extubation time in general surgical patients. One such study was conducted by Shafiq F et al., who studied the tracheal extubation time using isoflurane in the older age group (60 years and above) and found that the extubation time was significantly shorter in BIS group compared to ETAG group [6]. Thus, this study was planned to compare the effect of BIS monitoring and ETAG concentration on the tracheal extubation time using isoflurane as the inhalational agent of choice.

## MATERIALS AND METHODS

This prospective observational cohort study was conducted in the Department of Anaesthesiology at Mahatma Gandhi Memorial Government Medical College and MY Hospital, Indore, Madhya Pradesh, India, from June 2020 to June 2021. Due permission was obtained from the Institutional Ethics Committee (Letter No.-EC/MGM/FEB-20/35). The study involved 60 patients undergoing surgery under general anaesthesia.

**Sample size calculation:** Sample size was calculated using G\* power software. A two-tailed analysis was done at an effect size of 0.8, confidence interval of 95% and power of 80%. The sample size

obtained was 26 patients in each group. Finally, 30 patients were included in each group.

**Inclusion criteria:** Patients with American Society of Anesthesiologists (ASA) physical status I and II, aged from 18 to 60 years of either sex undergoing surgeries (except neurosurgery) under GA using isoflurane as the inhalational agent were included in the study.

**Exclusion criteria:** Refusal to take part in the study, chronic users of psychoactive medication, patients with known or suspected encephalopathy, patients with deranged liver functions, psychiatric patients, pregnant and lactating mothers, patient with anticipated difficult intubation, patient not getting extubated immediately after procedure and operation time more than 4 hour were excluded from the study.

The patients were allocated in equal numbers into two groups depending upon the modality being used by the anaesthesiologist to monitor and maintain the depth of anaesthesia.

- Group B received BIS guided anaesthesia, where BIS value was kept between 40 and 60.
- Group E received ETAG concentration guided anaesthesia, where MAC was kept between 0.7 to 1.3.

**Preanaesthetic procedure:** A thorough preanaesthetic evaluation was carried out before the surgery was planned and the required clinical and laboratory investigations were done accordingly. The procedure and purpose of the study was explained to each patient and written informed consent was obtained from each participating patient.

## Procedure

All patients were kept nil per oral for six hours prior to surgery. They were premedicated with inj. glycopyrrolate 0.004 mg/kg intramuscularly in the preoperative room. Patients were then taken into operation theatre. Upon arriving in the operating room, the patients were connected to the multipara monitor and an intravenous access with 18 G intravenous (i.v.) cannula was secured. The patient monitoring included electrocardiogram, Non Invasive Blood Pressure (NIBP), Heart Rate (HR) and percent oxygen saturation (SpO<sub>2</sub>). The baseline HR, NIBP and SpO<sub>2</sub> were recorded. Bispectral index monitoring electrodes were applied on the forehead of the patients in the BIS group. The BIS monitoring was initiated, and the patient's awake/baseline BIS were recorded.

Patients were preoxygenated with 100% oxygen for 3 minutes and given inj. midazolam 1 mg intravenously, followed by general anaesthesia induction with i.v. inj. fentanyl (2 mcg/kg) and inj. propofol (2 mg/kg). Immediately after induction, isoflurane was used to maintain the depth of anaesthesia. Laryngoscopy and intubation were facilitated by using intravenous administration of depolarizing muscle relaxant inj. succinyl choline (1.5 mg/kg). Haemodynamic parameters [Heart Rate (HR), Mean Arterial Pressure (MAP), SpO<sub>2</sub>], BIS in the group B patients and MAC (equivalent to ETAG) in the group E patients were recorded just after intubation (0 mins). Anaesthesia was maintained using 50% nitrous oxide in oxygen, isoflurane and i.v. inj. atracurium 0.5 mg/kg as loading dose and 0.1 mg/kg in divided doses for maintenance. The patients were mechanically ventilated using volume control mode. Isoflurane was titrated to maintain a BIS value of 40-60 in the BIS group and MAC of 0.7-1.3 in the ETAG group throughout the surgery.

All haemodynamic parameters were observed and recorded at 5 min, 15 mins, 30 mins, 60 mins, 90 mins, 120 mins, 150 mins, 180 mins, and after extubation of the patient. After the last skin suture, all the anaesthetic agents were stopped and after the onset of spontaneous respiration, residual neuromuscular blockade was reversed with intravenous inj. neostigmine (0.05 mg/kg) and inj. glycopyrrolate (0.01 mg/kg). Extubation was done when:

- Patients started following commands,
- Had a sustained head lift for 5 sec and
- Maintained adequate SpO<sub>2</sub>.

Patient's characteristics and variables such as duration of surgery and duration of anaesthesia were documented. Any intraoperative complication was recorded and managed. The time duration from the discontinuation of isoflurane and other anaesthetic agents to the tracheal extubation was observed and recorded as tracheal extubation time which was the primary outcome.

## STATISTICAL ANALYSIS

Online statistical software GraphPad and Epi Info were used. Association between two non parametric variables, like gender and ASA grades were done using Pearson Chi-square test. Comparison between the means of two groups was done using unpaired t-test. A p-value <0.05 was taken as statistically significant. Descriptive statistics was presented in the form of numbers and percentages. The final data has been presented in the form of tables and graphs.

## RESULTS

One patient in each group was excluded by the end of study, as due to intraoperative complications, they did not get extubated in the operating room. Though the complications were managed intraoperatively, they were planned to be kept on postoperative mechanical ventilation for their better outcome. Observations of the remaining 58 patients were recorded and analysed. The groups were well-matched regarding age, gender, and the ASA grade [Table/Fig-1].

Variables	Group B (n=29)	Group E (n=29)	p-value
Age (years) (mean±SD)	35.66±11.99	36.86±11.97	0.703
<b>Gender</b>			
Male	10	13	0.421
Female	19	16	
<b>American Society of Anesthesiologists (ASA)</b>			
Grade I	7	7	1
Grade II	22	22	

**[Table/Fig-1]:** Demographic profiles of patients. Unpaired t-test applied for age; Pearson Chi-square test applied for gender and ASA grade; p-value <0.05 was considered as significant

Type of surgery consisted of open and laparoscopic cholecystectomy, pyelolithotomy, transabdominal preperitoneal hernia repair, laparoscopic hernioplasty, hydatid cyst removal, dermoid cyst excision, fundoplication, laparoscopic removal of hydatid cyst, and mastectomy. Both the groups were comparable regarding the type of surgery and duration of surgery as well as anaesthesia. The difference in the duration of surgery and duration of anaesthesia were not significant in the two groups (p-value=0.304, p-value=0.970, respectively). The mean tracheal extubation time in group B was 21.14±2.23 minutes and in group E was 15.20±1.27 minutes. The difference was found to be statistically significant (p-value=0.001), showing a significantly lower mean tracheal extubation time in group E in comparison to group B [Table/Fig-2].

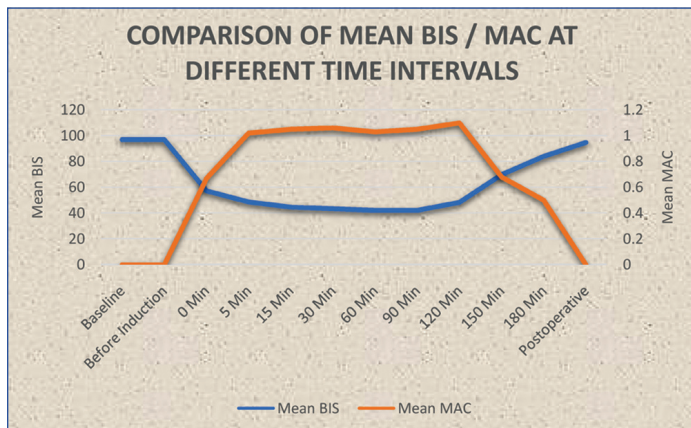
Parameters	Group B (Mean±SD)	Group E (Mean±SD)	p-value
Duration of surgery (min)	138.03±15.07	142.28±16.06	0.304
Duration of anaesthesia (min)	165.41±17.29	165.24±17.13	0.970
Time to tracheal extubation (min)	21.14±2.23	15.20±1.27	0.001

**[Table/Fig-2]:** Mean duration of surgery, anaesthesia and time to tracheal extubation. Unpaired t-test applied; p-value <0.05 was considered as significant

The mean baseline BIS was 96.93±1.03. Immediately after induction, the mean BIS value was found to be 57.34±1.9. Then there was fall in the BIS values which continued till 90 minutes, but remained between 40 and 60. Then, there was an increase at 150 minutes and this rise continued till 180 minutes. The mean baseline MAC was 0, which increased slightly at 0 minutes, reached almost 0.7 MAC just after induction and then increased continuously till 120 minutes and remained between 0.7-1.3 throughout these

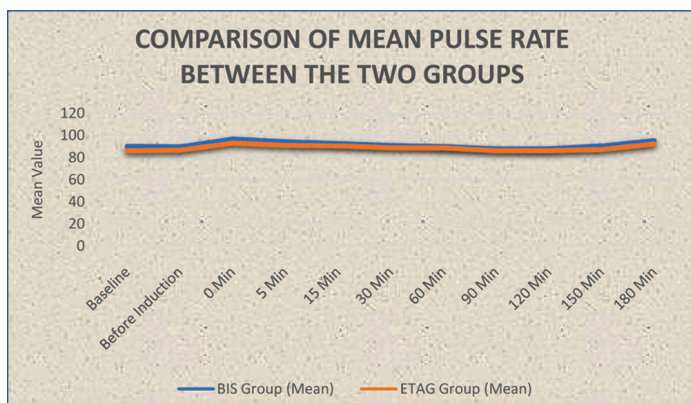


intervals. Then there was a fall at 150 minutes and this fall continued till 180 minutes. After stopping all the anaesthetic agents and Isoflurane, the values of BIS and MAC returned near to the baseline at the time of extubation [Table/Fig-3].



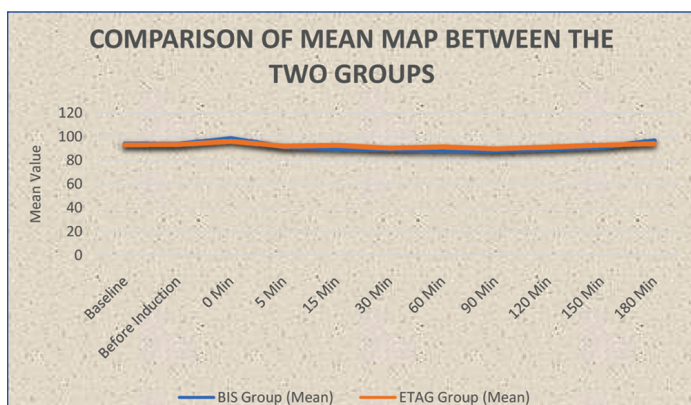
[Table/Fig-3]: Line diagram showing mean BIS/MAC at different time intervals.

All haemodynamic parameters i.e., pulse rate, mean arterial pressure and oxygen saturation remained within normal limits (20% of baseline) and were comparable between the two groups at all the time intervals ( $p$ -value  $>0.05$ ) [Table/Fig-4-6].



[Table/Fig-4]: Line diagram showing comparison of mean pulse rate between the two groups at different time intervals.

Unpaired t-test applied;  $p$ -value  $<0.05$  was considered as significant

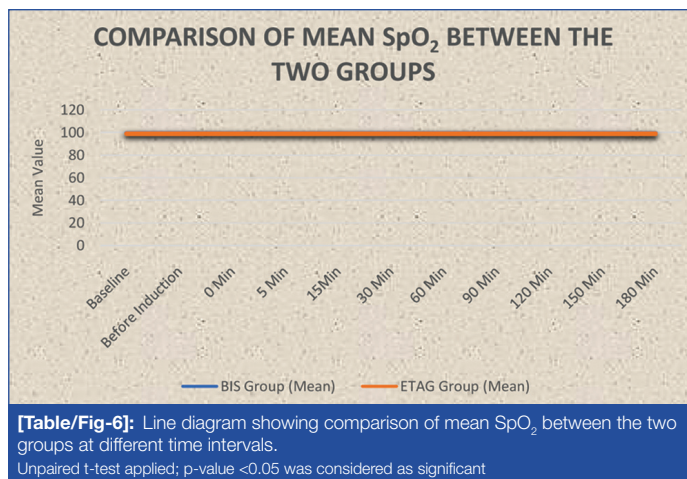


[Table/Fig-5]: Line diagram showing comparison of mean MAP between the two groups at different time intervals.

Unpaired t-test applied;  $p$ -value  $<0.05$  was considered as significant

## DISCUSSION

Along with adequate depth of anaesthesia, early extubation is also important for patient's well-being, as prolonged intubation duration is usually associated with respiratory complications and a longer hospital stay [2]. Though various studies have been done to assess modality which helps in providing proper depth, also very few studies have been performed to evaluate modality which provides early extubation. The present study compared tracheal extubation time using BIS and ETAG concentration guided monitoring in



[Table/Fig-6]: Line diagram showing comparison of mean  $SpO_2$  between the two groups at different time intervals.

Unpaired t-test applied;  $p$ -value  $<0.05$  was considered as significant

Isoflurane based general anaesthesia. It was found that the tracheal extubation time was significantly longer in BIS guided anaesthesia as compared to ETAG guided anaesthesia.

Jain N et al., studied extubation time using halothane as the inhalational agent found that extubation time was significantly greater in the BIS group compared to ETAG group [1]. However, Shukla U et al., used sevoflurane as the inhalational agent and found a significantly shorter extubation time in the BIS group. They suggested that sevoflurane's less partition coefficient might be a factor in early recovery from anaesthesia [5].

In the present study, the mean tracheal extubation time in BIS group ( $21.14 \pm 2.23$  minutes) was found to be significantly longer than the mean tracheal extubation time in the ETAG group ( $15.20 \pm 1.27$  minutes), suggesting that the use of BIS monitoring though helped in maintaining adequate anaesthesia, does not necessarily help in early extubation. A similar study done by Vance JL et al., on cardiac surgery patients found that the difference between the two means was not significant (307 minutes in the BIS group and 323 minutes in ETAG group, respectively). It was concluded that the use of BIS monitoring did not reduce the extubation time [7]. However, contrary to the index study, Shafiq F et al., had found that the extubation time was significantly shorter in BIS group compared to ETAG group ( $7.83 \pm 2.6$  minutes vs  $11.23 \pm 3.1$  minutes). They studied the effects of BIS monitoring and ETAG monitoring (including HR and blood pressure monitoring also) on the tracheal extubation time using Isoflurane as the inhalational agent in the older age group (60 years and above), posted for abdominal surgeries. This can be due to decreased requirement of anaesthetic agents in the older age group [6].

Villafranca A et al., compared extubation time in fast-track cardiac surgeries, titrating the inhalational agents using BIS protocol and ETAG protocol. They found no significant association between BIS monitoring and early extubation, and suggested that extubation mainly depended on patient's characteristics [8].

Equi-tidal minimum alveolar concentration studies that have been done to compare the BIS values of different agents at equal MAC concentrations and have shown different BIS values for agents, suggesting that different agents require different concentrations to attain a particular MAC [9,10]. This has an indirect effect on patient's recovery profile, as a higher blood: gas partition coefficient will require longer washout time than those with lower partition coefficient [11]. Such studies have concluded that the BIS values are drug specific for different inhaled and other anaesthetics [9-12].

These studies justify the present findings of delayed extubation in the BIS group as higher concentration of isoflurane is required to attain the target BIS value (40-60) due to its higher blood gas participation coefficient which further increases its washout time.

## Limitation(s)

This study was conducted in a single centre, paediatric and geriatric patients were excluded. Also, correlation between the MAC and BIS values in the same patient could not be done in order to prevent the bias. This study was also confined to short duration surgeries, and can be done for longer duration surgeries as the increased duration of anaesthesia might have a different impact on extubation time.

## CONCLUSION(S)

It can be concluded that the tracheal extubation time is significantly longer in BIS guided anaesthesia as compared to ETAG guided anaesthesia. End tidal anaesthetic gas monitoring promotes earlier extubation of patients as compared to BIS monitoring in Isoflurane based general anaesthesia. Both the modalities are comparable in maintaining the haemodynamic stability of the patients during the procedure, thus helping in maintenance of adequate depth of anaesthesia throughout the procedure.

## REFERENCES

- [1] Jain N, Mathur PR, Khan S, Khare A, Mathur V, Sethi S. Effect of bispectral index versus end-tidal anesthetic gas concentration-guided protocol on time to tracheal extubation for halothane-based general anesthesia. *Anesth Essays Res.* 2016;10(3):591-96.
- [2] Zettervall SL, Soden PA, Shean KE, Deery SE, Ultee KH, Alef M, et al. Early extubation reduces respiratory complications and hospital length of stay following repair of abdominal aortic aneurysms. *J Vasc Surg.* 2017;65(1):58-64.
- [3] Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: Executive summary: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;124(23):2610-42.
- [4] Fitch ZW, Debesa O, Ohkuma R, Duquaine D, Steppan J, Schneider EB, et al. A protocol-driven approach to early extubation after heart surgery. *J Thorac Cardiovasc Surg.* 2014;147(4):1344-50.
- [5] Shukla U, Yadav U, Yadav JB, Agrawal S. Comparison of end-tidal anesthetic gas concentration versus bispectral index-guided protocol as directing tool on time to tracheal extubation for sevoflurane-based general anesthesia. *Anesth Essays Res.* 2020;14(4):600.
- [6] Shafiq F, Naqvi HI, Ahmed A. Effects of bispectral index monitoring on isoflurane consumption and recovery profiles for anesthesia in an elderly Asian population. *J Anaesthesiol Clin Pharmacol.* 2012;28(3):348.
- [7] Vance JL, Shanks AM, Woodrum DT. Intraoperative bispectral index monitoring and time to extubation after cardiac surgery: Secondary analysis of a randomized controlled trial. *BMC anesthesiology.* 2014;14(1):01-07.
- [8] Villafranca A, Thomson IA, Grocott HP, Avidan MS, Kahn S, Jacobsohn E. The impact of bispectral index versus end-tidal anesthetic concentration-guided anesthesia on time to tracheal extubation in fast-track cardiac surgery. *Anesth Analg.* 2013;116(3):541-48.
- [9] Bharti N, Devrajan J. Comparison of bispectral index values produced by isoflurane and Halothane at equal end-tidal MAC concentrations. *Anesth Essays Res.* 2007;51(5):401-04.
- [10] Gupta M, Shri I, Sakia P, Govil D. Comparison of equi-minimum alveolar concentration of sevoflurane and isoflurane on bispectral index values during both wash in and wash out phases: A prospective randomised study. *Indian J Anaesth.* 2015;59(2):79.
- [11] Khan KS, Hayes I, Buggy DJ. Pharmacology of anaesthetic agents II: Inhalation anaesthetic agents. *Continuing Education in Anaesthesia Critical Care & Pain.* 2014;14(3):106-11. <https://doi.org/10.1093/bjaceaccp/mkt038>.
- [12] Schwab HS, Seeberger MD, Eger EI, Kindler CH, Filipovic M. Sevoflurane decreases bispectral index values more than does halothane at equal MAC multiples. *Anesth Analg.* 2004;99(6):1723-27.

### PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of Anaesthesiology, Mahatma Gandhi Memorial Government Medical College and MY Hospital, Indore, Madhya Pradesh, India.
2. Postgraduate Resident, Department of Anaesthesiology, Mahatma Gandhi Memorial Government Medical College and MY Hospital, Indore, Madhya Pradesh, India.
3. Professor and Head, Department of Anaesthesiology, Mahatma Gandhi Memorial Government Medical College and MY Hospital, Indore, Madhya Pradesh, India.
4. Assistant Professor, Department of Anaesthesiology, Mahatma Gandhi Memorial Government Medical College and MY Hospital, Indore, Madhya Pradesh, India.

### NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Neetu Gupta,  
1404, Ophira-2, Apollo DB City, Nipania, Indore, Madhya Pradesh, India.  
E-mail: dr.neetu2022@gmail.com

### PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Apr 13, 2022
- Manual Googling: May 11, 2022
- iThenticate Software: Jun 08, 2022 (23%)

### ETYMOLOGY: Author Origin

### AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Apr 08, 2022**  
Date of Peer Review: **Apr 28, 2022**  
Date of Acceptance: **May 31, 2022**  
Date of Publishing: **Jul 01, 2022**