

THESIS FOR THE DEGREE OF DOCTOR OF  
PHILOSOPHY (PhD)

**Investigation of the effectiveness of innovative monitoring  
procedures for the safety of anesthesia**

by

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Doctoral School of Neurosciences

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The Examination takes place at the Library of Department of  
Anesthesiology and Intensive Care, Faculty of Medicine,  
University of Debrecen, 08th May, 2019. 11.00 am

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Department of Internal Medicine, Faculty of Medicine,  
University of Debrecen, 08th May, 2019. 13.00 pm

## **I. Introduction**

The modern monitoring methods used in anesthetic practice are the subject of numerous scientific publications, which determine not only the professional protocols for patient observation in the operating room, but also the main directions of medical technology developments. Although uncertainty about the use of unknown device or the lack of training and experience often hinder the spread of a new test method, the need for continuous improvement of patient safety and avoidance of anesthesiological “accidents” has inevitably coincided with the continuous technological development of intraoperative patient monitoring tools. While the prevalence of general anesthesia-related deaths has decreased significantly in recent decades, high-risk patients and high-risk surgical interventions continue to be associated with a high incidence of life-threatening complications. They are difficult to distinguish from risk factors depending on the type of disease or the type of surgery based on mortality tests, but there is often a human omission and inexperience in which the ignorance or misinterpretation of the data and alarms obtained during patient observation play a significant role. The latter factors may be partly related to the toxic residues of the evaporating anesthetics entering the operating airspace of the operating room, which,

due to the long exposure time, poses a number of potential hazards to the medical staff. The continuous improvement of monitoring techniques with the highest technical standards, which can detect multiple parameters in parallel, can only further reduce the health risk of anesthetic activity if it serves the safety of both pillars - the patients themselves or the staff responsible for their treatment - of perioperative care.

## **II. Background**

### **Alternative monitoring of the depth of muscle relaxation based on change of the stapedius reflex threshold**

*The significance of the residual neuromuscular block, its effect on morbidity*

Research into the physiological functioning of neuromuscular junction was established by Claude Bernard's pioneering work in the second half of the 19th century, but the practical use of muscle relaxants during narcosis only spread after the introduction of endotracheal intubation worldwide. Although the development of modern surgical and anesthesiological procedures has been associated with the increasing use of different types of muscle relaxants, however, there remains a significant problem the prevention of "postoperative residual neuromuscular block" (PRNB) in the

wake-up phase. This means a residual muscle relaxant effect at the end of the surgery, after the removal of the tube, which reduces the patient's muscle mass to various degrees and can be a source of serious complications. The prevalence of this phenomenon depends on both the drug used and the anesthetic method, but can be detected at a very high rate (20-40% on average) in addition to modern anesthetic procedures. The main reason for this is that the effect of muscle relaxants is influenced by a number of factors, regardless of their type, so that insufficiency of given drug at the end of narcosis cannot be expected with complete safety in clinical practice.

The neuromuscular block that may still exist after the extubation can cause significant dysfunction in the muscles of the pharynx, larynx, esophagus, and depletion of the manifested swallowing coordination and respiratory protection reflexes, leading to aspiration and postoperative pneumonia. In addition, malfunctioning of the upper respiratory muscles may cause obstruction, a decrease in the oxygen saturation of the blood, which is particularly harmful in certain underlying diseases (obesity, COPD, sleep apnea). The symptoms associated with the residual relaxant effect (general weakness, suffocation, vision, speech, swallowing, and cough) are subjectively perceived by the awakening patients. Overall, the harmful

effects of residual muscle relaxation (aspiration, upper respiratory tract obstruction, atelectasis, pneumonia, hypoxia) are independent risk factors for postoperative respiratory failure.

*Characteristics of muscle relaxant monitoring, difficulties in recognizing and preventing postoperative muscle weakness during general anesthesia*

The essence of the pharmacological action of neuromuscular blockers is that they inhibit skeletal muscle by blocking the transmission of stimuli on the motor endplate. Non-depolarizing muscle relaxants, as antagonists, bind to the receptor of the physiological transmitter, but do not cause muscle contraction but competitively inhibit the attachment of acetylcholine. The relaxant effect is ceased due to the distribution, gradual metabolism, and excretion of the drug used, or by the use of specific antidotes. The latter either inhibit acetylcholinesterase enzyme activity and increase the concentration of acetylcholine in the neuromuscular junction, or bind the muscle relaxant drug to form an ineffective complex.

Muscle relaxants used in anesthesia can only significantly reduce muscle strength by blocking more than 75% of the acetylcholine receptors, while 90% of the receptors

are required to inhibit clinically effective muscle relaxation. Unfortunately, the routine monitoring procedures currently used in the practice are only able to detect muscle relaxant activity at 75% of the acetylcholine receptors or above, but in patients with a higher degree of inhibition (0-75% receptor coverage), patients may not yet have adequate safety. Because of the potential risk of a latent block, quantitative monitoring is being used to determine the extent of receptor coverage as accurately as possible.

The recognition of postoperative muscle weakness and the return of muscle strength are considered safe at the end of surgery which may be based on the evaluation of clinical criteria and instrumental tests. None of the criteria which are determined on the basis of clinical signs are ideal, their reliability is uncertain, because at the end of the anesthesia, even before extubation they require the patient to wake up and cooperate. Qualitative and quantitative monitoring procedures are also available for anesthesia for objective determination of muscle relaxation. With these methods, the current depth of muscle relaxation can be estimated by the magnitude of muscle contraction induced by the „supramaximal” stimulation of the motor nerve of the neuromuscular junction. For measuring reasons, the measurement of the intensity of muscle twitching

on the m. adductor pollicis (thumb opposition) by the stimulation of the ulnar nerve has been widely accepted. With the use of the easiest-to-use acceleromyography, the incidence of residual relaxant effects decreased significantly.

#### *The acoustic (stapedius) reflex test*

The acoustic reflex threshold determination and the tympanometry are commonly used to assess middle ear function and are considered best practices. Although the methods of the two tests are closely related, the information they have obtained is different, they serve different purposes. The principle of the measurement is to determine the absorption or reflection of the test tone on the eardrum at different auditory pressures. The acoustic reflex, also known as the stapedius reflex refers to an involuntary muscle contraction of the stapedius muscle in response to a high-intensity sound stimulus.

The physiological role of the reflex is to protect the integrity of the inner ear against strong, especially low-frequency sounds. The excitation through the auditory, and facial nerve causes the contraction of the m. stapedius and tensor tympani which are the smallest skeletal muscles in the body. Contraction of the muscles stiffen the middle ear ossicles and tilts the stapes in the oval window of the cochlea which



effectively decreases the vibrational energy transmitted to the cochlea. The muscle contraction is clinically apparent by a marked change in the impedance properties of the middle ear. The smallest volume (normally 70 dB) that can trigger the reflex is the threshold of the stapedius reflex (acoustic reflex threshold).

### **Non-invasive pulse wave analysis for monitoring the cardiovascular effects of CO<sub>2</sub>-pneumoperitoneum during laparoscopic cholecystectomy**

*Pathophysiological consequences of CO<sub>2</sub>-pneumoperitoneum used in laparoscopic surgery*

Adequate surgical conditions during laparoscopic surgeries can be achieved by abdominal or extraperitoneal insufflation of a gaseous substance, but in addition to the many advantages of the method, studies have also demonstrated the potential risks of using CO<sub>2</sub>-pneumoperitoneum. Changes in cardiovascular, neuroendocrine, and renal function are primarily due to increased intra-abdominal pressure (IAP), significant haemodynamic processes resulting from posture and absorbed CO<sub>2</sub>, and in particularly high-risk patients, precise anesthetic risk estimates and extended multiparametric intraoperative monitoring are warranted. Cardiovascular side

effects do not always correlate properly with conventional non-invasive patient monitoring parameters (blood pressure, pulse rate, ECG), and the resulting pathological processes are often detected only by invasive hemodynamic monitoring. However, the latter is not indicated for all patients due to its risks, especially when considering the relatively short duration and low risk of surgery.

The most typical reaction of the initial phase of laparoscopic surgery is the decrease of the circulating blood volume and the different degree of hypotension. This is primarily due to the side effects of the applied anesthetics and the reduction of the venous return (cardiac „preload“) from the abdominal organs to the heart due to the positioning of the patient. In the second phase following abdominal insufflation the increase in abdominal pressure activates the renin-angiotensin-aldosterone system, resulting in a gradual increase in peripheral systemic and pulmonary vascular resistance (cardiac „afterload“) and arterial pressure. Partial regeneration is observed about 10 to 15 minutes after insufflation. Peripheral vascular resistance begins to decline slowly, but the heart index is fully normalized only at the end of laparoscopic intervention, along with decline of abdominal pressure. The positioning of the patients according to the phases of surgery („head-up“ or

Trendelenburg) and the side effects of the applied anesthetics may further modify the pathophysiological changes in the circulatory system.

Comorbidity plays a major role in the phase of insufflation during laparoscopic cholecystectomy. Patients with normal cardiovascular function generally tolerate well the changes in the circulatory system. However, high-grade patients (ASA III-IV) are not able to compensate low filling pressure, simultaneous increase in arterial blood pressure and decreased oxygen transfer capacity.

*Non-invasive peripheral arterial pulse wave analysis by SphygmoCor device*

It is generally accepted that the characteristics of the peripheral pulse reflect the changes in arterial diameters, wall elasticity, wall thickness and the condition of the peripheral vascular beds. The principal basis of the SphygmoCor pulse wave analysis system is that the peripheral arterial pressure waveform may be used for the reconstruction of central (aortic) pressure. The method behind this is applanation tonometry, which ensures the sensitive detection of the radial artery pulse waveform. As a result of the "sequential transformation" of the peripheral pulse wave, by means of contour analysis, a central

pressure wave can be generated, so that both the peripheral reflection and the central pulse pressure rise can be described and analyzed. The main attribute of SphygmoCor is its ability to derive the central aortic pressure waveform non-invasively from the pressure pulse recorded at a peripheral site, usually at the upper arm (radial artery).

### **Does standing or sitting position of the anesthesiologist in the operating theatre influence sevoflurane exposure during craniotomies?**

*Health effects of workplace, chronic exposure to evaporative anesthetics*

Although most of the inhaled anesthetics entering the lungs during inhalation leave the body unchanged (in fact without metabolic transformation), the potential hazard associated with the toxicity of the preparations is not negligible. The anesthetic gases that are rapidly absorbed through the large respiratory surface, bypassing the hepatic metabolism, directly enter the circulation. Fortunately, the rate of biotransformation is generally low, but significant differences can be observed between the individual inhalational anesthetics. Although inhaled narcotics inevitably enter into the closed airspace of the operating room compared to the anesthetized patients, the

known side effects of the drugs may accumulate due to the long exposure time.

The potential for mutagenic, genotoxic effects of evaporating anesthetics in the air of the operating room is suggested by many studies. The exact mechanism is unclear, but with prolonged exposure, the increase in oxidative stress, the decrease in antioxidant capacity can cause different chromosomal damage (fiber break, basal exchange, cross-link breakdown) on the DNA.

Many epidemiological studies have investigated the effect of chronic anesthetic exposure on fertility disorders, fetal developmental disorders, premature births, and spontaneous abortions, but the scientific validity of the conclusions is currently not conclusive.

Several studies showed that high concentrations of anesthetic gas in the air into the operating air help to temporarily develop the central nervous system symptoms (headache, dizziness, nausea, fatigue, memory, coordination, attention disorder, irritability) which usually disappear after leaving the workspace.

*Limit values for the concentration of anesthetic gas detected in the operating airspace, the most frequent sources of exposure, and options to reduce it.*

There is a clear positive correlation between the amount of volatile anesthetics released into the atmosphere and the symptoms of occupational health damage. In some countries, for workplace risk, the threshold for acceptable levels of individual anesthetic gases in the work area is extrapolated to a time-based average of 8 hours. At the same time, there is no single regulatory requirement in the European Union, the individual provisions are only formulated as recommendations and it is not necessary to determine routinely the level of contamination caused by inhaled drugs in the operating rooms.

Evaporating anesthetics may come from several sources into the airspace. Leakage may occur from the anesthesia respiratory circuit, from the anesthesia machine, from the extraction and air exchange systems, or from the patient's respiratory tract. Differences in air anesthetic concentrations are due to the type, concentration, duration of exposure and room air exchange of the applied anesthetic, and the position of the surgical team. According to the reports, the main source of air pollution is the patient's respiratory zone. As a result, the exposure of the medical staff to the medical and

assistant exposure of the anesthetist is usually the most pronounced, but by changing the work area, positioning the staff, and adequately designing the surgical isolation, the concentration of evaporating anesthetics can be significantly affected and effectively reduced.

### **III. Objectives**

*Alternative monitoring of the depth of muscle relaxation based on change of the stapedius reflex threshold*

In our prospective study, stapedius reflex threshold determination was performed during surgical operations to monitor the effect of a non-depolarising muscle relaxant. Until then this method has not been used for this purpose.

*Questions to answer in our investigation:*

- Does muscle relaxation have a significant effect on the stapedius reflex response?
- Does the continuous detection of stapedius reflex change prove to be a suitable method for intraoperative monitoring of neuromuscular function?
- Determining the optimal frequency of stimulation.

- Comparison of the results of the stapedius reflex test and the traditional acceleromyography techniques (TOF stimulation and 1 Hz single twitch stimulation).

*Non-invasive pulse wave analysis for monitoring the cardiovascular effects of CO<sub>2</sub>-pneumoperitoneum during laparoscopic cholecystectomy*

In our prospective study, non-invasive pulse wave analysis was used to monitor hemodynamic effects of CO<sub>2</sub> pneumoperitoneum during laparoscopic cholecystectomy. During the study, the parameters were monitored using a SphygmoCor device which has never been used for this purpose in anesthesia practice.

Questions to answer in our investigation:

- Is the method of peripheral pulse wave analysis suitable for monitoring cardiovascular parameters under intraoperative conditions?
- In the case of laparoscopic cholecystectomy, are the hemodynamic changes detected by the SphygmoCor device due to CO<sub>2</sub> insufflation correlated with the invasive monitoring data reported in the literature?



*Does standing or sitting position of the anesthesiologist in the operating theatre influence sevoflurane exposure during craniotomies?*

The concentration of anesthetic gas entering the operating air in the operating room due to anesthesia is not measured in our country regularly, organized manner, and the method of determination has recently appeared in international practice. In our prospective study, the determination of sevoflurane concentration at fixed sampling points (in a laminar flow zone modeling standing position and in a turbulent flow zone modeling the sitting position) was performed.

Questions to answer in our investigation:

- Does sevoflurane concentration in the operating room airspace exceed the safe limit?
- Does the air concentration of sevoflurane differ in the laminar flow zone of the air exchange system and in the turbulent flow zone generated by the surgical isolation?
- Can the anesthetist's exposure to anesthetic gas be affected by changing the work area?

#### **IV. Patients and methods**

##### *Alternative monitoring of the depth of muscle relaxation based on change of the stapedius reflex threshold*

A total of 20 consecutive patients undergoing elective laparoscopic cholecystectomy with the American Society of Anesthesiologists (ASA) categories of I–II were subjects of the present study.

Neuromuscular monitoring was performed throughout the course of anaesthesia using TOF Watch SX acceleromyograph (Organon, Oss, Holland). The first evoked response of train of four (TOF) was considered the twitch height and was expressed as a percentage of the control. Stapedius reflex parameters as measured at different occasions were off-line compared to twitch height values as measured by acceleromyography. Thus, acceleromyographic measurement results were used as standard for the monitoring of neuromuscular blockade and stapedius reflex threshold levels (as an indirect measure of the stapedius muscle activity at different stages of anaesthesia) were compared with acceleromyographic results.

The stapedius reflex was assessed using a MT10 Handheld Impedance Tympanometer (Interacoustics, Assens,

Denmark). The device always records the smallest sound energy at which the reflex may be evoked. In our study the absence of the stapedius reflex at maximal sound energy emitted by the device (110 dB) indicated the total blockade of the stapedius muscle. The reappearance of the reflex at different higher than baseline sound energies allowed the quantification of the stapedius muscle recovery from curarisation. These stapedius reflex threshold differences in dB were used for comparison with twitch recovery.

In the present study stapedius reflex measurements were performed on different occasions during the course of clinical anaesthesia:

- After premedication but before anaesthesia induction.
- After induction, but before administration of muscle relaxant.
- After administration of muscle relaxant when twitch height decreased to 5%.
- During the course of surgical anaesthesia.
- Continuously during the recovery phase of the neuromuscular blockade (twitch > 10%) until the stapedius reflex returned to the initial value.

The primary endpoint of the study was the return of the stapedius reflex threshold to its initial value. The twitch height values measured at this point were taken into account for comparison. In addition we aimed to establish the correlation between stapedius reflex differences and twitch values during the recovery from curarisation.

*Non-invasive pulse wave analysis for monitoring the cardiovascular effects of CO<sub>2</sub>-pneumoperitoneum during laparoscopic cholecystectomy*

A total of 41 consecutive patients undergoing elective laparoscopic cholecystectomy for symptomatic cholelithiasis without cholangiography or choledochotomy were enrolled in this prospective case-series study. The patients were all in good health, classified as ASA I and II.

The SphygmoCor pulse wave analysing system was used for monitoring cardiovascular function, which is a noninvasive method based on applanation tonometry. During the present study we measured systemic and central aortic pressure, augmentation pressure, augmentation index, ejection duration and subendocardial viability ratio.

Hemodynamic measurements were repeated in different phases of the procedure:

- before induction of anesthesia
- 5 minutes after induction of anesthesia
- 5 minutes after inflation of the peritoneal space followed by repeated measurements every 10 minutes
- 5 minutes after deflation of the peritoneal cavity.

*Does standing or sitting position of the anesthesiologist in the operating theatre influence sevoflurane exposure during craniotomies?*

We included 27 patients undergoing craniotomy for the removal of intracerebral tumors.

To collect the evaporated amount of sevoflurane a setup was used consisting of a portable air sampling pump (224-51 TX Air Sampling Pump SKC, Dorset, England), an attached tube system and an absorber ampule coupled to the tube system; the details of the sampling were described elsewhere in detail. The suction pump ensured a continuous flow through the absorber ampule where sevoflurane was collected for later analysis using gas chromatography. Sample collection was started at skin incision and terminated at dural closure.

To answer the present study's question, three detectors were placed at the different sites of the OR as follows:

1. on an infusion stand at the side of the patient at a height of 175 cm in the laminar flow zone (modeling of standing position)
2. on an infusion stand at the side of the patient at a height of 100 cm in the turbulent flow zone (modeling of sitting position)
3. in the indifferent corner of the operating room for control ("background" measurement of sevoflurane concentration).

## **V. Results**

### **1. Alternative monitoring of the depth of muscle relaxation based on change of the stapedius reflex threshold**

Parallel stapedius reflex and acceleromyographic measurements were performed on 20 patients (11 males and 9 females) undergoing cholecystectomy. The mean age of the patients was  $43.7 \pm 5.8$  years. Since the frequency of the applied test tone did not affect the reflex change, a 1 kHz pitcher was used.

*Assessment of the neuromuscular blocking effect of rocuronium on the stapedius reflex test*

The intensity of the reflected sound energy at which the stapedius reflex is detectable was similar ( $89.5 \pm 9.9$  dB) at the stages of premedication and anaesthetic induction. However, after administration of the muscle relaxant rocuronium, when the twitch height reached the level of 5% (indicating clinically effective muscle relaxation), the stapedius reflex could not be evoked even with 110 dB stimulation (the maximum setting of the device), indicating the total blockade of the stapedius muscle. This blocked of the stapedius muscle was observed throughout the course of clinical muscle relaxation.

*Neuromuscular function and the stapedius reflex during recovery phase of anesthesia*

During the recovery phase the sound energy needed to evoke the stapedius reflex has decreased (indicating a return of the muscular activity), but the sound energy values required to induce the reflex showed significant variability. Along with this, the twitch height gradually increased until the initial value. In many cases, the stapedius reflex threshold returned to normal levels, while a significant residual block could be detected by acceleromyography. When evaluating all data for monitoring muscle relaxation, the sensitivity of stapedius reflex measurements was 10.5% only. It was clearly demonstrated that

at the end of the neuromuscular block, at the 95% safe TOF value, the stapedius reflex could always be induced.

## **2. Non-invasive pulse wave analysis for monitoring the cardiovascular effects of CO<sub>2</sub>-pneumoperitoneum during laparoscopic cholecystectomy**

### *The effect of anesthetic induction on hemodynamic parameters*

The induction of anesthesia resulted in a statistically significant reduction in both peripheral blood pressure and central aortic pressures, accompanied by a decrease in augmentation pressure and augmentation index.

### *The effect of peritoneal insufflation on hemodynamic parameters*

Peripheral blood pressures did not change markedly along with peritoneal cavity insufflation, except for a moderate increase in systolic blood pressure. In contrast to this, a marked increase could be observed in central aortic pressure values which was accompanied by increased augmentation pressure and augmentation index, indicating a rise in peripheral arterial stiffness. Despite changes in the central aortic blood pressure, subendocardial viability ratio remained relatively stable during and after peritoneal cavity insufflation.



### *Comparison of hemodynamic parameters at preeinduction and peritoneal insufflation phase*

Peripheral and central blood pressures returned to the preinduction values after peritoneal insufflation. The only parameter that showed a gradual increase was the augmentation index. After deflation of the abdominal cavity both peripheral and aortic pressure values returned to the levels observed after induction of anesthesia. Although augmentation pressures were still higher than before inflation, augmentation index (the main indicator of peripheral arterial stiffness) also returned to the pre-insufflation value.

### **3. Does standing or sitting position of the anesthesiologist in the operating theatre influence sevoflurane exposure during craniotomies?**

At the height of the sitting position the captured amount of sevoflurane was somewhat higher than that at the height of standing, but this difference did not reach the level of statistical significance. A significantly lower sevoflurane concentration was measured at the indifferent corner of the OR.

## **Conclusions**

In our first study, we examined how the threshold of stapedius reflex is affected by muscle relaxation with rocuronium. Previously, the depth of the neuromuscular block was not evaluated using tympanometry or stapedius reflex test and no data are available of the effect muscle relaxants on m. stapedius. The results of the present study are mainly physiological and their clinical usefulness is limited. We have demonstrated that the neuromuscular block can be assessed by stapedius reflex measurements, but it is also clear that the method cannot be used as a routine alternative to neuromuscular block monitoring due to its poor sensitivity.

However, our results may have important implications for both the ear-nose-throat and the anesthetic practices. The effects of muscle relaxants should be taken into consideration in the case of surgical interventions performed in clinical practice with electrophysiological monitoring. By pharmacological inhibition of the musculus stapedius, the sounds of the environment can intensify and this may be of particular importance in different phases of narcosis and in the case of patients with sustained respiration with muscle relaxation in the intensive care unit.

In our second cohort study we used a non-invasive pulse wave analysis to study cardiovascular changes in laparoscopic cholecystectomy. The SphygmoCor device has been studied for a number of systemic diseases affecting the peripheral vascular system (hypertension, diabetes, systolic heart failure, pre-menopause), but the method for haemodynamic monitoring of intraoperative surgery has not been used in anesthesia.

After the induction of anesthesia, the significantly decreasing augmentation index confirmed that the resistance of peripheral arteries was reduced by the anesthetic drugs. In the next phase of the intervention, insufflation of the abdominal cavity and the placement of the patient's in reverse Trendelenburg position causes a marked increase in arterial mean blood pressure, peripheral vascular resistance and augmentation index. In this study, we also confirmed that peritoneal insufflation is the most dangerous period of laparoscopic surgery.

Based on our results, in the case of operations where non-invasive methods and intermittent measurements provide sufficient information to follow changes in circulatory parameters, the method is suitable for intraoperative use.

Harmful health effects associated with chronic exposure to inhaled anesthetics cannot be excluded. In order to prevent occupational injury, potential sources of contamination and the impact of factors arising from the working environment should be identified to minimize contamination of operating room personnel.

Based on the results measured so far, the anesthetic team is not an area adjacent to the patient, but rather a position at the end of the leg because there is a significant reduction in exposure by surgical isolation. In our third investigation we would like to study where the gas exposure to the workers is the lowest in the anesthetic work area beside the patient's side. Measurements from air samples showed that when an anesthetist isolated on the side of the operating table is in a standing position (laminar flow zone), the cumulative amount of anesthetics in the air is lower than in the sitting position (turbulent flow zone).

## **Summary**

1. The stapedius reflex test is not suitable for intraoperative assessment of the degree of neuromuscular block.
2. Using a non-depolarizing muscle relaxant, the function of the musculus stapedius can be inhibited.
3. In the case of intra-operative application of tympanometry and stapedius reflex test, or when examining the effect of different anesthetics on the reflex, the actual degree of muscle relaxation should be taken into consideration.
4. The SphygmoCor device is suitable for the non-invasive detection of hemodynamic changes during laparoscopic surgery.
5. The degree of contamination of the inhaled anesthetics in the operating room depends on the layout of the work area, the location of the workers and the characteristics of the air exchange system.
6. The technical design of the work environment should take into account the specific characteristics of the operating room that affect exposure to a particular field.



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### List of publications related to the dissertation

1. **Sárkány, P.**, Tankó, B., Simon, É., Gál, J., Fülesdi, B., Molnár, C.: Does standing or sitting position of the anesthesiologist in the operating theatre influence sevoflurane exposure during craniotomies?  
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