KÜTAHYA UNIVERSITY OF HEALTH SCIENCES

RECTORATE

INTERVENTIONAL CLINICAL TRIALS

TO THE CHAIRMAN OF THE ETHICS COMMITTEE

I kindly request your information and necessity for the examination of our research titled "Evaluation of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth " by your board.

Responsible Researcher

Assistant Professor Bedreddin Cavlı

KÜTAHYA HEALTH SCIENCES UNIVERSITY RECTORATE INTERVENTIONAL CLINICAL RESEARCH ETHICS COMMITTEE RESEARCH BUDGET FORM

A. RESEARCH INFORMATION

Supportive
Asst. Professor, Bedreddin Cavlı bedreddin.cavlı@ksbu.edu.tr 05051590606
Legal Representative
Bedreddin Cavlı bedreddin.cavlı@ksbu.edu.tr +905051590606

Name of the study			
Evaluation of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth			
Protocol number/code			
The number/code given to the research by the Turkish Medicines and Medical Devices Agency (TİTCK) and the Ethics Committee (EK)			
TİTCK		**EK**	

B. RESEARCH CENTRES

Please indicate the centres participating in the research from our country:
1. Kütahya Health Sciences University Faculty of Dentistry, Department of Oral, Dental and Maxillofacial Surgery

C. SERVICE PROCUREMENT

Services to be received from Turkey

1. Specify the services to be received from the research centre and their number	
Process Name	**Number of transactions for one volunteer**
Monitoring of patients	1

2. Specify the services to be received from outside the research centres and their number	
Process Name	Number of transactions for one volunteer
-	-

Services to be received from outside Turkey

3. Specify the services to be received from outside Turkey and their number	
Process Name	Number of transactions for one volunteer
-	-

D. PAYMENTS

Please indicate the amounts stated in this section in Turkish Lira.

1. Please indicate the amount to be paid to the research centre, excluding researcher payments, for each subject who completes the study:	
Centre Name	Amount (for 1 volunteer)
-	0 TL

2. State the amount to be paid to the research centre on behalf of the researcher for each volunteer who completes the study:	
Centre Name	Amount (for 1 volunteer)
-	0 TL

3. If volunteers will be paid, explain in detail and indicate the maximum amount of payment planned to be paid to a volunteer during the study:
Volunteer patients will not receive any payment.

4. Indicate other payments, if any, and the amount:	
Process name	Amount
-	-

E. BUDGET SOURCE

The researcher himself	X
Finance organisation/institution	☐
Description:	Disposable ECG electrodes used to monitor patients will be paid for by the investigators.

F. SUPPORTER'S DECLARATION (SIGNATURE)

Please indicate the total* budget allocated for the research in Turkey (in Turkish Lira)	340 TL
The budget was calculated considering the transaction costs dated. It is not the total amount allocated for one volunteer, but the total amount including investigator payments, centre payments and operational expenses allocated for our country during the whole research.	

Work with this budget form;

- The information stated in the form is correct,

- I undertake that the payments related to the research protocol, other concurrent treatment and research-induced rescue treatment costs foreseen to be made during the research specified in the research protocol will not be paid to the volunteer and the Social Security Institution, and will be paid by the sponsor (person or organisation).

Handwritten name and surname		
Telephone number		
Email address		
Date (in days/months/years)		
Signature		

KÜTAHYA HEALTH SCIENCES UNIVERSITY RECTORATE INTERVENTIONAL CLINICAL RESEARCH ETHICS COMMITTEE RESEARCH PROTOCOL FORM

Title of the study: Evaluation of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth

Title, name, field of specialization and place of duty of the principal investigator: Asst. Professor Bedreddin Cavlı

Oral and Maxillofacial Surgery- Kütahya Health Sciences University Faculty of Dentistry

Title, names, fields of specialization and duty stations of all researchers who will be involved in the study:

Responsible Researcher: Asst. Professor, Bedreddin Cavlı

Oral and Maxillofacial Surgery- Kütahya Health Sciences University Faculty of Dentistry

Assistant Researcher: Research Assistant, Aykut Şaylığ

Oral and Maxillofacial Surgery- Kütahya Health Sciences University Faculty of Dentistry

Assistant Researcher: Research Assistant, Şeyma Kale

Oral and Maxillofacial Surgery- Kütahya Health Sciences University Faculty of Dentistry

Counsellors:

Asst. Professor Necmiye Şengel

Anesthesiology and Reanimation- Gazi University Faculty of Dentistry

Professor Ziver Ergun Yücel

Oral and Maxillofacial Surgery- Gazi University Faculty of Dentistry

Place of the study: Kütahya Health Sciences University Faculty of Dentistry, Department of Oral, Dental and Maxillofacial Surger

PHASE AND TYPE OF RESEARCH	Phase 1	☐
	Phase 2	☐
	Phase 3	☐
	Phase 4	☐
	Observational drug study	☐
	Medical device clinical research	☐

	Performance evaluation studies conducted with in vitro medical diagnostic devices	☐
	Non-drug clinical research	☒
	Please specify if other:	

Research hypothesis:

μ ≠ 0 hypothesis:: During extraction of mandibular impacted wisdom teeth, the trigeminocardiac reflex does not occur with stimulation of the peripheral branches of the trigeminal nerve.
μ = 0 hypothesis:: During extraction of mandibular impacted wisdom teeth, a trigeminocardiac reflex occurs by stimulation of the peripheral branches of the trigeminal nerve.

Introduction-Purpose Section

The trigeminocardiac reflex (TCR) has entered the scientific literature as an oculocardiac reflex with strabismus surgeries (1). In cases where the V1 branch of the trigeminal nerve forms the afferent pathway of the V1 branch of the trigeminal nerve, a clinical phenomenon with vagal stimulation findings has been encountered. Since the publication of TCR in ophthalmological surgery in 1908, it has become a well-known clinical picture for ophthalmologists and anesthetists (2). The anesthetist's mastery and experience in this picture, which is met by manipulation of the ocular muscles, is of great importance. Recognition that the picture is a brainstem reflex involving the vagal pathway is critical in mastering the clinical situation. In the literature, it has been reported that V2 and V3 branches of the trigeminal nerve can also produce the reflex picture and the reflex can be seen under local anesthesia. (3,4). Reflex is diagnosed under local anesthesia as well as under general anesthesia with hemodynamic data (blood pressure, heart rate) that can be monitored non-invasively.

TCR is a physiological, life-threatening response with sudden onset of severe bradycardia, hypotension and asystole with parasympathetic activation of the heart due to stimulation of the vagal nerve as a result of stimulation of any of the three branches of the trigeminal nerve. (1). It is defined as a decrease in heart rate and mean arterial blood pressure by more than 20% from baseline or a heart rate of less than 60 beats per minute due to intraoperative traction or manipulation of the trigeminal nerve. The afferent branch of the trigeminocardiac reflex arc is formed by the sensory nerve endings of the fifth cranial nerve. Neuronal signals are sent to the trigeminal sensory nucleus via the Gasserian ganglion. The sensory nucleus of the afferent reflex branch of the trigeminal nerve connects to the efferent pathway via short internuncial fibres in the reticular formation with the more distant motor nucleus of the vagus nerve. Cardioinhibitory efferent fibres originate from the motor nucleus of the vagus nerve. It transmits vagus-mediated negative chronotropic and inotropic responses to the heart and terminates in the myocardium (5).

In the maxillofacial surgery literature, there are case reports reporting the development of trigeminocardiac reflex in orthognathic surgery, dental implant surgery and maxillofacial trauma surgery and prevalence studies for major surgeries (6,7,8). Haemodynamic changes and neurological-based emergencies (e.g. vasovagal syncope) are quite common in routine oral surgical procedures performed under local anaesthesia (9).

In addition, in a study, it was noted that a significant decrease in heart rate and blood pressure occurred during extraction of posterior mandibular teeth and this may be related to the trigeminocardiac reflex (10). Extraction of impacted wisdom teeth is one of the commonly performed procedures in the field of oral and maxillofacial surgery. To the best of our knowledge, there is no study in the literature evaluating the development of TCR during mandibular impacted wisdom tooth extraction.

Our aim was to investigate the trigeminocardiac reflex during oral surgical procedures routinely performed under local anaesthesia. Our reasons for choosing mandibular impacted wisdom tooth surgery among oral surgeries for this purpose are; the proximity of the inferior alveolar nerve, which is the largest terminal branch of the V3 branch of the trigeminal nerve, to the tooth roots and the frequent observation of traction on the nerve, the fact that there may be differences in the depth of effect between anaesthetic techniques due to the variation of the mandibular nerve, and our clinical experience. There are no studies in the literature evaluating the development of trigeminocardiac reflex during surgical treatment of mandibular wisdom teeth.

Materials and Methods Section:

The study will be conducted on patients referred to KSBÜ Faculty of Dentistry, Department of Oral, Dental and Maxillofacial Surgery from Oral, Dental and Maxillofacial Radiology, who have an indication for extraction of impacted mandibular wisdom teeth under local anesthesia, who will undergo extraction of impacted wisdom teeth for the first time, who agree to have the surgical extraction of these teeth performed at KSBÜ Faculty of Dentistry, Department of Oral, Dental and Maxillofacial Surgery and who agree to participate in the study.

If there is a clinical necessity, cone beam computed tomography will be taken to evaluate the relationship of impacted wisdom teeth with the nervus alveolaris inferior and to evaluate their localization in the mandible in three dimensions. In patients who do not need tomography, the evaluation will be performed with Orthopantomogram film. The distance of the relevant wisdom tooth roots from the inferior alveolar nerve will be recorded.

During the procedure, Gow-Gates and nervus alveolaris inferior anesthesia techniques, which are the two most commonly used local anesthesia techniques in oral, dental and maxillofacial surgery practice, will be applied for the extraction of mandibular impacted teeth.

Patients will be divided into 2 groups according to the proximity of the wisdom tooth roots to the inferior alveolar nerve (1 mm and closer to the nerve / more than 1 mm away from the nerve) and 2 groups according to the anesthesia technique to be applied (Gow-Gates Block - Inferior alveolar block). Total research arm is 4.

In the research arms we have established, the follow-up of TKR that may occur during the procedure will be provided by monitoring the patients (Contec Medical Systems, Hebei, China.) Heart rate, systolic and diastolic blood pressure, oxygen saturation will be recorded during the procedure. The records will be taken in 4 stages: before starting the surgical procedure, during the application of local anaesthesia, during the incision, during the elevation of the crown and root. Sudden changes that occur during the procedure will be recorded together with the process in which they occur.

(e.g. during local anesthesia)
Initial heart rate: 80 beats/min
End of procedure heart rate: 78 beats/min
Sudden presence of bradycardia or tachycardia during the procedure;
Sudden change in heart rate: 80>58 or 80>98)

During extraction of impacted wisdom teeth, a 20% decrease in heart rate and a decrease in heart rate below 60 will be considered as the development of TCR in parallel with the literature. The prevalence of TKR will be evaluated in 4 separate groups according to whether Gow-Gates anaesthesia or nervus alveolaris inferior anaesthesia is applied and whether the wisdom teeth are closer than 1 mm and 1 mm or further than 1 mm from the nervus alveolaris inferior.

During mandibular impacted wisdom tooth extraction, patients will be monitored and the following parameters will be evaluated:
1. Systolic blood pressure
2. Diastolic blood pressure
4. Oxygen saturation
5. Heart rate

The anxiety level of the patients will be assessed with the Amsterdam Preoperative Anxiety and Information Score Scale (APAIS) and State-Trait Anxiety Inventory (STAI-S) in order to differentiate TKR from common neurological emergencies (e.g. vasovagal syncope) due to dental phobia. State Anxiety Scale was developed in 1970 and its Turkish form was adapted in 1983 and validity and reliability study was conducted. APAIS was translated into Turkish for the first time in our country in 2007 and it was found that APAIS and STAI-S were correlated with each other in the studies conducted(11).

STAI-S (The State-Trait Anxiety Inventory)

Amsterdam Preoperative Anxiety and Information Scale (APAIS)

	Not all 1	2	3	4	Very much 5
I am worried the about anesthetics					
The anesthetics is on my mind continually					
. I would like to know as much as possible about the anesthetic					
I am worried about the procedure.					
The procedure is on my mind continually.					
I would like to know as much as possible about the procedure					

		No t at all	A little	So me wha t	Very Much So
1.	I feel calm	(1)	(2)	(3)	(4)
2.	I feel secure	(1)	(2)	(3)	(4)
3.	I feel tense	(1)	(2)	(3)	(4)
4.	I feel strained	(1)	(2)	(3)	(4)
5.	I feel at ease	(1)	(2)	(3)	(4)
6.	I feel upset	(1)	(2)	(3)	(4)
7.	I am presently worrying over possible misfortunes	(1)	(2)	(3)	(4)
8.	. I feel satisfied	(1)	(2)	(3)	(4)
9.	I feel frightened	(1)	(2)	(3)	(4)
10.	I feel uncomfortable	(1)	(2)	(3)	(4)
11.	I feel self confident	(1)	(2)	(3)	(4)
12.	I feel nervous	(1)	(2)	(3)	(4)
13.	I feel jittery	(1)	(2)	(3)	(4)
14.	I feel indecisive	(1)	(2)	(3)	(4)
15.	I am relaxed	(1)	(2)	(3)	(4)
16.	I feel content.	(1)	(2)	(3)	(4)
17.	I am worried	(1)	(2)	(3)	(4)
18.	I feel confused	(1)	(2)	(3)	(4)
19.	I feel steady	(1)	(2)	(3)	(4)
20.	I feel pleasant.	(1)	(2)	(3)	(4)

Inclusion criteria:

Patients aged 18-30 years

Patients without any systemic problems

Patients with an indication for extraction of mandibular wisdom teeth

Patients have no previous experience of impacted tooth extraction

Exclusion criteria:
Female patients who are pregnant or breastfeeding
Patients with systemic problems
Patients with mental or neurological disorders
Patients taking antidepressants
Patients with cardiovascular problems

Sample Selection and the statistical method to be used:
Since the study population was not known, the power and sample level of the study were calculated with reference to the study of Bohluli (2011). Bohluli (2011) studied with n=20 patients in his study. According to the study of Bohluli (2011), it is seen that n=20 patients planned to be included in the study planned the study with 90% power (in studies, values of 0.70 and above are considered valid and 0.80 is considered to be quite sufficient). In the study, it was determined that the effect size level was 0.42. The study is planned to be conducted on a total of 40 patients. The groups were determined equally as Group 1 (IAS / less than 1 mm distance) n=10, Group 2 (IAS / more than 1 mm distance) n=10, Group 3 (IAS / less than 1 mm distance) n=10 and Group 4 (IAS / more than 1 mm distance) n=10.
Regarding the analysis of the data; descriptive statistics will be presented with mean-d.deviation, median-IQR, frequency and percentage values. In order to examine whether the measurements in the study are different according to the characteristics of the study groups, independent Mann Wihtney U test and Kruskall Wallis test analyses are considered. Paired Wilcoxon test and Friedman test analysis can be applied in the evaluations of repeated measurements. In determining the times that are significant as a result of Friedman test, it is considered to be determined by All-pairwise method. Spearman correlation analysis will be applied to examine the relationships between the measurement values of the groups. Chi-square analysis will be performed for the proportional evaluations of the groups. In the study, p values less than 0.05 are considered significant. The analyses will be analysed with SPSS 25.0. Power level and effect size calculations calculated in the study were determined with G*PowerVersion 3.1.7.

List of References

1. Schaller, B., Probst, R., Strebel, S., & Gratzl, O. (1999). Trigeminocardiac reflex during surgery in the cerebellopontine angle. Journal of neurosurgery, 90(2), 215-220.
2. Aschner, B. (1908). Ueber einen Bisher noch nicht Beschriebenen Reflex vom Auge auf Kreislauf und Atmung: Verschwinden des Radialispulses bei Druck auf das. Review of Oculocardiac Reflex When Facial Surgery.
3. James, I., Huang, S., Yu, H. C., & Chang, Y. C. (2017). Occurrence of trigeminocardiac reflex during dental implant surgery: an observational prospective study. Journal of the Formosan Medical Association, 116(10), 742-747.
4. James, I., Huang, S., Chang, H. H., Lin, C. P., Liao, W. C., Kao, C. T., & Huang, T. H. (2018). Trigeminocardiac reflex during non-surgical root canal treatment of teeth with irreversible pulpitis. Journal of the Formosan Medical Association, 117(6), 512-517.
5. Meuwly, C., Golanov, E., Chowdhury, T., Erne, P., & Schaller, B. (2015). Trigeminal cardiac reflex: new thinking model about the definition based on a literature review. Medicine, 94(5).

6. Bohluli, B., Schaller, B. J., Khorshidi-Khiavi, R., Dalband, M., Sadr-Eshkevari, P., & Maurer, P. (2011). Trigeminocardiac reflex, bilateral sagittal split ramus osteotomy, Gow-Gates block: a randomized controlled clinical trial. Journal of oral and maxillofacial surgery, 69(9), 2316-2320.
7. Mhamunkar, P. A., Kolari, V., & Sequeira, J. (2022). Evaluation of Trigeminocardiac Reflex in Patients Undergoing Elevation of Zygomatic Fractures. Cureus, 14(2).
8. Elsayed, S. A. H., Hegab, A. F., & Alkatsh, S. S. Y. (2019). Does surgical release of TMJ bony ankylosis increase the risk of trigeminocardiac reflex? A retrospective cohort study. Journal of Oral and Maxillofacial Surgery, 77(2), 391-397.
9. Edmondson, H. D., Gordon, P. H., Lloyd, J. M., Meeson, J. E., & Whitehead, F. I. H. (1978). Vasovagal episodes in the dental surgery. Journal of Dentistry, 6(3), 189-195
10. Alemany-Martínez, A., Valmaseda-Castellón, E., Berini-Aytés, L., & Gay-Escoda, C. (2008). Hemodynamic changes during the surgical removal of lower third molars. Journal of oral and maxillofacial surgery, 66(3), 453-461.
11. ARLI, Ş. K. (2017). Ameliyat öncesi anksiyetenin APAIS ve STAI-I ölçekleri ile değerlendirilmesi. Hacettepe Üniversitesi Hemşirelik Fakültesi Dergisi, 4(3), 38-47.

KÜTAHYA HEALTH SCIENCES UNIVERSITY RECTORATE INTERVENTIONAL CLINICAL RESEARCH ETHICS COMMITTEE APPLICATION FORMS

1. APPLICATION PETITION	☒
2. APPLICATION CONTENT FORM	☒
3. APPLICATION FORM	☒
4. CONTRACT	☒
4. RESEARCH BUDGET	☒
5. CVS	☒
6. INFORMED CONSENT FORM	☒
7. MATERIAL PURCHASE CONSENT FORM (if necessary)	☐
8. QUESTIONNAIRE ETC. FORMS USED	☒
9. APPROVAL CERTIFICATE OF THE RELEVANT DEPARTMENT HEAD / HEAD OF THE MAIN DISCIPLINE / LABORATORY SUPERVISORS	☐
10. INSTITUTIONAL PERMISSION CERTIFICATE	☒
11. CONFIRMATION WRITTEN THAT YOU ARE A STUDENT OF THE RELATED INSTITUTE (if the research is a thesis and the researcher is a student of the institute)	☐
12. 3 PUBLICATIONS RELATED TO RESEARCH	☒
13. DATA SECURITY AGREEMENT (For necessary researches)	☐
14. GCP, GLP AND HELSINKI DECLARATION COMMITMENT	☒
15. Delivery of the application file to the Ethics Committee secretariat	☒

Tick the relevant boxes with a cross.

Researches with incomplete application forms will not be evaluated.
I undertake that I have submitted all documents completely.

Title of the Study : Evaluation of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth
Responsible Researcher: Asst. Professor Bedreddin Cavlı
Signature and Date :

KÜTAHYA HEALTH SCIENCES UNIVERSITY RECTORATE INTERVENTIONAL CLINICAL RESEARCH ETHICS COMMITTEE CLINICAL RESEARCH APPLİCATİON FORM

A. SUMMARY OF RESEARCH	
Supportive	DDS, Asst. Professor, Bedreddin Cavlı bedreddin.cavlı@ksbu.edu.tr 05051590606
Legal representative	DDS, Asst. Professor, Bedreddin Cavlı
Tittle of the research	Evaluation of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth
Protocol code	-
Status of research	National – For academic purposes (Individual research project)
Nature of the research	– Method clinical trial
Phase of	– It is not a phase study.
Investigated medical condition or disease	Investigation of the frequency of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth
Research methodology	In mandibular impacted wisdom tooth extractions, patients will be monitored (heart rate, blood pressure, oxygen saturation) and trigeminocardiac reflex development will be followed.
Place of production	Research product will not be used .
Comparison product / method	Research product will not be used
Place of production	Research product will not be used
Placebo	Research product will not be used
Place of production	Research product will not be used
Research arms*(Arms-Interventions)*	The study will include impacted wisdom teeth in the mandible. There will be 2 separate groups with the 2 most commonly used anaesthetic techniques (gow-gates (GG)/inferior alveolar nerve block (IAS)). The

	tooth roots will be categorised as those that are between 1 mm and more than 1 mm closer to the nervus alveolaris inferior (Y-1) or more than 1 mm further away (Y-2). The research arms were planned as GG/Y-1, GG/Y-2, IAS/Y-1 and IAS/Y-2.
Purpose of the research	Trigeminocardiac reflex (TCR) was introduced to the scientific literature as an oculocardiac reflex with strabismus surgeries (1). In cases in which the V1 branch of the trigeminal nerve formed the afferent pathway, a clinical phenomenon in which vagal stimulation findings were observed was encountered. Since its publication in ophthalmological surgery in 1908, it has become a clinical picture well known to ophthalmologists and anaesthesiologists (2). The mastery and experience of the anaesthetist is of great importance in this picture which is met by manipulation of the ocular muscles. Recognition that the picture is a brainstem reflex involving the vagal pathway is critical in mastering the clinical situation. In the literature, it has been reported that V2 and V3 branches of the trigeminal nerve can also produce the reflex picture and the reflex can also be observed under local anaesthesia (3,4). The reflex is diagnosed with haemodynamic data (blood pressure, heart rate) which can be monitored non-invasively under local anaesthesia as well as under general anaesthesia. TCHR is a physiological, life-threatening response characterised by sudden onset of severe bradycardia, hypotension and asystole, in which parasympathetic activation of the heart is observed with stimulation of the vagal nerve as a result of stimulation of any of the three branches of the trigeminal nerve (1). It is defined as a decrease in heart rate and mean arterial blood pressure by more than 20% compared to baseline or a heart rate of less than 60 beats per minute due to intraoperative traction or manipulation of the trigeminal nerve. The patients are normotensive or hypotensive (5). The afferent branch of the TKR arc is formed by the sensory nerve endings of the fifth cranial nerve and neuronal signals are sent to the trigeminal sensory nucleus via the Gasserian ganglion. The sensory nucleus of the afferent reflex branch of the trigeminal nerve is connected to the efferent pathway via short internuncial fibres in the reticular formation with the more distant motor nucleus of the vagus nerve. Cardioinhibitory efferent fibres originate from the motor nucleus of the vagus nerve and transmit vagus-mediated negative chronotropic and inotropic responses to the heart, terminating in the myocardium. In the maxillofacial surgery literature, there are case reports reporting the development of trigeminocardiac reflex in orthognathic surgery, dental implant surgery and maxillofacial trauma surgery and prevalence studies for major surgeries (6,7,8). Haemodynamic changes and neurological-based emergencies (e.g. vasovagal syncope) are quite

	common in routine oral surgical procedures performed under local anaesthesia (9). In addition, in a study, a significant decrease in heart rate and blood pressure occurred during extraction of posterior mandibular teeth and it was pointed out that this may be related to the trigeminocardiac reflex (10). Extraction of impacted wisdom teeth is one of the commonly performed procedures in the field of oral and maxillofacial surgery. To the best of our knowledge, there is no study in the literature evaluating the development of TCR during mandibular impacted wisdom tooth extraction. Our aim was to investigate the trigeminocardiac reflex during oral surgical procedures routinely performed under local anaesthesia. Our reasons for choosing mandibular impacted wisdom tooth surgery among oral surgeries for this purpose are; the proximity of the inferior alveolar nerve, which is the largest terminal branch of the V3 branch of the trigeminal nerve, to the tooth roots and the frequent observation of traction on the nerve, the fact that there may be differences in the depth of effect between anaesthetic techniques due to the variation of the mandibular nerve, and our clinical experience. There is no study in the literature evaluating the development of trigeminocardiac reflex during surgical treatment of mandibular wisdom teeth.
Scope of the research	The study will be conducted on patients referred to KSBÜ Faculty of Dentistry, Department of Oral, Dental and Maxillofacial Surgery from Oral, Dental and Maxillofacial Radiology, who have an indication for extraction of impacted mandibular wisdom teeth under local anesthesia, who will undergo extraction of impacted wisdom teeth for the first time, who agree to have the surgical extraction of these teeth performed at KSBÜ Faculty of Dentistry, Department of Oral, Dental and Maxillofacial Surgery and who agree to participate in the study. If there is a clinical necessity, cone beam computed tomography will be taken to evaluate the relationship of impacted wisdom teeth with the nervus alveolaris inferior and to evaluate their localization in the mandible in three dimensions. In patients who do not need tomography, the evaluation will be performed with Orthopantomogram film. The distance of the relevant wisdom tooth roots from the inferior alveolar nerve will be recorded. During the procedure, Gow-Gates and nervus alveolaris inferior anesthesia techniques, which are the two most commonly used local anesthesia techniques in oral, dental and maxillofacial surgery practice, will be applied for the extraction of mandibular impacted teeth. Patients will be divided into 2 groups according to the proximity of the wisdom tooth roots to the inferior alveolar nerve (1 mm and closer to the nerve / more than 1 mm away from the nerve) and 2 groups according to the anesthesia technique to be applied (Gow-Gates Block - Inferior alveolar block). Total research arm is 4.

	In the research arms we have established, the follow-up of TKR that may occur during the procedure will be provided by monitoring the patients (Contec Medical Systems, Hebei, China.) Heart rate, systolic and diastolic blood pressure, oxygen saturation will be recorded during the procedure. The records will be taken in 4 stages: before starting the surgical procedure, during the application of local anesthesia, during the incision, during the elevation of the crown and root. Sudden changes that occur during the procedure will be recorded together with the process in which they occur. (e.g. during local anesthesia) Initial heart rate: 80 beats/min End of procedure heart rate: 78 beats/min Sudden presence of bradycardia or tachycardia during the procedure; Sudden change in heart rate: 80>58 or 80>98) During extraction of impacted wisdom teeth, a 20% decrease in heart rate and a decrease in heart rate below 60 will be considered as the development of TCR in parallel with the literature. The prevalence of TKR will be evaluated in 4 separate groups according to whether Gow-Gates anesthesia or nervus alveolaris inferior anesthesia is applied and whether the wisdom teeth are closer than 1 mm and 1 mm or further than 1 mm from the nervus alveolaris inferior. During mandibular impacted wisdom tooth extraction, patients will be monitored and the following parameters will be evaluated: 1. Systolic blood pressure 2. Diastolic blood pressure 3. Oxygen saturation 4. Heart rate The anxiety level of the patients will be assessed with the Amsterdam Preoperative Anxiety and Information Score Scale (APAIS) and State-Trait Anxiety Inventory (STAI-S) in order to differentiate TKR from common neurological emergencies (e.g. vasovagal syncope) due to dental phobia. State Anxiety Scale was developed in 1970 and its Turkish form was adapted in 1983 and validity and reliability study was conducted. APAIS was translated into Turkish for the first time in our country in 2007 and it was found that APAIS and STAI-S were correlated with each other in the studies conducted(11). References

1. Schaller, B., Probst, R., Strebel, S., & Gratzl, O. (1999). Trigeminocardiac reflex during surgery in the cerebellopontine angle. *Journal of neurosurgery*, *90*(2), 215-220.
2. Aschner, B. (1908). Ueber einen Bisher noch nicht Beschriebenen Reflex vom Auge auf Kreislauf und Atmung: Verschwinden des Radialispulses bei Druck auf das. *Review of Oculocardiac Reflex When Facial Surgery*.
3. James, I., Huang, S., Yu, H. C., & Chang, Y. C. (2017). Occurrence of trigeminocardiac reflex during dental implant surgery: an observational prospective study. *Journal of the Formosan Medical Association*, *116*(10), 742-747.
4. James, I., Huang, S., Chang, H. H., Lin, C. P., Liao, W. C., Kao, C. T., & Huang, T. H. (2018). Trigeminocardiac reflex during non-surgical root canal treatment of teeth with irreversible pulpitis. Journal of the Formosan Medical Association, 117(6), 512-517.
5. Meuwly, C., Golanov, E., Chowdhury, T., Erne, P., & Schaller, B. (2015). Trigeminal cardiac reflex: new thinking model about the definition based on a literature review. *Medicine*, *94*(5).
6. Bohluli, B., Schaller, B. J., Khorshidi-Khiavi, R., Dalband, M., Sadr-Eshkevari, P., & Maurer, P. (2011). Trigeminocardiac reflex, bilateral sagittal split ramus osteotomy, Gow-Gates block: a randomized controlled clinical trial. Journal of oral and maxillofacial surgery, 69(9), 2316-2320.
7. Mhamunkar, P. A., Kolari, V., & Sequeira, J. (2022). Evaluation of Trigeminocardiac Reflex in Patients Undergoing Elevation of Zygomatic Fractures. Cureus, 14(2).
8. Elsayed, S. A. H., Hegab, A. F., & Alkatsh, S. S. Y. (2019). Does surgical release of TMJ bony ankylosis increase the risk of trigeminocardiac reflex? A retrospective cohort study. Journal of Oral and Maxillofacial Surgery, 77(2), 391-397.
9. Edmondson, H. D., Gordon, P. H., Lloyd, J. M., Meeson, J. E., & Whitehead, F. I. H. (1978). Vasovagal episodes in the dental surgery. *Journal of Dentistry*, *6*(3), 189-195
10. Alemany-Martínez, A., Valmaseda-Castellón, E., Berini-Aytés, L., & Gay-Escoda, C. (2008). Hemodynamic changes during the surgical removal of lower third molars. *Journal of oral and maxillofacial surgery*, *66*(3), 453-461.
11. ARLI, Ş. K. (2017). Ameliyat öncesi anksiyetenin APAIS ve STAI-I ölçekleri ile değerlendirilmesi. *Hacettepe Üniversitesi Hemşirelik Fakültesi Dergisi*, *4*(3), 38-47.

Design of the research	Cross-sectional, prospective cohort	
Volunteer group	- Healthy volunteers - Male - Women - Adults	
Volunteer age range	18-30 age range	
Volunteers	Total	40
	Distribution	GG/Y-1 --- n=10 GG/Y-2 --- n=10 İAS/Y-1 --- n=10 İAS/Y-2 --- n=10
Inclusion criteria:	Patients aged 18-30 years Patients without any systemic problems Patients with an indication for extraction of mandibular wisdom teeth Patients have no previous experience of impacted tooth extraction	
Exclusion criteria	Female patients who are pregnant or breastfeeding Patients with systemic problems Patients with mental or neurological disorders Patients taking antidepressants Patients with cardiovascular problems	
Duration of research **Duration of research**	Total	3 months
	Volunteer Recruitment Start (Beginning of the research)	
	Volunteer Recruitment End	
Endpoint	The study will be finalised when information on the relevant parameters is obtained from 40 patients during the extraction of mandibular impacted teeth. .	

Evaluation of results *(Outcome/Endpoint)*	During extraction of impacted wisdom teeth, a 20% decrease in heart rate and a decrease in heart rate below 60 will be considered as the development of TCR in parallel with the literature. The prevalence of TKR will be evaluated in 4 separate groups according to whether Gow-Gates anaesthesia or nervus alveolaris inferior anaesthesia is applied and whether the wisdom teeth are closer than 1 mm and 1 mm or further than 1 mm from the nervus alveolaris inferior. During mandibular impacted wisdom tooth extraction, patients will be monitorised and the following parameters will be evaluated: 1. Systolic blood pressure 2. Diastolic blood pressure 3. Oxygen saturation 4. Heart rate Patients will be asked to fill out the Situational Anxiety Inventory (STAI-S) and the Amsterdam Preoperative Anxiety and Information Scale (APAIS) forms before the procedure in order to evaluate the relationship between the haemodynamic changes that may occur and anxiety..
Statistical Analysis	Since the study population was not known, the power and sample level of the study were calculated with reference to the study of Bohluli (2011). Bohluli (2011) studied with n=20 patients in his study. According to the study of Bohluli (2011), it is seen that n=20 patients planned to be included in the study planned the study with 90% power (in studies, values of 0.70 and above are considered valid and 0.80 is considered to be quite sufficient). In the study, it was determined that the effect size level was 0.42. The study is planned to be conducted on a total of 40 patients. The groups were determined equally as Group 1 (IAS / less than 1 mm distance) n=10, Group 2 (IAS / more than 1 mm distance) n=10, Group 3 (IAS / less than 1 mm distance) n=10 and Group 4 (IAS / more than 1 mm distance) n=10. Regarding the analysis of the data; descriptive statistics will be presented with mean-d.deviation, median-IQR, frequency and percentage values. In order to examine whether the measurements in the study are different according to the characteristics of the study groups, independent Mann Wihtney U test and Kruskall Wallis test analyses are considered. Paired Wilcoxon test and Friedman test analysis can be applied in the evaluations of repeated measurements. In determining the times that are significant as a result of Friedman test, it is considered to be determined by All-pairwise method. Spearman correlation analysis will be applied to examine the relationships between the measurement values of the groups. Chi-square analysis will be performed for the proportional evaluations of the groups. In the study, p values less than 0.05 are considered significant. The analyses will be analysed with

	SPSS 25.0. Power level and effect size calculations calculated in the study were determined with G*PowerVersion 3.1.7.	
Coordinator	Coordinating centre	Kütahya Health Sciences University Faculty of Dentistry Department of Oral, Dental and Maxillofacial Surgery Kütahya Health Sciences University Faculty of Dentistry Department of Oral, Dental and Maxillofacial Surgery
	Coordinator (principal investigator in single-centre studies)	Bedreddin Cavlı
	Contact	+905051590606 bedreddin.cavlı@ksbu.edu.tr
Administrative Responsible (if applicable)	Name and surname	-
	Place of assignment	-
	Contact	-

Research centres

	Research centres	Principal Investigator (Area of Expertise) (Telephone)
1	Kütahya Health Sciences University Faculty of Dentistry Oral, Dental and Maxillofacial Surgery	Bedreddin Cavlı +905051590606

Information for bioavailability/bioequivalence studies

Licence status	Not a bioavailability/bioequivalence study.
Analytical centre/department	Not a bioavailability/bioequivalence study.
Tested research product	Not a bioavailability/bioequivalence study.
Reference product	Not a bioavailability/bioequivalence study.
Study design	Not a bioavailability/bioequivalence study.
Working periods	Not a bioavailability/bioequivalence study.
Previous studies	Not a bioavailability/bioequivalence study.

Properties of active substance

Resolution	No active substance will be used.
Bioavailability	No active substance will be used.
AUC	No active substance will be used.
C_{max}	No active substance will be used.
t_{max}	No active substance will be used.
Elimination Half Life ($t_{1/2}$)	No active substance will be used.
Volume of Dispersion	No active substance will be used.
Binding to Proteins	No active substance will be used.
Food Effect	No active substance will be used.
Metabolism and Metabolites	No active substance will be used.
Breakthrough	No active substance will be used.
Accumulation	No active substance will be used.
Blood collection times	No active substance will be used.
Substance covered by biosafety	No active substance will be used.
Intra-individual variability constant of the active substance (%CV)	No active substance will be used.
Substance to be analysed	No active substance will be used.

B. OTHER INFORMATION

Risk / Benefit evaluation

There were no risk factors related to the study.
In this study, the development of trigeminocardiac reflex, which is an important issue during the extraction of impacted wisdom teeth and can be life-threatening in some cases, will be evaluated and important information about the frequency of trigeminocardiac reflex will be obtained.

Sensitive population/Vulnerable Group ***(Vulnerable subjects)***

No sensitive population/vulnerable groups.

Payment to volunteers

Volunteers will not receive any payment.

Volunteer services

Volunteers will not receive any payment..

Research / volunteer documents ***(additional documentation and recruitment procedure)***

In the study, patient cards will be created to note the age, gender, distance of the mandibular impacted wisdom teeth to the nervus alveolaris, systolic-diastolic blood pressure, heart rate, oxygen saturation and changes in these during the procedure.

At the same time, STAI-S (Situational Anxiety Test) and APAIS (Amsterdam Preoperative Anxiety and Information Form) will be used in adult patients to evaluate stress-anxiety and trigeminocardiac reflex development. The study will be conducted by including patients referred to KSBU Faculty of Dentistry, Department of Oral, Dental and Maxillofacial Surgery from Oral, Dental and Maxillofacial Radiology.

Independent data monitoring committee

There is no independent data monitoring committee in the study.

Sub-study

There is no sub-study in the research.

Biological material management

Biological material will not be transferred.

Facility / laboratory

No central technical facilities or laboratories will be used in the study

Delegation of tasks

There are no delegated duties.

Referral to other health authorities

There is no other country where research has been approved

Research-specific information

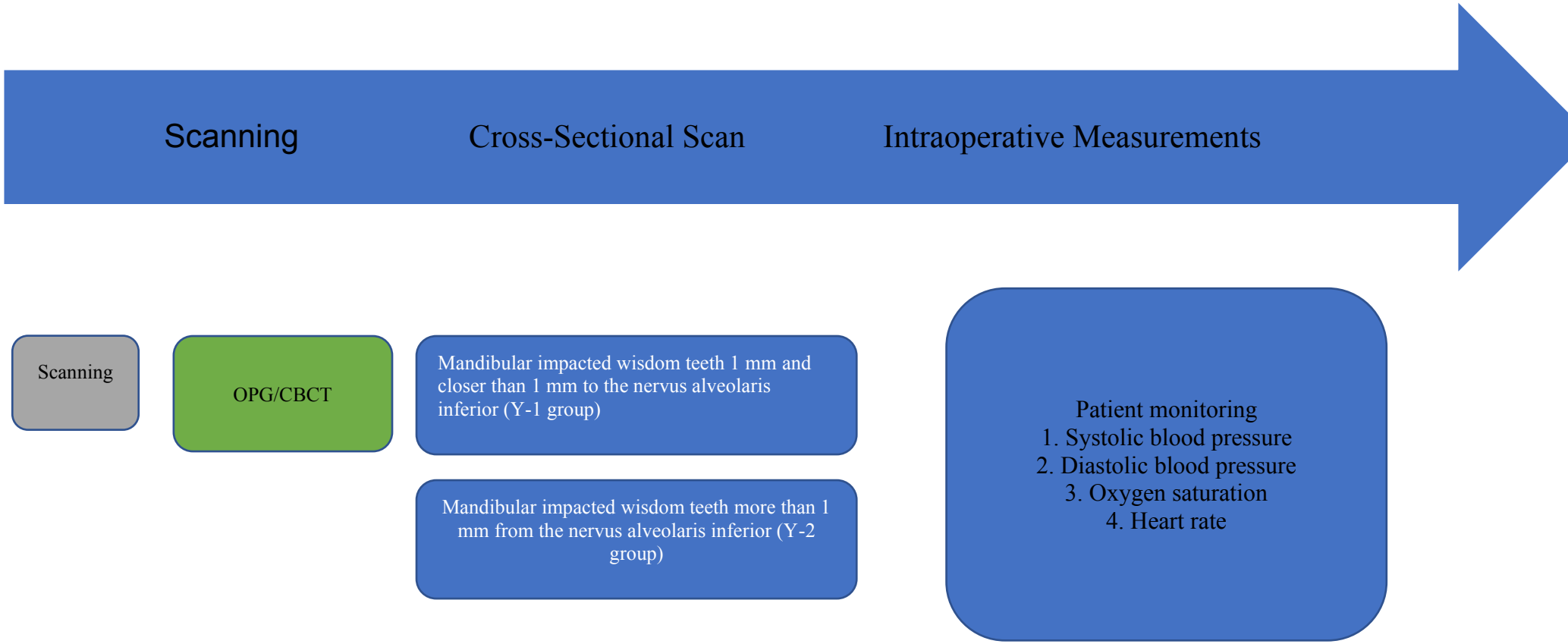
The trigeminocardiac reflex has been overshadowed by other vasovagal reflexes and is a well-defined clinical picture in ophthalmology. We believe that it should attract more attention in oral surgery where procedures are usually performed under local anaesthesia.

The study includes the addition of monitoring of patients to the treatment processes routinely performed in our clinic.

C. RESEARCH TEAM LIST

Centre Name	**Kütahya Health Sciences University Faculty of Dentistry Oral, Dental and Maxillofacial Surgery**			
Address	**İstiklal Neighbourhood Lala Hüseyin Paşa Street No:271 43100 KÜTAHYA**			
Mission	Name Surname	Title	**Education**	**İKU Training (present/absent))**
Principal Investigator	Bedreddin Cavlı	Asst. Professor	Oral and Maxillofacial Surgery	None
Assistant Researcher	Aykut Şaylığ	Resarch Asst	Oral and Maxillofacial Surgery	None
Assistant Researcher	Şeyma Kale	Resarch Asst	Oral and Maxillofacial Surgery	None
Counsellor	Necmiye Şengel	Asst. Professor	Anaesthesiology and Reanimation	None
Counsellor	Ziver Ergun Yücel	Professor	Oral and Maxillofacial Surgery	None

D. RESEARCH DESIGN DIAGRAM



E. ASSESSMENT CHART (Schedule of Assessments)

Evaluation	**Tarama**	**Operasyon**
Informed Voluntary Consent Form		**X**
Demographic information	**X**	
Medical history/ General physical examination	**X**	
Clinical data		**X**
CBCT	**X**	
Inclusion/exclusion criteria	**X**	
Intra-op data		**X**

F. ETHICS COMMITTEE INFORMATION		
☒	**There is a previous rejection decision by the ethics committee of the research**	
	Name of the ethics committee	Kütahya Health Sciences University Non-Interventional Clinical Research Ethics Committee
	Date of decision	
	Decision no.	
This section must be filled in when applying to the Turkish Medicines and Medical Devices Agency.		
☐	**Ethics committee application was made for approval of the research**	
	Name of the ethics committee	-
	Application date	-
☐	**There is ethics committee approval for the research.**.	
	Name of the ethics committee	-
	Date of decision	-
	Decision no.	-

G. RELATED DOCUMENTS

1. Research protocol
2. Protocol signature page (signed by the coordinator in multicentre studies and the principal investigator in single-centre studies)Bilgilendirilmiş gönüllü olur formu (BGOF)
3. Research brochure
4. Case report form
5. Insurance documents
6. (insurance certificate, insurance policy, insurance endorsements, general and special conditions of the policy)
7. Research budget form
8. CVs
9. (of the principal investigators)
10. Authorisation documents (if valid)
11. (with Turkish translations certified by a notary public or sworn translator)
12. Research team documents (if applicable)
13. (all documents used only by the research team or used to inform the research team, such as application instructions, information texts, doctors' letters, etc.)
14. Volunteer documents (if applicable)

15. (patient card, patient diary, questionnaire, instructions for use, application instructions, information texts, posters, brochures, information documents explaining the intended use of the materials to be given to volunteers (electronic diary, cooler bag, etc.))

16. Ethics committee decision (original and certified copy of the original)

17. Research product file (if required)

18. GMP Certificate/Document (apostilled) (if applicable)

19. If the research is for academic purposes, a wet signed document approved by an authorised person other than the applicant stating that the research is for academic purposes

Only for bioavailability/bioequivalence studies;

20. Certificate of supply of the investigational product and reference product(s) (invoice/package photocopy with serial number and expiry date)

21. Certificate of analysis of the research product

H. DOCUMENTS TO BE PHYSICALLY SUBMITTED

This section is only valid for applications to the Turkish Medicines and Medical Devices Agency.

All interested parties who are users of the Electronic Application System of the Agency must make their applications through the system. Documents that do not need to be physically submitted are submitted only through the Electronic Application System. The scanned versions of the documents that need to be physically submitted are submitted through the Electronic Application System; the originals are submitted by submitting them to the document unit of the Agency.

For applications made by real persons who are not users of the Electronic Application System of the Institution, all documents must be submitted physically.

The following documents should be submitted physically with wet signatures or preferably with electronic signatures.

1. Ethics committee decision

It is essential to submit the following documents with electronic signatures through the electronic application system. However, if these documents cannot be submitted with electronic signatures, their wet signed versions can be physically submitted.

1. Research budget form
2. Insurance documents
3. Authorisation certificate
4. CV
5. Protocol signature page
6. Proof that the research is for academic purposes
7. GMP certificate/document (apostilled) 1

İ. SIGNATURE OF THE APPLICANT

- All documents attached to the application file are identical to the original,
- The information provided in the application is correct,
- The research will be conducted in accordance with the protocol, relevant legislation, the current Helsinki Declaration and the principles of good clinical practice,

- The investigational product (including placebo) is manufactured in accordance with GMP rules,
- The Turkish label sample of the investigational product (including placebo) was prepared in accordance with GMP guidelines,
- That the research team (including laboratory team, research nurse, research pharmacist, etc.) is informed about the research
- That the proposed clinical trial is feasible,
- The research application is not made to more than one of the ethics committees established within the scope of the relevant Regulation at the same time,
- The progress of the research will be reported at least annually (with an annual notification form),
- Reports on serious adverse events/reactions and periodic safety reports will be submitted inaccordance with the periods specified in the legislation,
- That the research is recorded in a public database, provided that the confidentiality of personal data is respected,
- The publication of the information and research results of the research in a public database by the Authority, provided that the confidentiality of trade secrets and personal data is respected within the conditions determined by the Authority,

I agree and undertake to submit a copy of the summary of the final report within a maximum period of 1 (one) year after the end of the research (in all countries, if it is an international research).

Name and surname	Bedreddin Cavlı
Telephone number	+905051590606
Email address	bedreddin.cavlı@ksbu.edu.tr
Date (in days/months/years)	
Signature	

KÜTAHYA HEALTH SCIENCES UNIVERSITY RECTORATE INTERVENTIONAL CLINICAL RESEARCH ETHICS COMMITTEE RESEARCHERS CV FORM

A. PERSONAL INFORMATION

Name Surname	Bedreddin Cavlı
Academic title/position	Asst. Professor
Place of assignment	Kütahya Health Sciences University Faculty of Dentistry Department of Oral and Maxillofacial Surgery
Telephone number	05051590606
Email address	bedreddin.cavlı@ksbu.edu.tr

B. EDUCATION INFORMATION

Year	Section	Institution	Degree
2015	Faculty of Dentistry	Selcuk University	-
2020	Department of Oral and Maxillofacial Surgery	Gazi University	-

C. INFORMATION ON WORK EXPERIENCE

Date Range	Institution	Mission
2021-...	Kütahya University of Health Sciences / Department of Oral and Maxillofacial Surgery	Asst. Professor
2021	Eskisehir Oral and Dental Health Hospital	Specialist Dentist
2016-2020	Gazi University / Department of Oral and Maxillofacial Surgery	Research Asst.

D. GENERAL INFORMATION ABOUT CLINICAL RESEARCH

4. Training/certificate information on Good Clinical Practices (GCP) and clinical research: If there is a certificate regarding the training you have received, please attach a copy.	
Name and place of training/certificate	**Date**
-	-
5. Clinical research information:	

Responsible Investigator, Co-Investigator, Co-ordinator, Field Officer, Monitor, Pharmacist, etc. should be specified. Write the information in this section in date order.		
Clinical research	**Date Range**	**Mission**
-	-	-

E. SIGNATURE OF THE CV OWNER

I accept and declare that the information I have declared above is correct and up-to-date and that I will comply with the provisions of the relevant legislation and good clinical practices regarding the conduct of clinical trials.

Name Surname	Bedreddin CAVLI
Date (in days/months/years)	
Signature	

A. PERSONAL INFORMATION

Name Surname	Aykut Şaylığ
Academic title/position	Research Asst
Place of assignment	Kütahya Health Sciences University Faculty of Dentistry Department of Oral and Maxillofacial Surgery
Telephone number	05315643315
Email address	Aykut.saylıg@ksbu.edu.tr

B. EDUCATION INFORMATION

Year	Section	Institution	Degree
2018	Faculty of Dentistry	Ankara University	

C. INFORMATION ON WORK EXPERIENCE

Date Range	Institution	Mission
2020-….	Kütahya University of Health Sciences / Department of Oral and Maxillofacial Surgery	Research Asst.

D. GENERAL INFORMATION ABOUT CLINICAL RESEARCH

.

1.Training/certificate information on Good Clinical Practices (GCP) and clinical research: If there is a certificate regarding the training you have received, please attach a copy:	
Name and place of training/certificate	**Date**
--	-

2. Clinical research information: Responsible Investigator, Co-Investigator, Co-ordinator, Field Officer, Monitor, Pharmacist, etc. should be specified. Write the information in this section in date order..		
Clinical research	**Date Range**	**Mission**
-	-	-

E. SIGNATURE OF THE CV OWNER

I accept and declare that the information I have declared above is correct and up-to-date and that I will comply with the provisions of the relevant legislation and good clinical practices regarding the conduct of clinical trials.

Name and Surname	Aykut Şaylığ
Date (in days/months/years)	
Signature	

A. PERSONAL INFORMATION

Name Surname	Şeyma Kale
Academic title/position	Research Asst
Place of assignment	Kütahya Health Sciences University Faculty of Dentistry Department of Oral and Maxillofacial Surgery
Telephone number	05533618111
Email address	seyma.kale@ksbu.edu.tr

B. EDUCATION INFORMATION

Year	**Section**	**Institution**	**Degree**

2018	Faculty of Dentistry	Eskişehir Osmangazi University	

C. INFORMATION ON WORK EXPERIENCE

Date Range	Institution	Mission
2020-….	Kütahya University of Health Sciences / Department of Oral and Maxillofacial Surgery	Research Asst.

D. GENERAL INFORMATION ABOUT CLINICAL RESEARCH

.

1.Training/certificate information on Good Clinical Practices (GCP) and clinical research: If there is a certificate regarding the training you have received, please attach a copy:	
Name and place of training/certificate	**Date**
--	-

2. Clinical research information: Responsible Investigator, Co-Investigator, Co-ordinator, Field Officer, Monitor, Pharmacist, etc. should be specified. Write the information in this section in date order..		
Clinical research	**Date Range**	**Mission**
-	-	-

E. SIGNATURE OF THE CV OWNER

I accept and declare that the information I have declared above is correct and up-to-date and that I will comply with the provisions of the relevant legislation and good clinical practices regarding the conduct of clinical trials.

Name and Surname	Şeyma KALE
Date (in days/months/years)	
Signature	

A. PERSONAL INFORMATION

Name Surname	Necmiye Şengel
Academic title/position	Asst. Professor
Place of assignment	Anaesthesiology and Reanimation - Gazi University Faculty of Dentistry

Telephone number	0505 629 10 06
Email address	necmiyesengel@hotmail.com

B. EDUCATION INFORMATION .

Year	Section	Institution	Degree
2008	Faculty of Medicine	Gazi University	Licence
2013	Anaesthesiology and Reanimation	Gazi University	Expertise

C. INFORMATION ON WORK EXPERIENCE

Date Range	Institution	Mission
2018	Gazi University Faculty of Dentistry	Asst. Professor
2008-2013	Gazi University Department of Anaesthesiology and Reanimation	Research Asst.

D. GENERAL INFORMATION ABOUT CLINICAL RESEARCH

.

1.Training/certificate information on Good Clinical Practices (GCP) and clinical research: If there is a certificate regarding the training you have received, please attach a copy:	
Name and place of training/certificate	**Date**
--	-

2. Clinical research information: Responsible Investigator, Co-Investigator, Co-ordinator, Field Officer, Monitor, Pharmacist, etc. should be specified. Write the information in this section in date order..		
Clinical research	**Date Range**	**Mission**
-	-	-

E. SIGNATURE OF THE CV OWNER

I accept and declare that the information I have declared above is correct and up-to-date and that I will comply with the provisions of the relevant legislation and good clinical practices regarding the conduct of clinical trials.

Name and Surname	Necmiye Şengel
Date (in days/months/years)	

Signature	

A. PERSONAL INFORMATION

Name Surname	Ziver Ergun Yücel
Academic title/position	Professor
Place of assignment	Oral and Maxillofacial Surgery- Gazi University Faculty of Dentistry
Telephone number	0532 395 55 58
Email address	erguny@gazi.edu.tr

B. EDUCATION INFORMATION

Year	Section	Institution	Degree
1980	Faculty of Dentistry	Ankara University	
1984	Department of Oral and Maxillofacial Surgery	Gazi University	

C. INFORMATION ON WORK EXPERIENCE

Date Range	Institution	Mission
1984	Gazi University Department of Oral and Maxillofacial Surgery	Research Asst.
1985	Gazi University Department of Oral and Maxillofacial Surgery	Asst. Profesor
1986	Department of Maxillofacial Surgery, Freie Universität Berlin	Researcher
1988	Gazi University Department of Oral and Maxillofacial Surgery	Assoc. Professor
1991-1992	Guys & St. Thomas Hospital, University of London	Researcher
1995	Gazi University Department of Oral and Maxillofacial Surgery	Profesor

D. GENERAL INFORMATION ABOUT CLINICAL RESEARCH

1.Training/certificate information on Good Clinical Practices (GCP) and clinical research: If there is a certificate regarding the training you have received, please attach a copy:	
Name and place of training/certificate	**Date**

--	-

2. Clinical research information: **Responsible Investigator, Co-Investigator, Co-ordinator, Field Officer, Monitor, Pharmacist, etc. should be specified.** **Write the information in this section in date order..**		
Clinical research	**Date Range**	**Mission**
-	**-**	**-**

E. SIGNATURE OF THE CV OWNER

I accept and declare that the information I have declared above is correct and up-to-date and that I will comply with the provisions of the relevant legislation and good clinical practices regarding the conduct of clinical trials.

Name and Surname	Ziver Ergun Yücel
Date (in days/months/years)	
Signature	

COMMITMENT
KÜTAHYA UNIVERSITY OF HEALTH SCIENCES
CHAIRMAN OF THE ETHICS COMMITTEE FOR CLINICAL RESEARCH

As the undersigned researchers participating in the study titled " Evaluation of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth ", we declare and undertake that we have read the latest version of the World Medical Association Declaration of Helsinki and the current Good Clinical Practices Guide / Good Laboratory Practices Guide published by the Ministry of Health, that the study will be conducted in accordance with the World Medical Association Declaration of Helsinki, GCP / GLP, that we assume all legal and financial responsibilities that may arise in the study, and that all units and staff participating in the study have been informed about the study.

Responsible Researcher:
Asst. Professor Bedreddin Cavlı Signature

Assistant Researcher
Reacher Asst. Aykut Şaylığ Signature

Assistant Researcher
Reacher Asst. Şeyma Kale Signature

Counsellor
Asst. Professor Necmiye Şengel Signature

Counsellor
Professor Ergun Yücel Signature

COMMITMENT
KÜTAHYA UNIVERSITY OF HEALTH SCIENCES
CHAIRMAN OF THE ETHICS COMMITTEE FOR CLINICAL RESEARCH

Title of the Study: Evaluation of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth
During the above-mentioned research, I undertake that no procedure that is not included in the research budget and that will impose an additional burden on the volunteer or the social security institution will not be applied and that I will fulfil my responsibilities in this regard.

Research Responsible
Name-Surname-Title **Signature** **Date:**
Asst. Professor Bedreddin CAVLI

RESPONSIBLE RESEARCHER COMMITMENT FOR THE PROTECTION OF PERSONAL DATA

This confidentiality undertaking ("Undertaking") has been signed on 01.09.2023 between Kütahya Health Sciences University Oral and Dental Health Application and Research Centre ("Centre") located at İstiklal Neighbourhood Lala Hüseyin Pasha Street No:271 and the principal investigator [Dr. Bedreddin Cavlı] residing at [KSBÜ Oral and Dental Health Application and Research Centre Department of Oral, Dental and Maxillofacial Surgery].

With the Letter of Undertaking, the Employee irrevocably accepts, declares and undertakes the following matters, fully understanding and assimilating the consequences.

MATTER 1

PROTECTION OF PERSONAL DATA

a) Within the scope of the relationship established between the Centre and the Responsible Researcher, the Centre processes the personal data of all employees and patients as a data processor in accordance with the General Data Protection Regulation No. 6698 ("GDPR") in order to fulfil its obligations arising from the relevant legislation, especially Law No. 2547, to protect its justified and legitimate

interests regarding the management of the Centre and scientific research, to fulfil its obligations to authorised third parties, competent administrative and judicial bodies, public institutions and organisations, and to ensure data security, and may be transferred to third parties, especially authorized public institutions and organisations, within the scope of Article 8 of the GDPR

b) The scientific research officer and the entire team involved in the study will show the highest level of sensitivity and care regarding the processing and protection of personal and special quality personal data that they have learnt due to their duties and made available to them. In the event that the employee causes the disclosure of personal data or in case of security vulnerability, cyber-attack, data leakage or accidental loss or destruction of data in any way, the employee accepts, declares and undertakes that he / she will notify Kütahya University of Health Sciences, which has the title of data controller ("Data Controller") and the persons authorised by the Data Controller immediately and in writing from the date he / she becomes aware of the event in question.

c) The Principal Investigator and the entire team involved in the study 01.10.2023 between 31.12.2023 for the research titled " Evaluation of trigeminocardiac reflex development during extraction of mandibular impacted wisdom teeth ", agrees, declares and undertakes that they will not illegally record the personal data of any person during and after the research, that they will anonymise all data to be used by the patients and destroy them after the end of the data usage period, that they will forward the records regarding the destruction to the Centre, and that they will not illegally give, disseminate or seize the personal data of any person. The responsible researcher and the entire team involved in the study accept and declare that they are aware that the acts in question constitute a criminal offence under the Turkish Penal Code.

RESPONSIBLE RESEARCHER DECLARATION	RESEARCHER DECLARATION
Asst. Professor Bedreddin Cavlı	Research Assistant Aykut Şaylığ