National Cheng Kung University Hospital, College of Medicine
Human Research Information and Consent Form

Scope of Application: Human research, questionnaires, interviews, and specimen collection not regulated by Article 8 of the Medical Care Act.

(This consent form should be explained in detail by the principal investigator to the participant, who must then sign it after careful consideration.)

You are being invited to participate in this study. This information and consent form provides you with relevant information about the study. The research principal investigator will explain the study content to you and answer any questions you may have.

Project Name：
(Chinese) 口腔舌咽肌肉功能訓練介入達文西手術後之阻塞性睡眠呼吸中止症患者之成效

(English) Efficacy of oropharyngeal myofunctional therapeutic training for obstructive sleep apnea patients after transoral robotic surgery

NCT number: NCT04876482

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Research Funding Source: NCKU Hospital

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Participant's Name:
Gender:
Date of Birth:
Mailing Address:
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I. Study Overview:

The Department of Physical Therapy and the Institute of Health Care Science at National Cheng Kung University have collaborated to study the effectiveness of rehabilitation interventions for Obstructive Sleep Apnea Syndrome (OSA). This consent form provides you with information about the study. The principal investigator or co-investigators will explain the study details and answer any questions you may have. We sincerely invite you to participate in this research.

Obstructive Sleep Apnea Syndrome is characterized by complete or partial obstruction of the upper airway, resulting in repeated episodes of breathing cessation or hypoventilation during sleep, along with uncoordinated chest and abdominal movements, intermittent hypoxia, decreased blood oxygen levels, and even sudden death. It is a common condition in middle-aged individuals, though its prevalence is often underestimated due to undiagnosed cases. In Taiwan, the prevalence is 4% in adult males and 2% in females. The disease progression involves both structural and non-structural predisposing factors, making the clinical symptoms variable and complex. The intermittent hypoxia associated with OSA leads to systemic oxidative stress and a cascade of oxidative reactions, which are risk factors for cardiovascular diseases. This explains why cardiovascular diseases are the most prevalent comorbid condition among OSA patients. Research has also found a high correlation between daytime sleepiness and emotional state in OSA patients. Treatment options for OSA include sleep surgery, continuous positive airway pressure (CPAP), anti-snoring devices, weight loss, and oropharyngeal muscle training.

Previous studies using drug-induced sleep endoscopy have shown that OSA patients' upper airways are more prone to collapse during sleep, with 81% of collapses occurring at the soft palate, 46.6% at the base of the tongue, and 38.7% at the hypopharynx. Normal respiratory control decreases during sleep, narrowing the upper airway, but OSA patients often experience insufficient muscle responsiveness in the pharyngeal dilators or age-related fat accumulation, especially during the rapid eye movement (REM) stage when muscle tone is lowest, making airway collapse more likely. Thus, the aim of our study is to investigate the clinical effectiveness of surgical removal of excess soft tissue and neuromuscular re-education training of the pharyngeal dilator muscles based on clinical examination of airway collapse sites.

This study will measure biomarkers in the blood, including 8-hydroxy-2'-deoxyguanosine (8-OHdG), malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), nuclear factor kappa B (NF-κB), tumor necrosis factor-α (TNF-α), interleukin 6 (IL-6), and matrix metalloproteinase 9 (MMP-9). Previous literature indicates that recurrent ischemia and reperfusion injuries in OSA lead to excessive production of reactive oxygen species (ROS), oxidative stress markers (such as 8-OHdG and MDA), and inflammatory precursors (such as TNF-α and IL-6), damaging antioxidant defenses. Oxidative stress markers increase ROS concentrations, which activate NF-κB. NF-κB stimulates the production of inflammatory precursors and regulates the transcription of matrix metalloproteinases. Activation of TNF-α, IL-6, and MMP-9 leads to endothelial dysfunction and contributes to cardiovascular diseases. Research has found significant increases in 8-OHdG, MDA, NF-κB, TNF-α, IL-6, and MMP-9 concentrations in OSA patients' serum, while antioxidant markers (SOD and CAT) show significant decreases. MDA, NF-κB, and MMP-9 concentrations are highly positively correlated with the duration of nighttime oxygen saturation below 85% and negatively correlated with average blood oxygen saturation. Additionally, MMP-9 is positively correlated with IL-6 and TNF-α in plasma. This study aims to understand the relationship between the severity of OSA and cardiovascular disease risk factors and to explore whether surgical and exercise interventions can improve these risk factors.

II. Research Objectives

According to clinical examination of upper airway collapse sites, multiple interventions, including surgery and neuromuscular re-education training of the pharyngeal dilator muscles, will be implemented. The treatment modalities include sleep surgery and orofacial myofunctional therapy, to investigate their clinical efficacy for OSA. Using G power analysis, with a power level set at 80% and an alpha level at 0.05, the effective sample size is estimated to be about 28 subjects per group. The planned number of subjects for the experiment is 35 per group. The experiment is divided into two groups: the experimental group and the control group. The experimental group includes (1) a post-upper airway surgery group undergoing 12 weeks of orofacial myofunctional therapy (n=35) and (2) an upper airway surgery group (n=35). The control group consists of patients undergoing self-directed weight loss, using CPAP, and waiting for mandibular advancement devices (n=35). Given that the fabrication of mandibular advancement devices takes approximately 3-4 months, relevant measurements will be taken during the waiting period. For patients attempting self-directed weight loss, the principal investigator will inquire in the clinic if they are willing to receive professional weight loss consultation. (1) If the patient is willing, they will be referred to Dr. Chang Chin-Sung's weight loss clinic in the Family Medicine Department. (2) If the patient is unwilling, they will receive self-directed weight loss education materials, and a follow-up appointment will be scheduled 6 weeks later in the ENT clinic to check the weight loss status. If weight loss is unsatisfactory, research assistant (physical therapist Lai Yi-Ju) will arrange bi-weekly visits to measure weight and inquire about dietary status, providing food diaries, weight control diaries from the Family Medicine Department, and exercise diaries to ensure accurate recording and monitoring of weight loss. After 12 weeks, a follow-up appointment in the ENT clinic will confirm the weight loss status. All three groups will undergo pre- and post-intervention measurements and follow-up tests in a longitudinal study design to assess the effectiveness of functional training in physical therapy for post-surgical OSA patients.

III. **Study Duration:** From the date of ethical approval until December 31, 2022.

Estimated Number of Participants or Samples: 105

IV. **Main Inclusion and Exclusion Criteria:**

1. **Inclusion Criteria:**
   - Age between 20 and 65 years.
   - Diagnosed with mild to severe pure obstructive sleep apnea syndrome by PSG sleep study.
   - Epworth Sleepiness Scale score ≧10.
   - Agreement to weight loss, use CPAP, wait for anti-snoring appliance production, or undergo sleep surgery.
2. **Exclusion Criteria:**
   - Smoking, alcohol, or drug abuse within the past year.
   - Pregnancy.
   - Severe obstructive or restrictive pulmonary disease.
   - High-risk cardiovascular disease.
   - History of central or peripheral neurological disorders that prevents participation in exercise prescriptions.
   - Musculoskeletal or psychological disorders that prevent participation in exercise prescriptions.
   - Other non-respiratory sleep disorders.
   - Coexisting central or mixed sleep apnea disorders.

V. Experimental Procedures and Methods:

1. Assessment Process:

Experimental Procedures and Testing Items: The experimental steps primarily follow standard clinical procedures, detailed as follows:

i. Screening through the sleep clinic to determine if further sleep-related assessments are needed (current clinical procedures).
ii. Establishing the diagnosis of obstructive sleep apnea syndrome through sleep examinations (current clinical procedures, requiring overnight sleep studies at a sleep center).
iii. Participants agree to self-weight management, use CPAP, await the fabrication of an anti-snoring dental appliance, or undergo sleep surgery.
iv. Recruiting clinical participants based on inclusion and exclusion criteria, providing comprehensive study information, and informing participants of their right to withdraw from the study at any time. Participants will complete the consent form and will be orally introduced to the study grouping method during the clinic visit. Participants will choose their group based on personal preference and officially enter the clinical research study.
v. Using computed tomography (CT) and drug-induced sleep endoscope examination to understand the pre-surgical pharyngeal anatomy.
vi. Performing tongue muscle function tests, recording the results to understand pre-intervention functional indicators (approximately half an hour).
vii. Conducting biomarker tests to understand pre-intervention biomarker indicators.

Assessment Location: NCKU Hospital Physical Therapy Center

2. Research Procedures and Participant Cooperation:

Collect basic participant information (body mass index, body fat, etc.), followed by muscle function tests (muscle strength parameters, posture assessment) conducted by a physical therapist. The treatment plan includes 12 weeks of post-surgical or post-intervention orofacial myofunctional training, with pre- and post-surgical measurements and follow-up tests (Figure 2). Measurement items include drug-induced sleep endoscope examination and CT scans performed by a sleep specialist, sleep assessments conducted by a sleep technologist, tongue muscle function tests performed by a professional physical therapist, and blood collection by a professional nurse. Blood samples (20 cc each) will be collected at Week 0, Week 6 after the start of the project or post-surgery, and Week 18 after the start of the project or post-surgery, totaling three blood collections.

3. **Surgical Methods:**

Excision of excess soft tissue and hypertrophic lingual tonsils at the base of the tongue, and performing uvulopalatopharyngoplasty (UPPP). The surgeon will clearly inform the patient of the surgical risks.

4.Training Regimen:

Functional training of the oral, lingual, and pharyngeal muscles consists of three sets of exercises targeting the temporomandibular joint, tongue muscles, and oropharyngeal muscle groups. Each exercise mode is performed 10-15 times, with a rest period of 60-90 seconds between exercises. The training session lasts 30 minutes, conducted 3 times a day, 3-5 days a week, for a duration of 12 weeks for the experimental group. Once the subjects have demonstrated proper execution of the exercises, they may choose to continue the training either at the clinic or at home. However, they are required to return to the clinic for follow-up every 1-2 weeks. Similar to rehabilitation training for other skeletal muscles, functional training of the oral, lingual, and pharyngeal muscles necessitates careful monitoring of exercise intensity to prevent issues such as cardiovascular endurance impairment and muscle soreness. Therefore, heart rate, respiration, blood pressure, and blood oxygen levels should be measured before and after exercise. If subjects experience symptoms such as dizziness, nausea, or other discomforts during training, they should stop the exercises immediately.

VI. Retention and Use of Research Data:

Any personal and health information collected in this study will be securely stored. During data analysis, real names will be replaced with codes, and no data will be disclosed to non-research personnel. Data will be securely stored on the computer hard drive in the Respiratory and Circulatory Physiology Laboratory of the Department of Physical Therapy at National Cheng Kung University. The hard drive will not be removed from the laboratory, and all data will be encrypted and password-protected. The passwords will be managed by the principal investigator and co-investigators. The data will be retained until 2029, after which it will be legally destroyed.

VII. Preservation and Use of Research Materials

1. **Preservation and Use of Samples (including their derivatives):** The samples collected from you for this study will be used according to the research plan and stored in the Respiratory and Circulatory Physiology Laboratory of the Department of Physical Therapy at National Cheng Kung University. Upon completion of testing, the samples will be legally destroyed. To protect your privacy, we will use a research code to replace your name and related personal information, ensuring complete confidentiality of your samples and related data. If you have any concerns about the use of your samples or wish to have them destroyed, please contact us immediately (Contact: Yi-Ru Lai, Phone: 0963123117; Contact Unit: Respiratory and Circulatory Physiology Laboratory, Department of Physical Therapy, National Cheng Kung University, Phone: 06-2353535 ext. 5945, Address: No. 1, University Road, East District, Tainan City). We will then destroy your samples. You may also contact the Human Research Ethics Committee (Phone: (06) 2353535 ext. 3635) to assist with any disputes regarding the use of your samples in the study.
2. **Preservation and Reuse of Subject Data:** Your data will be securely stored by the research team and destroyed after the retention period ends in 2029.

VIII. Foreseeable Risks and Remedial Measures:

Assessment and training will be personally conducted by senior clinical physical therapists. The process will be completed under the guidance and supervision of professional personnel. If any physical, mental, or emotional negative feelings occur during the study, the participant has the absolute right to withdraw from the study without any loss or sequelae. The following are explanations of possible incidents and corresponding measures:

1. Radiation Exposure:

According to the Atomic Energy Council of the Executive Yuan, the radiation dose for a head and neck CT scan is 2-3 millisieverts (mSV), approximately 100-150 times that of a head and neck X-ray (0.02 mSV). Some individuals may have allergic reactions to the contrast agent used in CT scans, such as headaches, nausea, or vomiting. The likelihood of death from the contrast agent is about 1-3 in 100,000 people. After removing the intravenous line used for the contrast agent, apply local pressure for 5-10 minutes to prevent bleeding or bruising at the injection site. If there is swelling, redness, or pain at the injection site, inform the nurse immediately. For large bruises, apply ice packs on the same day and heat packs for 10-15 minutes daily after 24 hours to help disperse the bruise, which should gradually disappear in about 7-10 days. Before injecting the contrast agent, participants will have a blood test to check creatinine levels and confirm normal kidney function.

2.Surgical Risks:

The surgeon will clearly inform the patient of the surgical risks.

3. Post-Surgical Discomfort:

Initially after surgery, there may be wound pain and a foreign body sensation during swallowing. Regular follow-ups with a sleep specialist for wound assessment will be scheduled within four to six weeks post-surgery. Once the sleep specialist confirms wound stability, exercise training will commence.

4.Adaptation to Exercise Training:

Participants might initially struggle with learning new exercise techniques. Instructional videos or educational leaflets will be provided, with step-by-step illustrations to guide the patient in understanding correct movement performance and self-assessment methods.

5.Exercise-Induced Symptoms:

Participants might experience breathlessness or fatigue during exercise training. During the training process, subjective feedback from the patient will be frequently solicited, and the trainer will objectively assess the patient's performance.

6.Compliance with Training Schedule:

Participants might find it challenging to adhere to the regular training schedule. Alternative training sessions will be arranged at times convenient for the participant to ensure compliance with the same frequency of training sessions.

IX. Expected Benefits of the Study:

By surgically removing excess soft tissue at multiple collapse sites in the upper airway and providing neuromuscular re-education training for the pharyngeal dilator muscles, it is estimated that obstructive sleep apnea syndrome (OSA) can be improved. The primary causes of OSA include the collapse of excess soft tissue, insufficient muscle tone, and reduced muscle activity, leading to upper airway obstruction or collapse during sleep. The intervention is expected to address these clinical issues, thereby improving sleep problems and enhancing sleep quality.

X. Compensation for Damage and Insurance:

1. If adverse reactions or damages occur as a result of this clinical research plan, NCKUH will be responsible for compensation. However, foreseeable adverse reactions that are documented in this consent form and cannot be prevented will not be compensated.
2. If adverse reactions or damages occur as a result of this study, NCKUH is willing to provide necessary assistance.
3. Apart from the aforementioned compensation and medical care, no other forms of compensation will be provided by this study. If you are unwilling to accept these risks, please do not participate in the study.
4. Signing this consent form does not result in the forfeiture of any legal rights.

XI. Rights of Subjects and Personal Data Protection Mechanisms:

1. Research Participation Subsidies: This trial groups subjects based on their own willingness. Subjects must bear the costs of follow-up/outpatient visits and surgery. The research project will subsidize the cost of one CT scan, two drug-induced sleep endoscopies, and three blood draws.

2. Privacy Protection: The data obtained from the study may be published in academic journals, but your name will not be disclosed, and the privacy of your personal information will be strictly maintained. The principal investigator will carefully protect your privacy rights. The central health authorities, the research sponsor, and the Institutional Review Board (IRB) of National Cheng Kung University Hospital have the right to review your data in accordance with the law, without compromising your privacy.

3. Provision of New Information: If any new information arises during the research process that may affect your willingness to continue participating in the study, it will be provided to you promptly.

4. Inquiry and Complaint: If you have any questions about the nature of the research work, concerns about your rights as a patient, or if you suspect that you have been harmed due to participation in the research, you can contact the IRB of National Cheng Kung University Hospital for consultation. The contact number is 06-2353535 ext. 3635, or you can email em73635@mail.hosp.ncku.edu.tw, or mail to: Institutional Review Board, Outpatient Building, 138 Shengli Road, North District, Tainan City 704, Taiwan.

This consent form is in duplicate, and a copy has been provided to you by the principal/co-principal investigator, who has also fully explained the nature and purpose of this research and answered your related questions.

XII. Commercial Interests and Applications Potentially Arising from the Research:

This research is not expected to generate patents or other commercial interests.

XIII. Withdrawal and Termination of the Research:

You are free to decide whether to participate in this research. You may also withdraw your consent and exit the study at any time during the research process, without providing any reason. This will not cause any unpleasantness or affect your future medical care by your physician. The principal investigator or sponsor may also terminate the study if necessary. During the study, subjects can express their desire to stop or exit the research at any time; and upon withdrawal, your data will be completely removed from the laboratory computer hard drive. If you wish to withdraw from the study, please contact Ms. Yi-Ju Lai at 0963123117.

XIV. **Signature Section:**

1. **The subject has thoroughly understood the above research methods and the potential risks and benefits involved. Any questions regarding this trial have been fully explained by the principal investigator. I agree to voluntarily participate as a subject in this clinical trial.**
   (1) If the subject is incapacitated (a child under 7 years old or a person under guardianship), consent must be obtained from their legal representative or guardian.
   (2) For individuals with limited capacity (over 7 years old but under 20, or a person under assistance), consent must be jointly obtained from the individual and their legal representative or assistant, and the consent form must be signed by both. (For children aged 7-11, please attach the child version of the consent form.)
   (3) Even if the subject is not incapacitated or of limited capacity, if they are unconscious or mentally disordered and unable to act on their own, the consent must be given by an authorized person. (The order of consent follows relevant legal regulations.)

   Subject's Signature:

   Date:

   Signature of Legal Representative/Guardian/Assistant/Authorized Person (if applicable):

   Relationship to Subject:

   Date:

2. **Use of Witness:**
   (1) When the subject, legal representative, or authorized person cannot read, a witness should be present for all discussions regarding the subject's consent. The witness should read the subject consent form and any other written materials provided to the subject, to verify that the principal investigator or their designated personnel has accurately explained the contents to the subject, legal representative, or authorized person and ensured their full understanding.
   (2) The subject, legal representative, or authorized person should still sign the subject consent form and indicate the date. A fingerprint can replace the signature if necessary.
   (3) The witness should sign and date the subject consent form after completing the verbal explanation and confirming that the subject, legal representative, or authorized person's consent is given freely.
   (4) Research personnel cannot serve as witnesses.

   Witness's Signature:

   Date:

3. **The principal investigator or research personnel have fully explained the nature and purpose of the research methods described above, and the potential risks and benefits involved in this research project.**

   Signature of Principal Investigator/Co-Principal Investigator/Research Personnel:

   Date:

國立成功大學醫學院附設醫院
人體研究說明及同意書

適用範圍：非醫療法第 8 條所規範之人體研究、問卷、訪談及檢體採集等

（本同意書應由計畫主持人親自向受試者說明詳細內容，並請受試者經過慎重考慮後方得簽名）

您被邀請參與此研究，本說明及同意書提供您有關本研究之相關資訊，研究主持人將會為您說明研究內容並回答您的任何疑問。

計畫名稱：

(中) 口腔舌咽肌肉功能訓練介入達文西手術後之阻塞性睡眠呼吸中止症患者之成效

(英) Efficacy of oropharyngeal myofunctional therapeutic training for obstructive sleep apnea patients after transoral robotic surgery

執行單位：國立成功大學附設醫院耳鼻喉部/成大醫院睡眠中心
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研究經費來源：成大醫院院內研究計畫

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受試者姓名：
性別：　出生日期：
通訊住址：
聯絡電話：

一、研究簡介：

國立成功大學物理治療學系暨健康照護科學所共同合作，針對阻塞性睡眠呼吸中止症候群（Obstructive sleep apnea syndrome, OSA）進行復健治療介入的成效之研究，本同意書將提供您有關本研究之相關資訊，計畫主持或協同主持人將會為您說明研究內容並回答您的疑問，誠摯邀請您參與此研究。

阻塞性睡眠呼吸中止症候群乃因為上呼吸道完全或部分阻塞，而在睡眠過程反覆發生呼吸中止或換氣不足的現象，合併不協調的胸腹運動，間歇性缺氧以及血氧濃度下降，甚至猝死，為中年族群常見的疾病，盛行率卻因為沒有被診斷出來常被低估，在台灣成年人男性盛行率 4%，女性 2%。其病程發展同時具有結構性以及非結構性相關的前置因子，使得臨床症狀變得多變而複雜。阻塞性睡眠呼吸中止症候群間歇性的缺氧問題，會導致系統性的氧化壓力以及一連串的氧化反應，是心血管疾病的危險因子之一，這也解釋了為什麼心血管疾病是阻塞性睡眠呼吸中止症候群族群中最高盛行率的共病症。另有研究發現阻塞性睡眠呼吸中止症候群患者白天嗜睡狀況與情緒狀態有高度相關性。阻塞性睡眠呼吸中止症候群的患者，其治療方式包含睡眠外科手術、連續正壓呼吸輔助器(CPAP)、止鼾牙套、減重及口咽肌肉訓練。

在過去世代研究中，根據藥物誘導式的睡眠內視鏡檢查發現，阻塞性睡眠呼吸中止症候群患者其上呼吸道於睡眠週期較容易發生坍陷的問題，發生坍陷的位置 81%為軟顎後方坍陷，46.6%為舌根後方坍陷，而 38.7%為下咽坍陷。正常人體的呼吸中樞的驅動能力在睡眠週期，會有減弱的現象，導致上呼吸道變窄，但是阻塞性睡眠呼吸中止症候群患者常因為咽部擴張肌（pharyngeal dilators）肌肉活動反應不足（insufficient muscle responsiveness）或老化脂肪堆積的問題，尤其在肌肉張力活動最低的快速動眼時期，使其上呼吸道會更容易發生坍陷的問題。因此我們的研究目的乃是：依臨床檢查上呼吸道癱陷位置多處進行手術切除多餘軟組織及介入咽部擴張肌之肌肉再教育訓練（neuromuscular re-education training），探討其對於阻塞性睡眠呼吸中止症候群的臨床成效。

本研究將檢測血液中 8-羥基-2´-脫氧鳥苷(8-hydroxy-2-deoxyguanosine, 8-OHdG)、丙二醛(Malondialdehyde, MDA)、超氧化物歧化酶(superoxidase dismutase, SOD)、過氧化氫酶(catalase, CAT)、細胞核因子-κB(nuclear factor kappa B, NF-κB)、腫瘤壞死因子-α(tumor necrosis factor-α, TNF-α)、介白質 6(interleukin 6, IL-6)及基質金屬蛋白酶 9(Matrix metalloproteinases, MMP-9)。過去文獻顯示阻塞性睡眠呼吸中止症候群產生的反覆性缺血及再灌流損傷，將造成活性氧化物(Reactive oxygen specie, ROS)、氧化壓力物質(如: 8-OHdG 及丙二醛)及發炎前驅物質(如：腫瘤壞死因子-α、介白質 6) 過度產生，並損傷抗氧化能力。氧化壓力物質會造成活性氧化物濃度上升，活性氧化物會活化細胞核因子-κB，細胞核因子-κB 會刺激產生發炎前驅物質，並同時調節基質金屬蛋白酶的轉錄，腫瘤壞死因子-α、介白質 6 及基質金屬蛋白酶 9 的活化會造成內皮細胞失能，進而造成心血管疾病，已有研究發現阻塞性睡眠呼吸中止症患者血清中之 8-OHdG、丙二醛、細胞核因子-κB、腫瘤壞死因子-α、介白質 6 及基質金屬蛋白酶 9 濃度有顯著性上升之情況，而抗氧化壓力物質(超氧化物歧化酶及過氧化氫酶)濃度有顯著性下降之情況，丙二醛、細胞核因子-κB 及基質金屬蛋白酶 9 濃度與夜間氧氣飽和濃度低於 85%持續時間呈高度正相關性，而與平均血氧飽和濃度呈負相關性，另基質金屬蛋白酶 9 又與血漿中介白質 6 和腫瘤壞死因子-α 呈正相關性。希望藉由此研究了解瞭解阻塞性睡眠呼吸中止症候群嚴重程度與心血管疾病危險因子之相關性，並探討手術及運動介入是否改善心血管疾病發生的危險因子。

二、研究目的：

依臨床檢查上呼吸道癱陷位置多處介入手術及咽部擴張肌之肌肉再教育訓練（neuromuscular re-education training），探討其對於阻塞性睡眠呼吸中止症候群的臨床成效。實驗分成兩組實驗組和控制組，實驗組分別為上呼吸道手術後進行 12 週口腔舌咽肌肉功能訓練(運動)組(n=35)及上呼吸道手術組(n=35)，控制組為自行減重、使用 CPAP 及等待配戴止鼾牙套之患者(n=35)，因止鼾牙套製作時間約需 3-4 個月，將於患者等待期間進行相關測量，而自行減重患者，主持人於診間會詢問自行減重患者是否願意接受減重門診專業諮詢。(1)若患者願意，將轉介至家醫科張秦松醫師之減重門診診療；(2)若患者不願意，將於診間給予自行減重衛教單張，如附件，並於 6 周後安排回耳鼻喉科門診，以確認患者減重狀況，若減重情形不理想，將請研究助理(物理治療師賴奕儒)安排每 2 周回院一次，測量體重並詢問飲食狀況，且給予飲食日記、成大醫院家庭醫學部體重控制門診體重日記及運動日記，如附件，要求患者確實記錄，以監控減重情形。持續 12 周後，將再次安排回耳鼻喉科門診，確認患者減重狀況。三組皆會進行介入前後量測以及追蹤量測等重複測試的縱向研究設計，探討物理治療的功能性訓練對於手術後阻塞性睡眠呼吸中止症候群病人的成效。

三、研究預計執行期間：人體研究倫理審查通過日～ 111 年 12 月 31 日

受試者數目：共計 105 名

四、研究之主要納入與排除條件：

(1) 收案條件: 年紀介於 20~65 歲，經睡眠多項生理檢查診斷為輕度到重度純粹阻塞性睡眠呼吸中止症病人，並且愛普渥斯嗜睡度量表≧10，且已同意自行減重、使用 CPAP、等待止鼾牙套製作或接受睡眠外科手術治療者。

(2) 排除條件：

i. 一年內有抽菸、酒精和藥物濫用者
ii. 懷孕
iii. 嚴重阻塞性或限制性肺部疾病
iv. 運動高風險心血管疾病
v. 中樞或周邊神經疾病病史導致無法執行運動處方
vi. 肌肉骨骼或心理障礙導致無法執行運動處方
vii. 其他非呼吸相關的睡眠疾患
viii. 合併中樞型或混合型睡眠呼吸中止症的睡眠疾患

五、研究方法、程序及受試者應配合事項：

(1) 評估流程：

- 實驗流程與檢測項目：

實驗執行步驟多屬臨床處置標準流程，其細節如下說明：

i. 透過睡眠門診篩檢是否需要進一步的睡眠相關檢測（現行臨床處置流程）。
ii. 透過睡眠檢查確立阻塞性呼吸中止症候群診斷（現行臨床處置流程，需要在睡眠中心進行過夜睡眠檢查）。
iii. 受試者同意自行減重、使用 CPAP、等待止鼾牙套製作或進行睡眠外科手術
iv. 依照收案以及排案條件徵收臨床受試者，提供完整詳細的研究說明，並告知受試者有權利隨時終止參與計畫，完成受試者同意書填寫，此外也會在門診時口頭介紹計畫分組方式，受試者將以自身意願決定進入之組別，正式進入臨床人體研究計畫。
v. 透過電腦斷層掃描及藥物誘導式睡眠內視鏡檢查，瞭解手術前口咽部解剖結構。電腦斷層掃描(CT) 是利用 X 光的光束穿透身體，在身體對側以 X 光偵測器接收穿透過身體的 X 光，再以電腦解讀接收器的 X 光而顯像。由於人體每個組織對 X 光的吸收（阻斷）能力不同，所表現出的特徵也不同，可藉由電腦斷層掃描了解骨骼及肌肉之相對位置。藥物誘導式睡眠內視鏡檢查(DISE)是用來定位上呼吸道阻塞位置的檢查工具，希望知道阻塞性睡眠呼吸中止症候群病患睡著時的上呼吸道肌肉塌陷位置在何處。
vi. 透過舌肌肌肉檢測，紀錄檢測結果，瞭解受試者介入前功能指標（約需半個小時左右完成）
vii. 透過生物標記檢測，瞭解受試者介入前生物標記指標

評估地點：成大醫院物理治療中心。

(2) 研究程序及受試者應配合事項：

蒐集受試者的基本資料（身體質量指數、體脂肪）等，再由物理治療師施行實驗相關之肌肉功能性測試（肌力參數、姿勢評估）等等，治療計畫分別為手術及術後介入口腔顏面肌肉功能訓練 12 週，並進行手術前後量測以及追蹤量測等重複測試。其量測項目包含睡眠專科醫師進行藥物誘導式的睡眠內視鏡檢查及電腦斷層掃描，睡眠專科技師進行睡眠檢查，專業物理治療師進行舌肌肌肉功能檢查，以及專業護理人員血液採集，分別在第 0 週、術後第 6 週和術後第 18 週採血，一次採血 20c.c，總共採血 3 次。上述第 0 週、第 6 週及第 18 週之量測將不提供受試者交通費用。

(3) 手術方式

切除舌根處的多餘軟組織及增生肥大的舌扁桃腺，並進行懸壅垂顎咽成形術。手術醫師將另行明確告知手術風險。

(4) 訓練模式 **(如附件資料:衛教單張)**

口腔舌咽肌肉的功能訓練，其訓練模式包含顳顎關節、舌肌以及口咽肌群等共 3 組動作訓練， 10-15 次/每個動作模式，每個動作模式中間休息 60-90 秒，30 分鐘/回，3 回/天，3-5 天/週，12 週/實驗組，確認受試者運動執行正確後，受試者可以選擇在診間或居家進行訓練，唯 1-2 週需回診再進行追蹤，就像其他骨骼肌群的復健訓練一樣，口腔舌咽肌肉的功能訓練需要留意運動強度的監控，避免過度運動影響心肺耐力表現以及肌肉酸痛的問題，因此要在運動前後量測受試者的心跳、呼吸、血壓以及血氧，如運動過程，受試者發生頭暈、噁心或其他不舒服的症狀，應立即停止訓練。

六、研究資料之保存期限及運用規劃：

本研究所收集關於您的任何個人資料及健康資訊將被妥善保存，資料分析時將以代號取代真實姓名，所有資料將不會向非研究相關者公開。資料將妥善儲存於國立成功大學物理治療學系呼吸循環生理實驗室電腦硬碟中，電腦硬碟不得攜出實驗室外，且所有資料都將進行加密，需有密碼方得打開資料，密碼將由主要主持人及共同主持人管理。資料將保存至 2029 年，之後我們將依法銷毀。

七、研究材料之保存與使用

1.檢體(含其衍生物)之保存與使用

為研究所需，我們所蒐集您的檢體，將依本研究計畫使用，檢體將保存於 國立成功大學物理治療學系呼吸循環生理實驗室，檢測完畢將直接依法銷毀。為了保護您的個人隱私，我們將以一個試驗/研究編號來代替您的名字及相關個人資料，以確認您的檢體及與相關資料受到完整保密。如果您對檢體的使用有疑慮，或您有任何想要銷毀檢體的需求，請立即與我們聯絡(聯絡人：賴奕儒 電話：0963123117；聯絡單位：國立成功大學物理治療學系呼吸循環生理實驗室 電話：06-2353535 轉 5945 地址：台南市東區大學路 1 號)，我們即會將您的檢體銷毀。您也可以聯繫人體研究倫理審查委員會(電話：(06) 2353535 轉 3635)，以協助您解決檢體在研究使用上的任何爭議。

2.受試者資料之保存與再利用

您的資料將由研究團隊妥善**保存至 2029 年屆滿**後即銷毀。

八、可預見之風險及造成損害時之補救措施：

評估及訓練皆由臨床資深物理治療師親自執行，在專業人員的指導及監督下完成受試過程，如中途發生任何身體、心裡或情緒負面感受，受試者有絕對權利可以主張退出研究計畫，不會造成任何損失或後遺症，故針對可能發生之事故及因應措施說明：

1. 根據中華民國行政院原子能委員會的資料，頭頸部電腦斷層輻射劑量為 2-3 毫西弗(mSV)，約為頭頸部 X 光攝影 0.02 毫西弗(mSV)的 100-150 倍。有些人會對於電腦斷層掃描的顯影劑有過敏反應，例如：頭痛、噁心或嘔吐等；至於顯影劑致死的機率，依據文獻，約十萬個人接受顯影劑注射，有 1~3 個人因此死亡。於靜脈注射顯影劑的管路移除後，請持續局部加壓 5-10 分鐘，避免注射部位出血或瘀血；若靜脈注射部位有腫脹、發紅以及疼痛之情況時，請立即告知護理師處理。若瘀血部位很大時，請當日回家先冰敷，24 小時後再每日熱敷 10-15 分鐘，以利瘀血消散，約莫 7-10 天瘀血會漸漸消散。受試者於打顯影劑前有抽血檢測肌酸酐(creatinine)數值，確認受試者腎功能正常，才會決定進行施打顯影劑。

2.手術過程，手術醫師將另行明確告知手術風險。

3.手術後初期，可能出現傷口疼痛及吞嚥時有異物感等現象: 於術後四至六周內，定期回院由睡眠專科醫師進行傷口評估。經睡眠專科醫師評估傷口穩定後，再進行運動訓練。

4.運動訓練初期，可能無法適應新的運動技巧的學習：準備影片或衛教說明單張，圖相式依步驟逐項分解說明，並引導病人瞭解正確動作表現的自我評估方式。

5.運動訓練過程，可能引起喘氣或疲累的現象：於運動過程，加強詢問病人主觀的反應，並客觀判斷病人的表現。

6.運動訓練過程，可能無法順從定期的訓練計畫：依照同樣的訓練次數，在病人可配合的時間點另外進行訓練。

九、研究預期效益：

依臨床檢查上呼吸道癱陷位置多處進行手術切除多餘軟組織及介入咽部擴張肌之肌肉再教育訓練，推估可以改善阻塞型呼吸中止症候群，其致病主因是多餘軟組織癱陷、肌肉張力不足以及肌肉活動度降低導致睡眠時期上呼吸道阻塞或癱陷的臨床問題，介入治療推估可進而改善其睡眠問題，增益其睡眠品質。

十、損害補償與保險：

(一) 如依本研究所訂臨床研究計畫，因而發生不良反應或損害，由成大醫院負損害補償責任。但本受試者同意書上所記載，而無法預防之可預期不良反應，不予補償。

(二)如依本研究進行因而發生不良反應或損害，成大醫院願意提供必要的協助。

(三)除前二項補償及醫療照顧外，本研究不提供其他形式之補償。若您不願意接受這樣的風險，請勿參加研究。

(四)您不會因為簽署本同意書，而喪失在法律上的任何權利。

十一、受試者權利及個人資料保護機制：

(一)參加研究之補助

本試驗依受試者自身意願進行分組，受試者須負擔回診/門診及手術費用，研究計畫將補助 1 次電腦斷層、2 次藥物誘導式睡眠內視鏡檢查費用及 3 次採血費用。

(二)保護隱私

研究所得資料可能發表於學術雜誌，但不會公佈您的姓名且對受試者個人資料之隱私絕對保密，同時計畫主持人將謹慎維護您的隱私權。中央衛生主管機關、研究委託者與成大醫院人體研究倫理審查委員會在不危害您的隱私情況下，依法有權檢視您的資料。

(三) 研究過程中如有新資訊可能影響您繼續參與研究意願的任何重大發現，都將即時提供給您。

(四) 如果你(妳)在研究過程中對研究工作性質產生疑問，對身為患者之權利有意見或懷疑因參與研究而受害時，可與成大醫院之人體研究倫理審查委員會聯絡請求諮詢，其電話號碼為：06-2353535 轉 3635 或 e-mail : em73635@mail.hosp.ncku.edu.tw 或郵寄至 704 台南市北區勝利路 138 號門診大樓人體研究倫理審查委員會。

本同意書一式兩份，主持人/共同主持人研究人員已將同意書副本交給你(妳)，並已完整說明本研究之性質與目的，也已回答您研究等相關問題。

十二、研究可能衍生之商業利益及其應用之約定：

本研究預期不會衍生專利權或其他商業利益。

十三、研究之退出與中止：

您可自由決定是否參加本研究；研究過程中也可隨時撤銷同意，退出研究，不需任何理由，且不會引起任何不愉快或影響其日後醫師對您的醫療照顧。研究主持人或贊助廠商亦可能於必要時中止該研究之進行。此研究進行，受試者可以隨時反應停止或退出研究；且退出研究後資料將會完全自實驗室電腦硬碟中移除。受試者若欲退出本案，聯絡方式 0963123117 洽本案研究人員賴奕儒小姐。

十四、簽名欄：

(一) 受試者已詳細瞭解上述研究方法及其所可能產生的危險與利益，有關本試驗計畫的疑問，業經計畫主持人詳細予以解釋。本人同意接受為臨床試驗計畫的自願受試者。

1. 受試者為無行為能力(未滿 7 歲之兒童或受監護宣告之人)，應得其法定代理人或監護人之同意。
2. 限制行為能力人(滿 7 歲以上至未滿 20 歲或受輔助宣告之人)，應得其本人及法定代理人或輔助人共同同意並簽署同意書。(7~11 歲請檢附兒童版同意書)
3. 受試者雖非無行為能力或限制行為能力者，但因無意識或精神錯亂無法自行為之時，應由有同意權人為之。(同意順序依相關法律規定辦理)

受試者簽名：_____

日期：_____ 年_____月_____日

法定代理人/監護人/輔助人/有同意權人簽名(如適用)：_____

與受試者關係：_____

日期：_____年_____月_____日

(二) 見證人使用時機：

1. 受試者、法定代理人或有同意權之人皆無法閱讀時，應由見證人在場參與所有有關受試者同意書之討論。見證人應閱讀受試者同意書及提供受試者之任何其他書面資料，以見證研究主持人或其指定之人員已經確切地將其內容向受試者、法定代理人或有同意權之人解釋，並確定其充分了解所有資料之內容。
2. 受試者、法定代理人或有同意權之人，仍應於受試者同意書親筆簽名並載明日期。但得以指印代替簽名。
3. 見證人於完成口述說明，並確定受試者、法定代理人或有同意權之人之同意完全出於其自由意願後，應於受試者同意書簽名並載明日期。
4. 研究相關人員不得為見證人。

見證人簽名：_____

日期：_____年_____月_____日

(三) 主持人或研究人員已詳細解釋有關本研究計畫中上述研究方法的性質與目的，及可能產生的危險與利益。

主要主持人/共同主持人/研究人員簽名：_____

日期：_____年_____月_____日

成大醫院受試者知情同意過程記錄表

Documentation of the Informed Consent Process

※受試者參與人體研究或臨床試驗案時，研究者須填本表記錄知情同意過程是否適切。
※如受試者有簽署「受試者同意書」，本表請與「受試者同意書」同時進行填寫與保存，以利後續審核。如無「受試者同意書」則請單獨保存。

1. 研究計畫名稱/Study Title:口腔舌咽肌肉功能訓練介入達文西手術後之阻塞性睡眠呼吸中止症患者之成效
2. 計畫主持人/PI:林政佑
3. 本會編號/IRB No.:A-BR-108-059
4. 受試者姓名或編號/Subject Name or Subject No.:
5. 取得同意之研究者/Consent obtained by:
   □計畫主持人/Principle Investigator　□共(協)同計畫主持人/Co-Investigator
   □其他研究人員Other: (身份/identity)　(姓名/name)
6. 取得同意之研究者說明日期/Date of Explanation(yyyy/mm/dd):
7. 受試者同意日期/Date of Consent(yyyy/mm/dd):
8. 勾選以下符合之項目/ Check all that apply:

勾選/Check	項目/Elements
□	(1)受試者初步符合研究納入之條件 The subject meets pre-screening requirements.
□	(2)確認受試者有足夠的能力理解--參與本研究所可能產生之風險與利益 The subject's comprehension is assessed to ensure that the subject understands the research and the risks and benefits involved in the study.
□	(3)對受試者充分說明、討論以及檢閱受試者同意書內容 Fully discussed, explained and reviewed the consent form with subject.
□	(4)研究者根據 IRB 核准之程序獲得受試者(法定代理人/監護人)書面同意 Written consent (legally acceptable representative consent) was obtained (per IRB approved consent process).
□	(5)確認受試者的疑問都得到解答 All of the subject's questions were answered/concerns addressed.
□	(6)讓受試者(法定代理人/監護人)有足夠的時間閱讀同意書，並曾和其他非參與者討論是否參與本研究 Subject was given time to review the consent form and to discuss participation in this study with family members/others
□	(7)受試者已同意參與研究，並於研究程序開始前簽署 IRB 核准之最新版本同意書 The subject has agreed to participate in the study and signed/dated the most current valid IRB approved consent form prior to the start of any study procedures.
□	(8)將正本同意書保存於研究記錄或單獨的資料夾中 The original signed and dated consent form was placed in the research record or separate binder.
□	(9)提供一份簽署完成之同意書副本予受試者 A copy of the signed informed consent form was provided to the subject.

執行之研究人員簽名: Signature	日期: Date

IRB核准日期/IRB Approval Date:2019.11.28

NCKUH IRB
2019.11.28
Approved

Institutional Review Board
National Cheng Kung University Hospital
138 Sheng-Li Rd, Tainan 704, Taiwan R.O.C.
TEL:886-6-2353535 ext.3635 FAX:886-6-2388190

國立成功大學醫學院附設醫院
第一人體研究倫理審查委員會
台灣.台南市勝利路138號
E-mail:em73635@mail.hosp.ncku.edu.tw

Human Study Approval

Date: 2019.11.29

Title: Efficacy of oropharyngeal myofunctional therapeutic training for obstructive sleep apnea patients after transoral robotic surgery
Protocol No/ IRB No: -- / A-BR-108-059
Period of Project: From 2019.11.28 to 2022.12.31
Period of Approval: From 2019.11.28 to 2020.11.27
Content/Version:
1. Protocol: Version: 3, Date: 2019/11/18
2. Informed Consent Form: Version 3, Date: 2019/11/18
3. Education Sheet: Version: 1, Date: 2019/9/6

Institute: National Cheng Kung University Hospital
Investigator: Dr. Cheng-Yu Lin (Department of Otolaryngology)
Co-Investigator: Professor Ching-Hsia Hung
Co-Researcher: Yi-Ju Lai

Approved Number of Participants: NCKUH: 105 persons. If the number of participants enrolled exceeds the approved number, please submit an application for amendment and approval.

The Institutional Review Board of National Cheng Kung University Hospital (NCKUH) is organized and operated according to the laws and regulations of ICH-GCP and of Central Competent Authorities.

This project is reviewed and approved by NCKUH IRB in **2019.11.28.** The period of approval is granted until **2020.11.27.**

Regarding multi-period project, please submit the Interim Report before **2020.10.27.** If the approval of the interim report is not granted on its expiry date, except safeguarding the health of the participants, the research is suspended.

Regarding completed project, the Final Report shall be submitted within three months of its approved expiry date. Except for the health of the participants, all the procedures of the project shall be terminated on its approved stated deadline.

If PI does not submit the Interim/Final Report on time, he/she will be recorded in the overdue list and received the suspension/ termination notice from NCKUH IRB. The overdue list will be reported to the IRB. After the resolution of the board meeting, NCKUH IRB will suspend all the new projects applied by PI until the Interim/Final Report is submitted.

Please submit the Interim/Final Report in written form and send to NCKUH IRB office. The lastest application forms can be downloaded in its website (http：// www.ncku.edu.tw/ ~nckuhirb)

Any changes or amendments to the project (including the project period), please submit an amendment application to NCKUH IRB within its approved period. Any changes or amendments in any other way will not be accepted. Before the approval of the amendment application, the project is carried out according to its previously approved plan.

For some reasons projects granted approval by NCKUH IRB couldn't be implemented, PI shall apply for suspension/termination.

During or after the project is completed, please report any unfavorable occurrence in a human study particant according to GCP.

Yours sincerely,
Ting-Tsung Chang M.D.
Chairman

Institutional Review Board
National Cheng Kung University Hospital

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National Cheng Kung University Hospital
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第一人體研究倫理審查委員會
台灣.台南市勝利路138號
E-mail:em73635 @mail.hosp.ncku.edu.tw

Human Study Amendment Approval

Date: 2020.07.03

Title: Efficacy of oropharyngeal myofunctional therapeutic training for obstructive sleep apnea patients after transoral robotic surgery

Protocol No/ IRB No: -- / A-BR-108-059

Period of Project: From 2019.11.28 to 2022.12.31

Period of Approval: From 2019.11.28 to 2020.11.27

Content/Version:

1. Protocol: Version: 6, Date:2020.06.09
2. Informed Consent Form: Version 6, Date: 2020.06.09
3. Add Diet Diary: Version: 1, Date:2020.06.09
4. Add Weight loss Education Sheet: Version: 1, Date:2020.06.03
5. Add Weight Management and Exercise Diary: Version: 1, Date:2020.06.09

Institute: National Cheng Kung University Hospital

Investigator: Dr. Cheng-Yu Lin (Department of Otolaryngology)

Co-Investigator: Professor Ching-Hsia Hung

Co-Researcher: Yi-Ju Lai

The Institutional Review Board of National Cheng Kung University Hospital (NCKUH) is organized and operated according to the laws and regulations of ICH-GCP and of Central Competent Authorities.

This project is reviewed and approved by NCKUH IRB in **2020.07.02**. The period of approval is granted until **2020.11.27.**

Regarding completed project, the Final Report shall be submitted within three months of its approved expiry date. Except for the health of the participants, all the procedures of the project shall be terminated on its approved stated deadline.

If PI does not submit the Interim/Final Report on time, he/she will be recorded in the overdue list and received the suspension/ termination notice from NCKUH IRB. The overdue list will be reported to the IRB. After the resolution of the board meeting, NCKUH IRB will suspend all the new projects applied by PI until the Interim/Final Report is submitted.

Please submit the Interim/Final Report in written form and send to NCKUH IRB office. The lastest application forms can be downloaded in its website (http://nckuhirb.med.ncku.edu.tw/)

Any changes or amendments to the project (including the project period), please submit an amendment application to NCKUH IRB within its approved period. Any changes or amendments in any other way will not be accepted. Before the approval of the amendment application, the project is carried out according to its previously approved plan.

For some reasons projects granted approval by NCKUH IRB couldn't be implemented, PI shall apply for suspension/termination.

During or after the project is completed, please report any unfavorable occurrence in a human study particant according to GCP.

Yours sincerely,
Ting-Tsung Chang M.D.
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E-mail:em73635@mail.hosp.ncku.edu.tw

Interim Report Approval

Date: 2020.10.27

Title: Efficacy of oropharyngeal myofunctional therapeutic training for obstructive sleep apnea patients after transoral robotic surgery

Protocol No/ IRB No: NCKUH-10902002/ A-BR-108-059

Period of Project: From 2019.11.28 to 2022.12.31

Period of Approval: From 2019.11.28 to 2021.11.27

Institute: National Cheng Kung University Hospital

Investigator: Dr. Cheng-Yu Lin (Department of Otolaryngology)

The Institutional Review Board of National Cheng Kung University Hospital (NCKUH) is organized and operated according to the laws and regulations of ICH-GCP and of Central Competent Authorities.

This project is reviewed and approved by NCKUH IRB in 2020.10.27. The period of approval is granted until 2021.11.27.

Regarding multi-period project, please submit the Interim Report before 2021.10.27. If the approval of the interim report is not granted on its expiry date, except safeguarding the health of the participants, the research is suspended.

Regarding completed project, the Final Report shall be submitted within three months of its approved expiry date. Except for the health of the participants, all the procedures of the project shall be terminated on its approved stated deadline.

If PI does not submit the Interim/Final Report on time, he/she will be recorded in the overdue list and received the suspension/ termination notice from NCKUH IRB. The overdue list will be reported to the IRB. After the resolution of the board meeting, NCKUH IRB will suspend all the new projects applied by PI until the Interim/Final Report is submitted.

Please submit the Interim/Final Report in written form and send to NCKUH IRB office. The lastest application forms can be downloaded in its website (http：// www.ncku.edu.tw/ ~nckuhirb)

Any changes or amendments to the project (including the project period), please submit an amendment application to NCKUH IRB within its approved period. Any changes or amendments in any other way will not be accepted. Before the approval of the amendment application, the project is carried out according to its previously approved plan.

For some reasons projects granted approval by NCKUH IRB couldn't be implemented, PI shall apply for suspension/termination.

During or after the project is completed, please report any unfavorable occurrence in a human study particant according to GCP.

國立成功大學醫學院附設醫院 第一人體研究倫理審查委員會

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Interim Report Approval

Date: 2021.10.26

Title: Efficacy of oropharyngeal myofunctional therapeutic training for obstructive sleep apnea patients after transoral robotic surgery

Protocol No/ IRB No: NCKUH-10902002/ A-BR-108-059

Period of Project: From 2019.11.28 to 2022.12.31

Period of Approval: From 2019.11.28 to 2022.11.27

Institute: National Cheng Kung University Hospital

Investigator: Dr. Cheng-Yu Lin (Department of Otolaryngology)

The Institutional Review Board of National Cheng Kung University Hospital (NCKUH) is organized and operated according to the laws and regulations of ICH-GCP and of Central Competent Authorities.

This project is reviewed and approved by NCKUH IRB in 2021.10.26. The period of approval is granted until 2022.11.27.

Regarding multi-period project, please submit the Interim Report before 2022.09.27. If the approval of the interim report is not granted on its expiry date, except safeguarding the health of the participants, the research is suspended.

Regarding completed project, the Final Report shall be submitted within three months of its approved expiry date. Except for the health of the participants, all the procedures of the project shall be terminated on its approved stated deadline.

If PI does not submit the Interim/Final Report on time, he/she will be recorded in the overdue list and received the suspension/ termination notice from NCKUH IRB. The overdue list will be reported to the IRB. After the resolution of the board meeting, NCKUH IRB will suspend all the new projects applied by PI until the Interim/Final Report is submitted.

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