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Cranio-spinal Neurosurgical Approaches: Qualitative and Quantitative Analysis and Validation of New Minimally Invasive Techniques on Cadaveric Anatomical Models

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TITLE

Cranio-spinal Neurosurgical Approaches: Qualitative and Quantitative Analysis and Validation of New Minimally Invasive Techniques on Cadaveric Anatomical Models.

Acronym: Neuro_SURGEM (Neurosurgical Simulation and Quantitative Evaluation Methods)

Promoter: Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy
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ABSTRACT

In recent years, the preclinical phase has become crucial for surgical research, as highlighted in the IDEAL framework (Idea, Development, Exploration, Assessment, Long-term study), which underscores the need for rigorous evaluation in the development of new surgical techniques (1-3). Our research focuses on the systematic analysis of different cranio-spinal surgical approaches, using an innovative quantification system (BrainChop software). This preclinical study is conducted at the "SURGEM" anatomical laboratory at the Catholic University of the Sacred Heart in Rome. The study spans 36 months and includes several stages of cadaveric dissection with the aim of obtaining:

1. Quantification methods of working volumes and exposed area;
2. Analysis of anatomical variants;
3. Anatomical simulations;
4. Validation of new instruments/techniques.

The goal of this study is to deepen, through laboratory simulations, cranial (craniotomy, macro and minimally invasive) and spinal approaches with particular emphasis on the quantification of working volume and exposed area, anatomical variant analysis, and validation of new techniques/instruments (14-24). Using anatomical specimens and a neuronavigation system, various surgical techniques will be simulated with different types of dedicated instruments. This study will also analyze vascular, nerve, and bone anatomical variants that may influence surgical outcomes and intraoperative management of anatomical anomalies. Tumor resections will be simulated, with the goal of analyzing in detail the surgical access trajectories and resection areas.

35 Anatomical specimens will be used, including the voluntary donation program of the Agostino Gemelli University Hospital IRCCS - Catholic University of the Sacred Heart, in compliance with Italian law. Dissections will be performed using neurosurgical instruments, and data will be cataloged and anonymized, with proper storage.

This research aims to improve the understanding and effectiveness of cranio-spinal surgical approaches, promoting continuous innovation in surgical techniques. At the end of the three-year project, we expect not only to provide a detailed and quantitative analysis but also to make a significant contribution to the scientific literature in surgery and neurosurgery.

INTRODUCTION

BACKGROUND

In recent years, the preclinical phase of research in surgery has been recognized as a critical moment for the development of new techniques and surgical approaches. The IDEAL framework (Idea, Development, Exploration, Assessment, Long-term study) represents a reference model for describing the various phases of surgical research, highlighting the importance of preclinical evaluation both in the development and validation of new surgical approaches (1–3).

In Italy, the Law Number. 10 of February 10, 2020, introduced specific regulations concerning the donation of one's body and tissues post-mortem for study, training, and scientific research purposes, limited to those who have given their consent during their lifetime. The use of the human body or post-mortem tissues is governed by the principles of solidarity and proportionality, and regulated in a way that ensures respect for the dignity of the human body. This law has enabled the Fondazione Policlinico Universitario Agostino Gemelli to expand its study, training, and research activities, including the possibility of accepting body and tissue donations from individuals who have consented during their lifetime, thus contributing to the advancement of medicine and biotechnology.

The anatomical laboratory provides a controlled environment, ideal for simulating surgical procedures, allowing the analysis of multiple variables that influence the effectiveness of the procedure and cannot be controlled in clinical practice (4–14). Recently, the Principal Investigator (PI) developed, in collaboration with the University of Toronto, a navigation system that allows for the quantification of the workspace to define a specific surgical approach (14–19). This new method has been used in several anatomy laboratories, including those at the Universities of Brescia, Toronto, and Geneva, to conduct comparative quantitative studies on various neurosurgical, otolaryngological, and skull base surgery approaches. Some of the results obtained have been published in international scientific journals (14–24).

Objective

The main objective of this study is to conduct a preclinical and systematic analysis of the various cranial and spinal surgical approaches to evaluate their potential and limitations in an objective manner. Attention will be particularly focused on the study of skull base approaches, spinal approaches, quantitative studies, exploration of anatomical variations, and the validation of new surgical approaches and related instruments.

Endpoints

Primary Endpoints:

1. Quantification of Work Volume and Exposed Area in Cranio-Spinal Surgical Approaches

Work volume represents the three-dimensional operative space created by each cranio-spinal surgical approach. Quantification will be performed using BrainChop imaging software on standardized CT scans. Segmentation will follow predefined protocols to ensure reproducibility. Higher values indicate a larger and more accessible operative corridor. Exposed area corresponds to the two-dimensional anatomical surface revealed by each surgical approach. Measurements will be obtained from CT-based reconstructions using the same standardized segmentation workflow. Higher surface values reflect wider surgical exposure.

Unit of Measure: cubic millimeters (mm^3) and square millimeter.

Time Frame: Measurements will be obtained twice with BrainChop software for each approach on every specimen: before the dissection using baseline CT imaging and after completing the approach using repeat CT imaging on the same day.

Secondary Endpoints:

1. Analysis of anatomical variations influencing surgical approaches.
2. Validation of new surgical instruments and techniques on cadaveric specimens.
3. Average operative time for each surgical approach: Determining the average time required to complete each type of surgery (macrosurgical, microsurgical) based on the adopted surgical approach. The analysis will focus on the duration of the intervention for each approach, comparing the relative efficiency of the techniques.
4. Assessment of the perceived difficulty by surgeons during the execution of surgical approaches: Collecting subjective evaluations on the difficulty of the procedure using a difficulty rating scale (e.g., Likert scale), considering factors such as familiarity with the technique, the anatomical complexity of the cadaver, and the ergonomics of the instruments used.
5. Assessment of the visibility of target anatomical structures through different visualization methods: Measuring the visibility of areas of anatomical interest using different visualization methods (macrosurgical, microsurgical). This endpoint will focus on the effectiveness of the different modes in providing clear visibility of critical anatomical structures during the surgical procedure.
6. Acceptability and feedback from surgeons on the use of new surgical techniques and instruments: Gathering feedback from participating surgeons on the new instruments and surgical techniques, evaluating their experience in terms of comfort, ergonomics, ease of use, and ease of learning the techniques employed during the simulation.
7. Effectiveness of dissection and surgical training courses: Measuring the effectiveness of dissection and hands-on training courses using cadaveric specimens, through pre- and post-training tests. This endpoint will focus on the improvement of participants' technical skills, with particular attention to their ability to apply the new surgical techniques learned during the simulations.

Methodology

Study Design

This study is a monocentric, observational, non-profit study that will be conducted on cadaveric anatomical specimens. No drugs or medical devices will be used on human subjects. The study will have a duration of 36 months and will begin after approval from the ethics committee.

The study will be divided into three distinct phases:

- **First and Second Year:** The main objective will be the quantitative analysis of the different surgical approaches. This will be accomplished using the innovative research method already applied by the Principal Investigator (PI) for the preclinical study of skull base surgical approaches.
- **Third Year:** The focus will be on macroscopically and microscopically visualized skull base and spinal approaches. Quantitative analyses will be conducted, relevant anatomical variations will be explored, and new surgical approaches and related instruments will be validated.

Setting

The anatomical dissections will be performed at the SURGEM Laboratory (located in the Settorian Room of the Institute of Pathological Anatomy at the Catholic University of the Sacred Heart in Rome). Recruitment of specimens began on 15/10/2025 and will continue throughout the study, which is expected to last for three years. The dissections, data collection, and analysis will be carried out continuously during this period.

Procedure

The anatomical specimens will be sourced from the Catholic University of the Sacred Heart's voluntary donation program and the Science Care Program. Sixty percent of the specimens will undergo specific preparations, including arterial and/or venous injections with silicone, consisting of a base and catalyst (Xiameter®, Midland, MI, USA) and colored with Pintasol® (Mixol® Red E-L3mix, Kirchheim unter Teck, Germany). The specimens will undergo high-resolution CT scans, and the DICOM images will be imported into a dedicated neuronavigation system (GTx-Eyes II Approach Viewer, University Health Network, University of Toronto, Toronto, Ontario, Canada). In some cases, CT scans will be repeated after dissection, and new calculations will be made using the neuronavigation software.

CT scans will be performed at the Institute of Forensic Medicine at the Catholic University of the Sacred Heart. The source of the specimens will be tracked and recorded, including:

- Voluntary donation program at the Catholic University of the Sacred Heart, Rome, Italy, in accordance with Italian law (LAW 10 February 2020, No. 10 and DECREE OF THE PRESIDENT OF THE REPUBLIC 10 February 2023, No. 47);
- Science Care, USA.

The dissections will be performed using neuro-surgical instruments specific for skull base surgery available at the SURGEM laboratory:

- Complete set of Rhoton dissectors (Rhoton Micro Dissector).
- Complete set for skull base surgery (Karl Storz®, Germany).

- Zeiss microscope (UCSC 119473).

The specimens will be cataloged according to their source, and anonymized data provided by the donor centers will be entered into a database. Proper storage of the specimens will take place at the Institute of Pathological Anatomy (Head: Dr. Vincenzo Arena) at the Catholic University of the Sacred Heart. Non-fixed specimens will be stored frozen at -20°C in dedicated freezers, while fixed specimens (with formalin) will be stored at 4°C in a solution (formaldehyde, glycerol, alcohol reagent, and water).

Variables

The approaches will be performed in a modular manner, from the least invasive to the most extensive. Various surgical approaches will be simulated using surgical instruments dedicated to skull base surgery, spinal surgery, and in both macrosurgical and microsurgical visualization modes.

The quantification of the working volume and the exposed area for each surgical approach will be calculated with an open-source software (BrainChop) on the CT scans of the specimens obtained before and after surgical dissection. For each specimen's CT scan, the area of interest exposed by the different approaches to be compared will be outlined using the BrainChop software (14-24).

Error and Control

To minimize potential sources of error, rigorous control methodologies will be implemented during data collection. Each analysis will be repeated multiple times to ensure the accuracy of the results.

Sample Definition

Given the descriptive nature of the study, a formal sample size determination is not required. However, we estimate that 35 cadavers will be enrolled over the three-year period.

Statistical Analysis

Quantitative variables will be summarized as means and standard deviations, while qualitative variables will be reported as absolute and relative frequencies (percentages). The effectiveness of the training will be evaluated by testing the mean difference of scores obtained in tests administered before and after the training, using the paired Student’s t-test or the Wilcoxon test.

The difference in execution times between different techniques will be tested using ANOVA or the Kruskal-Wallis test. Linear models with random intercepts will be used to compare surgical volumes and exposed areas. A 95% confidence interval will be estimated using the bootstrap resampling method.

Results with $p<0.05$ will be considered statistically significant. Statistical analysis will be performed using STATA software (StataCorp® LLC, College Station, TX, USA).

Ethical Issues and Informed Consent

The study will be conducted in accordance with the protocol. No new informed consent will be required from the donor's family, as each donor has already provided written informed consent for the use of their body in medical research prior to death. Regarding donors, the Institute of Pathological Anatomy provides adequate counseling to the families, informing them about the use of the body and the studies to be conducted.

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