

**„VICTOR BABEȘ” UNIVERSITY OF  
MEDICINE AND PHARMACY FROM TIMIȘOARA  
DOCTORAL SCHOOL  
MEDICINE DOMAIN**



# **HABILITATION THESIS**

**INNOVATIVE AND TRANSDISCIPLINARY  
APPROACHES IN ENT SURGERY**

## **A B S T R A C T**

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## **ABSTRACT**

The habilitation thesis, titled "ENT Surgery: Innovative and Transdisciplinary Approaches," represents a synthesis of my scientific, professional, and academic activities conducted during the period from 2002 to 2023, following the defense of my doctoral thesis, "Modern Diagnostic Criteria (Histopathological and Imaging) for Laterocervical Lymphnode Metastasis in Head and Throat Cancer". An academic didactic career within the medical field entails the harmonious integration of roles as a dedicated physician, an educator of future medical professionals, and a pioneer in advancing medical sciences. Mastering this triumvirate of excellence poses a challenge for anyone aspiring to such a career. The structuring of this thesis adheres to the recommendations provided by the National Council for Attestation of University Titles, Diplomas, and Certificates (CNATDCU) and follows the methodology of the Doctoral School at the "Victor Babeș" University of Medicine and Pharmacy in Timișoara.

The thesis is divided into three sections, encompassing an overview of my personal professional, academic, and scientific contributions, a discussion of scientific achievements, and an exploration of future development perspectives within the scientific, professional, and academic domains. In 1991, I attained the position of Junior Teaching Assistant through a competitive selection process, followed by progression to the roles of University Assistant in 1993, Lecturer in 2014, and, as of 2021, Assistant Professor at the University of Medicine and Pharmacy "Victor Babeș" Timișoara, specifically within the Faculty of Medicine and the ENT Discipline.

Over the course of 28 years, I have been actively involved in teaching within the ENT Discipline, conducting teaching activities, providing guidance during clinical internships, and offering practical demonstrations in the field of ENT Pathology. Additionally, I have contributed significantly to the training of resident doctors. In our efforts to develop and support clinical courses and internships, we have diligently maintained high-quality lecture standards, ensuring the seriousness and competence

of our presentations. We have also been committed to continuously updating and disseminating information to students and resident doctors.

Our didactical approach is rooted in sustained interaction between teaching staff and students, as well as teaching staff and resident doctors. In the transmission of clinical information, we employ teaching methods centered on solving real and concrete situations, encompassing problem-based learning and case studies. Ultimately, our goal is to equip students with the essential ENT examination techniques required by every practicing physician, including the ability to perform a correct ENT examination, conduct diagnostic patient evaluations, establish positive and differential diagnoses, determine therapeutic objectives, and apply ENT medical-surgical treatments.

In 1988, I achieved the designation of Senior Specialist ENT Doctor, as per Minister of Health Order No. 694 of 03/12/1998, at the Clinical Municipal Hospital of Timișoara, ENT Clinic. From 1991 to 2005, I served as a secondary doctor, specialist, and primary ENT specialist within the Timișoara Municipal Clinical Hospital, ENT Clinic. In 2005, I assumed the position of Clinic Head at the Pediatric ENT Clinic "Bega" of the Emergency County Clinical Hospital No. 1 Timisoara. During the period in which I was active at at the ENT Clinic of the Timișoara Municipal Clinical Hospital, I actively contributed to the implementation of modern surgical methods with diagnostic and therapeutic applications, including rigid naso-sinus endoscopy, flexible naso-pharyngolaryngeal endoscopy, and laryngeal, oropharyngeal, and nasal CO2 laser surgery.

I would like to emphasize my experience in ENT endocavitary surgery, supported by an extensive case report. This report specifically delves into endoscopic surgery for various laryngeal pathologies, including benign and malignant tumors, contact ulcers, juvenile and adult laryngeal papillomatosis, chronic laryngitis, posttraumatic laryngeal stenosis, and Gerhard syndrome.

The primary focus of my surgical practice has been oncological pathology within the ENT field. I have dealt with increasingly complex oncological cases by expanding the scope of operative procedures. These procedures have been applied to malignant tumors located in the nose, paranasal sinuses, oropharynx, parapharyngeal space, parotid gland, ear, and cervical adenopathies. This expansion has included techniques such as "functional neck dissection" and "radical neck dissection."

Laryngeal cancer has been a prominent area of interest for our ENT Clinic's scientific research efforts. We have strived to deepen our understanding of laryngeal tumor pathology, with the findings having direct and immediate applicability in the field of oncological surgery.

My involvement with specialists in the field of ENT Pediatrics, as demonstrated by my participation in all European Society of ENT Pediatrics (ESPO) congresses since 2006, inspired me to initiate the establishment and organization of the Romanian Society of ENT Pediatrics.

As a Founding Member and the President of the Romanian Society of ENT Pediatrics since 2007, I have successfully organized five national and international medical scientific events. These events have borne the banner of both the Romanian Society of ENT Pediatrics and the University of Medicine and Pharmacy "Victor Babeș" in Timișoara.

The recognition of my scientific and academic achievements inherently acknowledges the contributions of my mentors, as well as the institutions where I have dedicated my entire career, including the University of Medicine and Pharmacy "Victor Babeș" Timisoara, Faculty of Medicine, ENT Discipline, Clinical Municipal Hospital of Timisoara, ENT Clinic, and the Pediatric ENT Clinic "Bega."

In this context, the establishment of the Romanian Society of ENT Pediatrics in 2007, my election as President of the Romanian Pediatric ENT Society since 2007, the successful organization of the First National Congress of ENT Pediatrics with international participation in Timisoara from September 21-24, 2011, my election as a Member of the Council of the European Pediatric ENT Society (ESPO), and my election as a Member of the Board of the European Society of ENT Pediatrics, representing Eastern Europe from 2021 to the present, all stand as prestigious international acknowledgments of the value of the Timisoara ENT school.

Furthermore, my research contributions can be exemplified by the publication of numerous articles. To date, I have authored or co-authored 210 scientific reports. Among these, 77 have been published in full, and 143 in abstract books (including 116 in international abstract books and 27 in national abstract books).

I have also published 35 articles in prestigious journals indexed by Thomson ISI, including 12 as the lead author and 9 as a co-author. Additionally, I have contributed 3 ISI proceedings articles as the lead author and 11 as a co-author. These journals include the International Journal of Pediatric Otorhinolaryngology, Int

J Mol Sci., BMC Neurology, Pathogens, and Experimental and Therapeutic Medicine.

Furthermore, I have published an additional 57 articles in journals indexed in international and national databases, such as European Archives of Oto-Rhino-Laryngology and Head & Neck, Rhinology, Laryngo-Rhino-Otologie, Otolaryngology Head Neck Surgery, and The Journal of International Advanced Otology.

Throughout the years, I have delivered over 200 presentations and lectures at various ENT national and international conferences. I have been invited to speak at different symposia and have participated in numerous postgraduate and continuing medical education courses within the field of ENT.

Additionally, I have authored or co-authored 20 book chapters, including those featured in textbooks for students and residents. Some notable examples include:

- "XII Manual of the Argentine Association of ENT and Pediatric Phonoaudiology," where I contributed a key lecture on "Endoscopic Sinus Surgery in Children," pages 127-134.
- "CT Imaging in Rhinology," edited by Vlad Budu, in which I wrote Chapter 10, titled "Pediatric Rhinological Pathology." This book, published by Callisto Publishers in 2020, spans 258 pages and features ISBN 978-606-8043-44-9.

In 2002, I successfully obtained a doctoral degree in medicine by defending my thesis titled "Modern Diagnostic Criteria (Histopathological and Imaging) of Laterocervical Lymphnode Metastasis from Head and Throat Cancer" within the field of ENT at the "Victor Babeș" University of Medicine and Pharmacy in Timișoara, under the supervision of Prof. Dr. Ion Marin.

Throughout my doctoral studies and beyond, I have incorporated imaging and histopathological information into my surgical practice. This integration has played a crucial role in the staging, treatment planning, and postoperative monitoring of patients with head and neck cancer.

The primary conclusion drawn from my research is that all valid clinical and paraclinical data obtained before initiating treatment can be used for clinical staging. Consequently, I recommend supplementing clinical examinations with CT scans, MRI, endoscopy, or biopsies for accurate staging before commencing therapeutic procedures. This recommendation is rooted in the understanding that

underestimating the tumor stage can result in inadequate treatment, emphasizing the critical importance of precise staging.

A significant portion of my scientific activity has been dedicated to the investigation of laryngeal and nasopharyngeal tumor pathologies. The overarching objective has been to enhance patient care through the refinement of existing surgical techniques and the introduction of innovative ones. Moreover, I have prioritized interdisciplinary collaboration with specialties such as histology, immunology, neurology, endocrinology, genetics, and molecular biology.

One noteworthy study in this domain is the reference work titled "Clinical, Ultrasound, and Histopathological Correlation of Clinically N0 Neck Nodes in Patients with Cancers of the Pharynx and Larynx." In this study, I proposed the evaluation of ultrasonography's role in diagnosing cervical lymph node metastases in patients with pharyngeal and laryngeal cancer, especially when clinical examination did not reveal adenopathy (N0). The study involved comparing palpation, neck ultrasonography (US), and histopathological examinations in these patients. The results indicated that palpation is an inaccurate method for detecting lymph node involvement in head and neck patients, heavily dependent on the surgeon's experience. Neck US emerged as a cost-effective, reliable, and well-tolerated method for investigating cervical lymph node involvement, both for diagnostic and follow-up purposes. Histopathological and immunohistochemical examinations were identified as crucial methods for positive and differential diagnoses, as well as prognosis assessment.

Another study, included in the same area, titled "Histopathological Prognostic and Risk Factors in Patients with Laryngeal Neoplasms," revealed results that support the conclusion that histopathological examination provides valuable information regarding the prognosis of laryngeal neoplasms. Factors such as the grade of differentiation, inflammatory reaction, and tissue invasion were identified as the main prognostic factors for laryngeal neoplasms.

In a complex and comprehensive study related to the etiology of oropharyngeal squamous cell carcinoma (OPSCC) titled "HPV and Other Risk Factors Involved in Pharyngeal Neoplasm: Clinical and Morphopathological Correlations in the Southwestern Region of Romania," I conducted research to assess the association between different environmental risk factors and the presence or absence of HPV and p16INK4a in various tumors from this region.

Chronic smoking, alcohol consumption, or urban origin may contribute to the development of oropharyngeal tumors. However, the presence of HPV was more frequently associated with malignant tumor transformation and diagnosis at advanced stages. Further studies are required to clarify the role of HPV in tumor onset, progression, or enhancement, as the risk factors are often intricate.

HPV positivity markers exhibited a high expression rate in advanced stages, suggesting a rapid growth rate, as supported by the Ki67 index, which increased proportionally to anti-HPV and anti-p16 immunomarking.

The presence of HPV serves as a prognostic factor for overall survival and a predictive marker for response to post-interventional treatment. Additionally, the immunoreaction for p16 can be employed as a surrogate marker for HPV involvement in exposed tissues. Combining anti-HPV, anti-p16, and Ki67 immunomarking in the primary diagnosis of OPSCC may provide options for selecting the most suitable therapeutic approach, potentially minimizing the need for extensive surgery, especially for advanced cancers.

Our results endorse the implementation of strategies for OPSCC prevention and early diagnosis. These findings can serve as a foundation for future studies aimed at adapting surgical and oncological treatments based on HPV staging to achieve better therapeutic outcomes.

Furthermore, I have engaged in intriguing research with valuable results for the prognostic process and therapeutic direction, particularly focusing on benign tumors like juvenile nasopharyngeal angiofibroma and middle ear cholesteatoma.

In the study titled "Juvenile Nasopharyngeal Angiofibroma: Timisoara ENT Department's Experience," I highlight the intricacies of surgical treatment and outline the criteria and stages for making the correct therapy choice. Managing juvenile nasopharyngeal angiofibroma presents challenges for ENT surgeons. As the most frequent benign tumor in the rhinopharynx, JNA exhibits a significant potential for local invasion and carries a poor prognosis when treated inadequately. The choice of surgical approach remains a subject of debate, but surgery remains the preferred treatment, aiming for complete tumor resection. Various surgical methods, including transpalatal, transpharyngeal, Denker approach, medial maxillectomy, transfacial through lateral rhinotomy, midfacial degloving, Le Fort I osteotomy, infratemporal, and subtemporal lateral approaches, are traditionally employed for JNA removal. In

our series, the Denker-Rouge technique was the most commonly used for primary surgery, with recurrences being operated on using the paralateronasal technique.

In a study dedicated to middle ear cholesteatoma titled "High-Resolution Computed Tomography in Middle Ear Cholesteatoma: How Much Do We Need It?" we have continued to enhance medical care by introducing new techniques in collaboration with other medical branches, such as high-resolution computed tomography (HRCT). A comparison of HRCT findings with intraoperative observations revealed a strong correlation for tegmen tympani erosion, sigmoid plate erosion, scutum and malleus erosion, and a moderate-to-good correlation for lateral semicircular canal erosion, incus and stapes erosion, and fallopian canal erosion. In conclusion, HRCT is a valuable tool for preoperative cholesteatoma assessment, aiding in surgical decision-making. It can accurately predict the extent of the disease and is useful for detecting potential risks. However, it is less accurate in detecting fallopian canal and stapes erosion.

Another aspect of my scientific activity related to the field of pediatric ENT involved research on hearing loss, endoscopic sinus surgery in children, surgery for genetic and acquired ORL malformations, and ENT complications in genetic diseases such as cystic fibrosis. We have approached malformations such as choanal imperforation using modern methods, where nasal endoscopy played a crucial role in both performing the intervention and postoperative follow-up for these children.

I achieved remarkable results in the field of sinus pathology by contributing to the understanding of sinus mechanisms in allergies. In the study titled "Allergic Rhinitis Associated with Nasal Polyps and Rhinosinusitis - Histopathological and Immunohistochemical Study," initiated to identify new biomarkers in allergic rhinitis (AR), the obtained results revealed significant changes in the rhinosinusal mucosa of patients with AR.

At the level of the covering epithelium, we observed the reduction or disappearance of cilia from the pseudostratified epithelium, widening of intercellular spaces, a tendency toward squamous metaplasia of the epithelium, thickening of the basal membrane, and even necrosis and epithelial erosions. These microscopic changes indicate a significant alteration in the barrier function of the covering epithelium, allowing pathogens and allergens to penetrate deep into the rhinosinusal



mucosa, thereby inducing a local inflammatory process responsible for clinical symptoms.

Regarding my future activities in scientific research, I intend to further develop existing fields, such as:

- Introducing new minimally invasive surgical techniques, including laser therapy, ultrasound, transoral robotic surgery, and robotic surgery, while studying their extension to a wider range of ENT pathologies. An important aspect of these studies will focus on postoperative recovery with minimal side effects.
- Incorporating new parameters with biomarker value (including imaging, histopathological, immunological, genetic) for diagnosing, guiding treatment, monitoring therapy, and predicting outcomes for major ENT pathologies.
- Exploring the role of the microbiome in pediatric pathology (including otitis, sinusitis, and pharyngotonsillitis).
- Enhancing cross-border scientific collaboration with Serbia (Nis, Belgrade), Bulgaria (Varna), and Hungary (Szeged, Budapest) within ENT clinics.

Simultaneously, I aim to introduce and develop new research directions, such as:

- Investigating methods to regenerate damaged facial tissues, particularly in the context of facial plastic and reconstructive surgery. This involves utilizing intraoperative navigation systems and non-surgical treatments like laser therapy, ultrasound, 3D printing, and injectable materials to achieve natural-looking results with reduced downtime.
- Implementing precision medicine to tailor treatments based on individual patients' genetic profiles, medical histories, and lifestyles. This approach will utilize genetic, molecular, and clinical data to design targeted treatments with better outcomes and fewer side effects, benefiting conditions such as head and neck cancers, sinus disorders, and hearing loss.

- Researching the development of a new methodology for early vestibular diagnostics, as many congenital or perinatally acquired vestibular diseases remain unidentified and are often misinterpreted as specific neuro-motor or neurological pathologies, leading to inadequate treatment.
- Promoting a multidisciplinary approach to all ENT pathologies. Given the significant advancements in research and technology, ENT increasingly intersects with borderline pathologies (otoneurology, neurosurgery, vascular and cervical surgery, rhino-neurology), necessitating multidisciplinary teams. Monoprofile hospitals are no longer sufficient in otolaryngology, where specialists care for both children and adults with acute and chronic conditions, often requiring collaboration with other medical specialties. Examples include interdisciplinary management in ENT + Neurosurgery for pituitary gland and skull base tumor pathologies, and ENT + Immunology and Molecular Biology for rhinosinusitis and allergies.

Furthermore, building on the positive experience gained from participation in the "National Program for the Treatment of Deafness through Implantable Auditory Prostheses - Cochlear Implant," and focusing on a modern-based approach to malformative pathology, we emphasize reconstructive techniques and improved postoperative recovery.

Being part of the academic community at "Victor Babeș" University of Medicine and Pharmacy of Timișoara entails a special responsibility to maintain and elevate academic standards, translating into excellence in the roles of a doctor, professor, and researcher. This responsibility extends to both those who have trained us, our teachers and mentors, as well as those we train – students, residents, and young doctors.

In this context, the fact that the learning process never ceases for a doctor must be complemented by a continuous commitment to acquiring and applying new procedures, treatments, and techniques. Consequently, I am dedicated to providing cutting-edge and high-quality clinical care for all ear, nose, and throat conditions, training future leaders in Otolaryngology, and fostering research perspectives that will lead to new treatments for ENT patients.

## LIST OF 10 REPRESENTATIVE SCIENTIFIC PAPERS

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6. Raluca Tudor, **Gheorghe Iovanescu**, Daniela Reisz, Amalia Cornea, Cristina Potre-Oncu, Adrian Tutelca, Mihaela Simu Additional factors to correlate with a more than 30% NIHSS score improvement in patients 7 days after fibrinolytic and/or endovascular treatment for ischemic stroke, *BMC Neurol* 20, 417 (**2020**). ISSN: 1471-2377  
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7. **Gheorghe Iovanescu**, F. Barsesteanu, Veronica Madalina Manole, A. Apostol, E.H. Stefanescu, V.A. Budu, Flavia Baderca, Simona Corina Trifu, Carmen Aurelia Mogoanta, Diana Camelia Bonte, Mihaela Viviana IvanClinical, ultrasound and histopathological correlation of clinically N0 neck nodes in patients with cancers of the pharynx and larynx, *Rom J Morphol Embryol* **2020**, 61(2):433–439, ISSN (print) 1220–0522, ISSN (online) 2066–8279 doi: 10.47162/RJME.61.2.12  
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