



**TITU MAIORESCU UNIVERSITY OF BUCHAREST  
DOCTORAL SCHOOL IN MEDICINE**

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**CONTRIBUTIONS TO THE DEVELOPMENT OF  
HEPATOBIILIARY, COLORECTAL, AND DIGESTIVE  
ONCOLOGY SURGERY: FROM MANAGEMENT  
ALGORITHMS TO MULTIDISCIPLINARY  
APPROACHES AND THE OPTIMIZATION OF  
POSTOPERATIVE OUTCOMES**

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**ABSTRACT OF THE HABILITATION THESIS**

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## ABSTRACT

This habilitation thesis summarizes the scientific, professional, and academic achievements accumulated since the public defense of the doctoral dissertation in 2018, at the “Carol Davila” University of Medicine and Pharmacy in Bucharest (IOSUD), and sets out a plan for my career development with a view to obtaining the habilitation certificate and the right to supervise doctoral dissertations. The document is structured around three main research areas, prioritized in relation to my core expertise as a general surgeon with a primary focus on digestive oncology surgery, hepatobiliary-pancreatic (HBP) surgery, and minimally as well as abdominal parietal defects performed using minimally invasive techniques; and a strongly interdisciplinary area, linking my surgical experience with fields involving immuno-inflammation in surgery (the study of sepsis and septic shock mechanisms) as well as onco-immunological inflammation.

**The main research area—gastrointestinal and hepatobiliary-pancreatic oncological surgery—**forms the core of the thesis and constitutes the largest portion of the work. The central thesis I propose is that **the surgical outcome depends not only on the lesion itself but also, decisively, on the level of expertise of the center where it is treated.** This area is presented in layers, in order of its proportion within my current professional practice.

Within this first area, **iatrogenic biliary tract injuries during laparoscopic cholecystectomy** constitute the main subtopic, in which I am the first author of a 12-year multicenter study involving 108 patients selected from 16,559 cholecystectomies. The results confirm an incidence of 0.65%, comparable to the international threshold of 0.5%; intraoperative recognition of only 30.2% of the injuries, with severity not accelerating diagnosis ( $p = 0.796$ ); the association of a vascular injury in 19% of cases, with an increased risk proportional to proximity to the biliary convergence ( $p = 0.01$ ); the study enabled the development of a proprietary decision-making algorithm for managing these complications, based on various classifications into severity groups, which corrects older decision-making systems based on the inability of the Neuhaus, and Strasberg-Bismuth classifications to account for vascular lesions; and, crucially, the demonstration that repair at the center where the injury occurred is associated with a significantly worse prognosis ( $OR = 7.0$ ; 95% CI 2.5–19.6;  $p < 0.01$ ), structurally explained by the limited technical repertoire—restricted to two procedures—at centers lacking expertise. The central output of the research is a decision algorithm with five decision points, based primarily on the Strasberg classification.

**Reconstructive hepatobiliary surgery** is another distinct subtopic of the first research direction, arising from surgery for iatrogenic lesions, trauma, and oncological resection in hepatobiliary-pancreatic surgery. The conceptual contribution lies in the formulation of the four technical determinants of anastomotic success—stump vascularization, anastomotic tension, transanastomotic pressure regime, and suture gauge—and in the rational prioritization of reconstructive procedures based on the number of conditions each satisfies. **Colorectal and Proctological Surgery** presents a case series of 10,940 patients with hemorrhoidal disease, featuring a tiered therapeutic algorithm, the identification of the risk of stenosis associated with the use of high-energy electrosurgical platforms (8.3% vs. 1.8%) and an incidental colorectal cancer detection rate of 3.1%; this study also validates a gastropexy technique that reduces postoperative gastroparesis following right hemicolectomy for cancer from 38.7% to 12.1% ( $p = 0.014$ ).

**Liver resection in metastatic disease** demonstrates the benefit of tumor-reducing hepatectomy in refractory GIST metastases at 31 months of systemic therapy (overall survival of 55 months, with a postoperative benefit of 25 months) and confirms, through propensity score analysis and virtual cohort analysis, the superiority of resection in neuroendocrine metastases (52 vs. 31 months;  $p < 0.001$ ).

**Severe liver trauma** validates the staged strategy in AAST Grade V trauma with porto-biliary avulsion.

**The second research focus of my career**—perioperative optimization, ERAS protocols, anesthetic management, and metabolic-nutritional support—extends the surgical core to the entire patient-centered care pathway: adapting the principles of enhanced recovery to proctological and digestive surgery, the safety of deep sedation in complex endoscopic procedures (an institutional series of 700 patients), anesthetic management of pheochromocytoma, and the impact of anesthetic techniques on antitumor immunity, demonstrating the preservation of *natural killer* cell cytotoxicity through epidural analgesia (12% decline vs. 24%;  $p = 0.007$ ).

**The third research area** focuses on concepts such as surgical immunoinflammation, ranging from sepsis to the onco-immunological interface. The studies conducted provide the pathophysiological basis for the first two areas, integrating the analysis of the molecular mechanisms of septic shock, studies on immunomodulation induced by Bruton's tyrosine kinase inhibitors in chronic lymphocytic leukemia, the theoretical framework for the IL-

4/Brentuximab Vedotin combination in *mycosis fungoides*, the immunological evaluation of recurrent spontaneous abortion, and research on infection in immunocompromised hosts.

My scientific and research achievements are complemented by translational and interdisciplinary contributions—the *in vivo* evaluation of Mg–1Ca bioresorbable implants and the development of a myoelectric forearm prosthesis—based on my complementary training in the field of biomaterials (studies culminating in a master’s degree from the Polytechnic University of Bucharest, 2015).

Overall, my scientific portfolio comprises **44 ISI/JCR Web of Science-indexed articles**, of which **30 are indexed with a quantifiable impact factor - 17 as first author and 13 as co-author**, corresponding to a Hirsch index of 11; in addition, 7 more articles indexed in the JCR ISI Web of Science in conference proceedings and scientific event volumes, 2 abstracts indexed in Web of Science; 29 books published by national publishers; 33 articles indexed in international databases other than Web of Science. This publishing activity is complemented by experience as a reviewer for Web of Science-indexed journals, with a total of 93 reviews, 33 of which are visible on Publons (Web of Science).