Habilitation Thesis Summary

(The experience of a surgical team over the last ten years)

According to the recommendations, in my doctoral thesis I should present my post-doctoral in my professional and academic research activities. Since my main preoccupation has been the practice of general surgery in the Cantacuzino Hospital for over twenty-five years, all my scientific and academic concerns are indissolubly linked to this professional practice. Moreover, surgical practice and the teaching process with students, but especially with residents and young surgeons, are constantly interwoven with my everyday activities. Along with daily surgical and didactic work, I have been concerned with the amount of free time (and always at the expense of my family) to document myself in order to progress professionally and to be able to communicate my observations and professional experience, be it in papers published in journals or treatises or be it at professional events. Didactic activity also requires an almost continuous effort to be informed, an effort to synthesize, to express publicly or in writing the knowledge necessary for the teaching of others. Not to the extent that I wanted to, and without having where to learn from, I tried to address some research themes also related to surgical pathology. These themes will be presented below mainly in terms of quantity but also ordered by the main aspects of pathology that I have encountered in my surgical practice.

This was the initial plan of the thesis, but I realized that all my so-called achievements are in fact the work of a team that I tried to gather around me. This team of colleagues of different ages worked with me both on the elaboration and presentation of scientific papers and on teaching activities both with students and with residents, and especially on all the surgical interventions carried out during these ten years. So, in the following, I will present my work in this context. The results of this work remain to be assessed by the reader; I personally believe that at the present time each of

my younger colleagues has the ability to develop and present scientific papers, can carry out a practical and theoretical teaching process with students and residents, and can produce treatises, as they have demonstrated.

Throughout this period, we have tried to improve ourselves through participation in postgraduate courses and to acquire new professional skills, mostly in the country but also abroad. The most notable ones are: laparoscopic surgery, surgical oncology, hepatobiliopancreatic surgery, plastic surgery, echography and endoscopy. In our effort to tackle hepatic and pancreatic surgery, as well as oncological pelvic surgery, Dr. Sorin Petrea had, and still has, an important role in the team, seconded by Sorin Aldoescu whose surgical performance was improved permanently. The constant preoccupation of colleague Sorin Aldoescu with laparoscopic surgery has added value to the team by sucessfully tackling parietal, genital, bariatric and colic pathology.

Beyond my professional evolution in the past 10 years, I can not overlook my initial training in two prestigious clinics, that of Professor Pavel Simici, and that of Professor Ion Juvara, who, unfortunately, is no longer practicing. In these clinics, I had the chance to meet several people who helped me and who left a positive mark on me:

Professor Dan Radulescu, who stopped me in the clinic and thus I had the opportunity to meet one of the most fascinating minds, but getting close to him was not at all easy. I have the great satisfaction to have been with him in the wonderful hours of discussion outside of hospital hours, but also in the last and most unpleasant part of his life. I regret that I did not take more advantage of his presence.

Professor Corneliu Radu, from whom I learned how to handle instruments and who, with a great generosity, quite rare today, allowed me to operate some of his personal patients, obviously under his direct guidance or supervision. I became close to him to a great extent, or rather, as far as his constant anxiety over those around him allowed. Unfortunately - but of course - the last medical episodes of his old age we partook together.

Professor Ion Vereanu strongly supported me in my didactic promotion, probably because of my attriubutes, him being above all petty interests because of the moral aristocratic-type values that he stubbornly practices in this day and age. After his withdrawal from activity we remained - I dare to say - friends, keeping the distance imposed on us by our different ages. I believe our friendship was justified by the certain values that we share.

Professor Florian Popa, with whom I worked during my internship at Professor Simic's clinic and with whom I remained in a great relationship, gave me understanding and help, without reservations, whenever I encountered difficulties or needed advice or support. At some point during my internship, in the context of those times, there was an attempt to retain my services at the clinic run by Professor Simici, but unfortunately this was not possible at that time. It is paradoxical that I still consider myself as belonging to that collective, the explanation being Professor Popa's personality, but more exactly, how he managed to perpetuate that feeling of belonging in the "Pantelimon team".

Starting from the scientific and professional accumulations of the last ten years, I have described of the most important stages of my personal work and of the surgical team I co-ordinate. I have presented the experience gained in my post-doctoral period in chronological order and organized by themes on topics of interest both from a professional surgical perspective and from a scientific point of view. The most interesting aspects of the pathology that we have faced or tackled have been the subject of analysis, materialized in the form of scientific presentations at various events or published in specialized journals, some of which are mentioned in the thesis.

Scientific Activities

After sustaining my MD thesis with the theme **"Pericysto-jejuno-anastomosis in the Treatment of Hepatic Hydatid Cysts"**, carried out, under the guidance of the late Prof. Dr. Corneliu Dragomirescu, at the "Carol Davila" University of Medicine and Pharmacology in Bucharest, in 2002, I continued my academic, professional-surgical and research activities, managing, in 2006, to fulfill the

academic and research criteria necessary for promotion from the position of Assistant Professor to that of Associate Professor at the Cantacuzino Hospital surgery clinic.

My research activity quickly led to my participation in 4 research grants from the Romanian Academy, in two of them having been in the capacity of director (project co-ordinator):

- **Study of the parasiticidal effect of various substances used intraoperatively for the inactivation of hydatid cysts (2007-2008)**
- **Presometry and cutaneous thermometry, predictive factors for the occurrence and evolution of neuropathic ulcerations in the diabetic foot (2005-2007)**

In two other grants I was co-director of the project:

- **The significance of molecular mechanisms involved in HPV transformation for monitoring human cancers (2005-2006)**
- **Risk factors in the contraction of sexually transmitted diseases in adolescents (2003-2004)**

I was appointed as a **professional assessor for the Grants Commission of the Romanian Academy**.

I was the author or co-author of **82 scientific papers** presented at various national conferences and congresses on surgery and more.

I worked on and published as first author or co-author a total of 30 articles out of which:

- In **ISI indexed journals**: **12 articles**, (2 in progress)
- In **BDI, CNCSIS indexed journals: 26 articles** (6 emerging)

I am the **author of four specialized books**:

- **Small surgery, Medical Press, 2017**
- **Pericysto-jejuno-anastomosis in the Treatment of Hepatic Hydatid Cysts** Medical Press 2014

- **Practical surgery textbook – Tehnoplast Press, 2005**
- **Amputations of the thigh and calf in patients with chronic ischemia – Romanian Academy Press, 2004**

I am the author of 4 chapters and treatises after 2002. The most important and honorary journalistic contribution, entrusted to me by Professor Irinel Popescu, is the writing of two chapters: **Benign Biliary Stenosis, Biliary Fistulae** from the **Hepatobiliopancreatic Surgery and Liver Transplant Treatise** - **Romanian Academy Press, 2016**, chapters written together with Sorin Petrea, Eduard Catrina and Sorin Aldoescu.

Professional Surgical Activities

From the point of view of the professional surgical achievements, **in the last 10 years I have performed over 4200 surgical interventions**.

I have gone through all the stages of surgical training surrounded by several surgical personalities, but I do not wish to give myself any merit because of it or to consider myself as their successor. I have tried, within the limits of my ability, to apply what I learned from the masters I had the opportunity to meet and to go through the new era of minimally invasive surgery. With the accumulation of a surgical experience, I felt the need to broaden the range of oncological operations by enlarging and improving lymphadenectomy, by plurivisceral resections in advanced local cancers and by improving pancreatic resection techniques (duodenopancreatectomy, central pancreatectomy, spleen preservation). If these interventions were also practiced by the masters, hepatic resections represent a completely new chapter in surgery that I tackled together with the entire team.

For this, in the last three years, I have participated in postgraduate courses on surgical oncology and hepatobiliopancreatic surgery, having gained diplomas in these two fields of activity.

The preoccupation with biliar pathology has largely defined the activity of the clinic led by Professor Ion Juvara and his students. Until the onset of laparoscopic surgery, I had accumulated a satisfactory experience in biliary surgery, successfully practicing almost all types of interventions for biliary lithiasis, including early and late re-interventions. Minimally invasive surgery along with interventional endoscopy have greatly changed the way to treat this pathology. Laparoscopic cholecystectomy was the operation that imposed minimally invasive treatment for gastrointestinal surgery, and I participated from the beginning in an effort to learn the new surgical techniques. This beginning was in 1994, and since then I have accumulated sufficient experience in the laparoscopic surgery of biliary lithiasis, the number of these interventions currently surpassing 2,000 individual surgeries, with the total number of team surpassing 3,000 operations.

Fortunately, at present, not a single member of the team has ever recorded a main bile duct lesion. Perhaps the "legacy" of Professor Juvara's school has had a contribution here. Avoiding bile duct lesions in minimally invasive surgery has reopened discussions on this topic from open surgery. Particularities of minimally invasive surgery in the production of these lesions have been the subject of retrospective studies in which I participated. ("Injuries of the Extrahepatic Bile Ducts in Laparoscopic Surgery").

The difficulties of laparoscopic cholecystectomy, due to the acute or chronic inflammatory process, but especially due to previous interventions, have been another concern that has been the subject of presentations at national events.

We performed interventions for post-operative lesions of CBP either after open or laparoscopic surgery.

We have assisted in the transition from surgery to endoscopy in treatment of choledocytic lithiasis and biliary stenoses (see the papers: **"What has remained for the surgeon in bile duct lithiasis?", "Endoscopic treatment of CBP lithiasis"**)

As I have already stated, the most important journalistic contribution to this pathology is "**Benign Biliary Stenosis, Biliary Fistulae"** from the

“Hepatobiliopancreatic Surgery and Liver Transplant Treatise”, edited by Prof. Dr. Irinel Popescu.

We started practicing **hepatic resection surgery** in 2012. The beginning period was more difficult in terms of postoperative outcomes and the reluctance to change of my colleagues. In the present, analyzing the accumulated casuistry (96 hepatic resections) within three years, the results are comparable to those in the literature. Along with me, two colleagues have been very enthusiastic about the stages of the theoretical and practical training in hepatic and pancreatic surgery, Sorin Petrea and Sorin Aldoescu, forming a team with good experience in resection surgery as well as removing the liver for transplant.

The preoccupation with pancreatic surgery of the Cantacuzino Hospital team have been well known; the interest in this surgery has gradually diminished with the disappearance or withdrawal of our masters. Without having the pretention of rising to their performances from those times, we tried to tackle this surgery as well. My personal experience being modest, I turned again to my colleagues from Fundeni Hospital. Beyond the training courses, the friendship and collaboration with Dr. Vlad Braşoveanu was of real use. As a result of this collaboration, the percentage of curative interventions in neoplastic cephalopancreatic diseases increased from 10-15% before 2012 to more than 30% at present.

The interventions were performed for, both benign and malignant, pancreatic lesions, as well as combined interventions for multi-organ resections on neighbouring cancers. Thus, in 5 cases, right collectomy and cephalic duodenopancreatectomy were combined to treat invasive ascending colon tumors in the duodenum. In 13 cases, splenopancreatectomies were combined with colonic or gastric resections for neoplasms which had developed in these gastrointestinal segments.

To treat pancreatic insulinomas we have diversified the range of therapeutic solutions. Besides enucleation, subtotal or caudal pancreatectomy, we have practiced central pancreatectomy and pancreatectomy with spleen preservation.

Increasing the volume of interventions for this pathology also led to an increase in postoperative success, with postoperative morbidity having decreased, as well as postoperative mortality which at this time is at a level comparable to that of specialized centres.

The complexity of the interventions has increased progressively, having, this year, performed within the department the first pancreatic resection combined with a segmental resection of the portal vein with TT anastomosis, for a cephalopancreatic tumor with venous vascular invasion. Also, the number of oncologic pancreatic interventions or with a pancreatic coaffection has increased significantly over the past two years, with almost three quarters of the total interventions being performed over the past two years. The number of patients with this pathology is on a rising trend from 20 in 2013 to 45 in 2016, and in the first months of 2017, 8 duodenopancreatectomies have been performed.

Another preoccupation was **multi-organ surgery for the treatment of locally invasive cancers** that has imposed itself in recent years as an acceptable solution for extending the lives of patients. We have adopted this more "aggressive" attitude in the last 3 years in the case of tumors with pelvic localization with gastrointestinal or genital origin, practicing different types of pelvectomy. Another concern has been gastrointestinal cancer with different localizations that had invaded neighboring organs, and lately, the synchronous treatment of colonic cancers and hepatic metastases.

The approach to this type of complex surgery for pelvic cancer, considered "outdated", was a serious challenge in the context in which the traditional attitude of the profession is abstenence. The approach to this aggressive surgery involves a large surgical effort with mixed teams and is followed by morbidity and mortality not at all encouraging even in large centres. The results and efforts of building a multidisciplinary team make us look optimistically towards also tackling these complex cases in the future. A real gain for us was learning the surgical techniques of external urinary diversion after the operations that also lifted the urinary bladder. Initially, this was performed by our urology colleagues but ultimately we managed to perform these ourselves.

Stomach surgery was one of the preoccupations of the Juvara Clinic, a testimony to this being the monograph of surgical technique "Stomach Surgery". The base techniques of stomach surgery described at that time, which I have learned step-by-step since the beginning of my career, still preserve their value, although gastric pathology has steered wide from ulcerative cancer.

With the emergence of current medical treatment, I have witnessed the dramatic decrease in the number of operations for ulcerative disease, leaving only its complications - perforation, stenosis and malignancy – for the surgical field. The rapid development after 90 years of diagnostic endoscopy and later therapeutic endoscopy has enabled the treatment of ulcerous hemorrhages in this way. Thus, the main actor on the stage of gastric pathology has remained cancer and, in increasingly rarer cases, the complications of ulcer disease. In this context, at the instigation of Professor Dan Radulescu, I tried to address this change in the paper **"What is left for the surgeon in gastroduodenal ulcers?"** - presented at "Medical Days of the "Dr. I. Cantacuzino" Hospital, 25-26 November 2003.

From a surgical perspective, the technological advances were represented by the development of laparoscopy, which demonstrated its advantages in benign esogastric pathology, with the advantages already known, taking almost entirely the treatment of hiatal hernias, reflux diseases and achalasia.

We tried to remain “on the wave” also in laparoscopic treatment tackling the benign pathology of the upper gastric pole. Progressively, we have gained experience in the treatment of hiatal hernias with good results from the beginning, results which led us to deal with more and more complicated cases, including recurrences following laparoscopic treatment and also, diaphragmatic defects requiring alloplasty prostheses or rare forms such as Morgagni hernia.

During this time we also laparoscopically treated reflux disease, as well as achalasia of the cardia, with good results without post-operative complications. We have also tackled obesity surgery, although I personally do not believe that the solution will remain surgical.

Beyond these preoccupations with minimally invasive surgery of the stomach, our most intense concern was directed towards gastric cancer surgery. If in my period of surgical training no attention was paid except to perigastric lymphadenectomy (D1), over the last decade it seems that the principles of the Japanese surgical school are being imposed in Europe. Participation at scientific events and the reading of the literature have led me to change my view regarding the importance of lymphadenectomy in gastric cancer. Therfore, I initially began to perform D2 lymphadenectomy and ultimately systemic D3 on all operable tumors.

In this manner, between 2012 and 2015, together with the team, we operated on 47 patients with gastric tumors, most of them (40) having primary malignant tumors with 5 of these having GIST type tumors that could not be treated laparoscopically due to extralumenal development.

The evolution of parietal surgery has witnessed a period of accumulation over the last 30 years, the benchmarks being represented by the introduction of the concept of the tension-free operation, popularized especially by Lichtenstein in inguinal hernia surgery and more so by the introduction of the techniques of laparoscopic treatment in the last 10 years for both parietal inguinal defects and post-operative ones (post-operative eventrations).

In the last 15 years of medical activity, I have used, in the case of parietal defects, almost exclusively alloplasty materials of various types, structures, materials and thickness, yet, regardless of the type of its material or the clinic, all the prostheses have to ensure a rate of recurrence that does not exceed 5% and great tolerability on the part of the pacient, expressed by a low local inflammatory response and minimal post-operative pain syndrome.

The minimally invasive approach to inguinal parietal defects can now be done in two ways: one with an initial intraperitoneal treatment of the extraperitoneal space (TAPP) and the other with a direct and exclusive extraperitoneal treatment (TEP). Each one comes with advantages and disadvantages for the surgeon, but today I think both should be learned and used, chosen after clinical and judicious reasoning.

Although we have gone through all phases of parietal defect treatment, I have felt the need to encourage my younger collaborators to attempt the minimally invasive surgery of this pathology by giving them all my personal cases. Thus, the team has accumulated an experience that allows us to treat laparoscopic inguinal hernias almost exclusively and part of the eventrations.

Diabetic foot has represented and continues to represent an important part of the clinic's activities due to the proximity of the Paulescu Institute. Diabetic foot surgery, although lacking in glamor, must be adapted to each patient, depending on the type of lesion and vasculopathy or neuropathy, to remove or at least delay the moment of amputation. We were concerned with finding the best technical variants for all types of amputations, but especially for the main ones (calf, thigh), applicable with good results to patients with chronic circulatory insufficiency of the pelvic limbs, such as arteriopathic diabetics. I published a small work describing these techniques accompanied by a CD containing a film of the operations trying in this way to popularize our experience in the surgical environment.

Another concern of the team was a pathology less well-known in practice, **Charcot osteoarthropathy**. The results of this concern can be summed up by moving from surgical treatment in the acute inflammatory phase, to illnesses that consisted of unnecessary incisions and debridement and which did not otherwise do anything but provide an entryway for microbes, to conservative treatment by combining orthopedic treatment with pharmaceutical treatment. Surgery remains to be used in case of the failure of the conservative approach, when arthropathy makes the foot unusable when walking or when the infection causes irreversible destruction. The mainstay of conservative treatment is to immobilize the foot and calf in a cast ("Total contact cast").

Tegumentary defects resulting from surgical interventions on diabetics (necrectomy, fasciectomy, drainage incisions of accumulations and various amputations) represent another problem that has been of concern to us. The first step I made was covering these defects with skin fragments, a painstaking technique that does not allow the coverage of too large an area. We progressed and began the coverage of these defects with split loose skin

harvested from the thigh. Used especially in diabetic patients with neuropathy, grafting with split loose skin has significantly reduced the duration of healing and allowed for greater defects to be covered. And in patients with arteriopathy with the possibility of revascularization, grafting is viable after performing vascular procedures.

The treatment of the chronic wounds of diabetics has enjoyed new methods in recent years. Many types of dressings have appeared with antiseptic, moisturizing and absorbent properties or which stimulate granulation. The debridermrnt of wounds can now be done using new methods (electrical stimulation, electromagnetism of the wound edges, local lazer therapy, hyperbaric oxygen therapy, systemic therapies, ultrasounds), to which negative pressure therapy has been added.

The numerous participations of the collective at various conferences focusing on updates in diabetic foot management (including Los Angeles, USA-DFCon 2013 Diabetic Foot Global Conference, March 2013) have paved the way for these modern treatments. These methods are, in certain conditions, the solution to healing wounds, while in other circumstances, the stage preceding the grafting or secondary suturing.

The development of endovascular surgery has opened a new front in the fight with diabetic arteriopathy, offering additional chances to these patients. Improvement of the circulatory bed in the diabetic with wounds with prolonged or unfavorable evolution often makes the difference between major amputation and amputation at the source.

Projects Related to Didactic Activities

Regarding the preparation of the students, I also bear in mind, besides the increase in quality of the courses for the students, the drafting of a volume of lectures on surgical pathology for 4th and 5th year students, with a didactic presentation exemplified by drawings and schemes, attempting to continue the

good traditions of our professors (the courses of Professors Dan Radulescu and Ion Vereanu).

In the activity of preparing the residents I propose to organize a multi-annual lecture programme of surgical techniques, diagnosis protocols and treatment, as well as the publishing of the literature in medical journals at weekly meetings. At the same time, we want to develop a model for the periodical verification of their theoretical knowledge by means of questionnaires and free discussions with the department collective. We contacted Professor Pezet from the Clermont Ferrand Hospital through one of our former residents in order to organize a mini-internship, concerning hepatobiliopancreatic surgery, for all members of the team including residents.

The professional activity will be completed – on the base of the experience gained by all the members of the surgical team after obtaining their diplomas in hepatobiliopancreatic surgery - by tackling more and more complex cases. Another objective is the treatment of hepatic and pancreatic lesions using minimally invasive techniques.

An increse in our experience in surgical oncology will be acheived by performing multiorgan resections in loco-regional advanced cancers as well as by the multidisciplinary treatment of each case of neoplasia, in which will participate: surgeons, residents, anesthesiologists, ICU medics, oncologists, gastroenterologists, imagistics technicians, pathological anatomists.

The experience gained in the surgical treatment of breast cancer can provide a solid foundation for collaboration with plastic surgery specialists in breast reconstruction.

Projects Related to Scientific Activities

Diabetic foot pathology remains the main research field of the department due to the large number of patients. That is why I propose:

- The drafting of a tome of **surgical techniques for diabetic foot**, thus completing one of the older concerns in the field.
- An epidemiological study of the relation between the field of arteriopathy or neuropathy and the nature of bacterial infection.
- Analysis of the impact of nutritional status on the evolution of diabetic foot ulcers.
- Studying transcutaneous oxygen pressure ($tcPO_2$) for assessing the healing prognosis of diabetic foot lesions.
- The assessment of pre- and post-operative sole pressure to determine the risk of ulceration on the sole
- The comparative assessment of diabetic foot lesion classification to determine the risk of amputation of diabetic foot lesions.

In the category of morphological studies, together with Professor Dr. Constantin Ionescu-Targoviste, we initiated a study of morphological pancreatic lesions in diabetic patients, which will be continued.

Together with Professor Dr. Mugurel Rusu, from the Department of Anatomy of the Faculty of Dentistry in Bucharest, we began a series of studies related to: vascular anatomical variants, diabetic neuropathy, Charcot osteoarthropathy, fetal embryology.

All the findings from the research projects mentioned above will be published in indexed journals ISI, BDI-CNCSIS.