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MEDICAL UNIVERSITY - PLOVDIV

REVIEW

OF THE DISSERTATION WORK

**“INTRAOPERATIVE ULTRASOUND IN NON-PALPABLE
TUMOR FORMATIONS OF THE BREAST GLAND
- APPLICATION AND SIMULATION TRAINING”**

of Dr. VALENTIN VALENTINOV IVANOV

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Special Surgery at MU Plovdiv for awarding the educational and scientific
degree "Doctor" in the professional field "Medicine", scientific specialty
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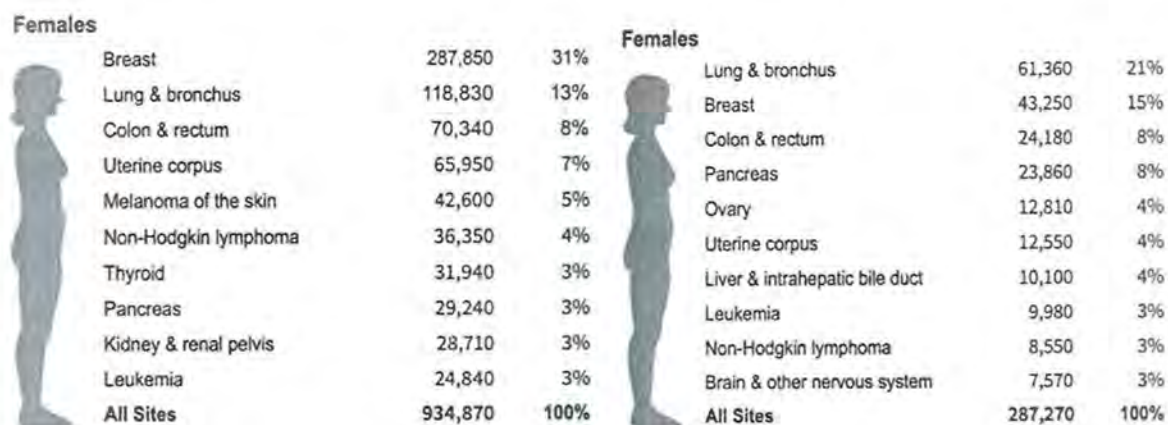
**Medical University Plovdiv, Medical Faculty, Department of Propaedeutics
of Surgical Diseases, Section of General Surgery**

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The presented set of materials on paper and electronic media is in accordance with Art.115/1/ of the procedure of acquiring the educational and research degree “PhD” in Medical University Plovdiv regulation and includes all the necessary documents, arranged according to the requirements.

Dr. Valentin Valentinov Ivanov graduated at the Medical University of Plovdiv in 2016 with a master degree in “Medicine” and in Health Management in the Faculty of Public Health of Medical University of Plovdiv in 2021. The work on the dissertation started in 2016 at the Clinic of Surgery of the University Hospital "Kaspela" Plovdiv, the author being an assistant professor in the Department of Special Surgery at MU Plovdiv since 2018, when he became an assistant professor at the Medical Simulation and Training Center of MU Plovdiv. He holds a language certificate from the University of Cambridge - level B2; he has participated in 35 national, 51 international scientific events and specialization courses from 2014 to 2021; where only in 2021 - the number is 34! He has 2 awards and participated in two projects.

The dissertation is a complex of randomized, prospective and experimental studies on the surgical treatment of non-palpable breast tumors, and in particular - breast cancer. According to GLOBOCAN and the Cancer Journal for Clinicians, breast cancer in women in 2022 will be the leading in frequency / 31%, n 287 850 / and second in mortality / 15%, n 43 250 / of all cancers.



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The 50 years accumulated experience and the critical, statistically and clinically significant 10 year recent analysis of multicentric and prospective randomized trials have led to the adoption of unified, objective criteria for evaluating results and creating preconditions for building international databases consensus statements, Evidence Based Surgery Guidelines and Recommendations for the diagnosis and treatment of breast cancer. From the summarized data, the best results are obtained in specialized and profiled surgical centers with the largest number of operations.

Regional lymph node (LM) metastases are one of the most important prognostic factors in breast cancer. Patients with metastatically affected lymph nodes have lower survival and require adjuvant chemotherapy. Sentinel lymph node (SLV) biopsy allows more accurate determination of nodal status, detection of micrometastases, aberrant lymphatic drainage and ectopic lymph nodes, leading to more precise staging and radicalism.

The choice of the surgical approach and the exactness of the surgical intervention are of key importance for the complex oncological treatment of breast cancer. Therefore, Dr. Valentin Ivanov's research, owing a scientific-synthesis nature, surgical research and practical focus, deserves positive evaluation.

The dissertation is structured correctly - it is written on 154 standard typewritten pages and contains 50 figures, 22 images, 15 tables. which is sufficient in volume. The style is professional, the language - rich and accurate.

The distribution by chapters is as follows:

Introduction - 1 page.

Literary review - 32 pages.

Purpose and tasks - 1 page.

Material and Methods - 14 pages.

Results - Own research - 68 pages.

Discussion - 13 pages.

Conclusions - 1 page.

Scientific contributions - 2 pages.

Bibliography - 15 pages.

The bibliography contains 226 authors, of which 6 in Cyrillic and 220 in Latin.

The Literary Review is detailed, clear, up-to-date, relevant in terms of content and presented critically. Here, Dr. Ivanov places the surgical approach to breast cancer to the current, modern level. This strategy is based on the latest innovations in the diagnosis and surgical treatment of breast cancer. The literary review is in-depth, extensive and made with the aim of comprehensiveness. It consists of 6 main subchapters. The systematic manner of writing includes in-depth topographic-anatomical and current epidemiological data; organ-preserving operative and neoadjuvant therapeutic methods, focusing on the essence of the study - methods for intraoperative navigation in non-palpable breast lesions. They are based on modern perioperative ultrasound, the application of effective and radioactive and magnetic markers, fluorescent methods and the SAVI SCOUT system providing, clean resection, lines at optimal volume of excision, without compromising oncological radicalism.

The broadness of the sub-chapters for surgical treatment, including a historical overview and types of surgical techniques, suggests the experience and good knowledge of the types of operations by the author.

The systematicity and precision of the exposition in this part, convince us that Dr. Ivanov knows and applies the most optimal modern concepts for the complex

treatment of breast cancer. Moreover - Dr. Ivanov, historically and contemporary, presents the positive role of simulation training and sets himself the ambitious task of creating, comparable to the intervention, a realistic model for simulation training, which is lacking in the available literature.

In general, the literature review is balanced, informative and richly supported by literary sources, from which the critical selection of citations of important publications on the issue is impressive.

These findings and the fact that breast cancer is currently the first in the world in incidence and mortality of all cancers in women are more than sufficient grounds to justify the problem under study as relevant.

The goal is ambitious, formulated accurately and clearly.

The tasks are 3, but the second main task regarding the nature and analysis of the study consists of 6 sub-tasks, which meet the set goal and are feasible.

In the section "Material and Methods" the author presents a comparative analysis of epidemiological and clinical data for all cancer patients, including those with breast cancer from Plovdiv, Pazardzhik and Smolyan from the Cancer Registry of the "Complex Cancer Center". Plovdiv, for the period 2010-2019.

The study includes a prospective multicentre comparative analysis of data from 53 patients with non-palpable breast tumors, 48 operated in the Department of Oncological Surgery at KOC Plovdiv and 5 in the Clinic of Surgery at Kaspela University Hospital Plovdiv; all 28 with organ-saving procedures - sectoral excision and 25 with intraoperative ultrasound navigation.

On 16 pages the Dr Ivanov reveals the classical objective and imaging studies, supplemented by BI-RADS classification, biopsy and pathoanatomical samples, including immunohistochemical typing and metric calculations. Alongside with non-surgical, documentary methods show preoperative skin marking of the exact

location of the tumor formation, with or without intraoperative ultrasound, all illustrated with color photographs and the original intraoperative protocols for taking study data separately. In the description of the individual operative techniques it is evident that the basic modern surgical and oncological principles are observed and applied - intraoperative ultrasound navigation, organ-preserving methods, exvivo ultrasound. The stages of creating the model, the matrix and the simulation phantom itself are described in parallel.

The studies are richly illustrated with original photographs and appropriate figures / diagrams and tables /, facilitating the optimal implementation of the set tasks and goals.

Modern statistical research methods were used - metric, nominal and ordinal - Smirnov, Fisher, Student's t test, X², Mann Whitney, and the specialized statistical product SPSS - version 27. Minitab 19 Medicalc 20.008 with graphical analysis.

In the chapter "Results", the data from the regional surveys occupy 34 pages, which can be reduced in volume, despite the epidemiological nature of these, otherwise relevant and valuable studies. In the remaining 34 pages, the author presents the perioperative characteristics of patients, showing significant workload for monitoring, recording, systematizing and analyzing statistical and clinical outcomes. The indications and data on the type of organ-preserving operative intervention are described in detail and the postoperative results are thoroughly analyzed.

The essential part of the research is the oncological technique, based on the intraoperative ultrasound navigation, which determines the optimal volume and distance of the radical resection line. The express intraoperative tumor verification, the volume of the excision, as well as the postoperative final pathoanatomical diagnosis, after immunohistochemical examinations and typing, are excellently

illustrated. The statistically significant differences in the volume of excision (up to several times) in the two groups are indicative, emphasizing the advantages of intraoperative ultrasound.

The “Discussion” section provides us with up-to-date regional data on breast cancer morbidity and mortality and is of great informative value.

The author rightly points out the indisputable advantages of ultrasound navigation - 100% diagnosis, smaller resection volume, allowing organ-sparing operations, especially in smaller mammary glands, without compromising on oncological radicalism, reexcision on indications, comparable operative time, less complications, short hospitalization and improved quality of life. Critically compared with similar literature data, the method of intraoperative ultrasound shows significant advantages in the surgical treatment of breast cancer, thwarting expensive, invasive diagnostic and therapeutic procedures. The principles of behavior and the results of one's own research and the data from the available current publications on the topic are discussed. There is a noticeable similarity between authors' approaches and those of the world's recommendations and guidelines.

The experimental studies, which ended with the construction of an original model for simulation training are of scientific interest. The phantom allows simulated mapping, fine, core- needle biopsy and even excision under ultrasound control, which is of great didactic and practical importance.

The 8 conclusions logically present the most significant findings from the analysis of the results, which show recommendations mostly of a practically applied nature, referring to the modern approach in the diagnosis and treatment of breast cancer.

The scientific contributions of the dissertation are the following:

1. A critical up-to-date overview of the historical development and current principles of diagnosis and treatment of breast cancer, with the most important aspects of the indications, principles and methods of modern intraoperative ultrasound navigation and organ-preserving surgical techniques is offered.
2. The in-depth epidemiological study of the region with current data on the incidence and mortality of breast cancer has great informative value.
3. For the first time in our country a complex of randomized, prospective and experimental studies on the surgical treatment of non-palpable tumors, and in particular - breast cancer is performed
4. An original algorithm for diagnosis and determination of the optimal resection volume based on intraoperative ultrasound navigation is proposed, which is easily applicable in oncosurgical practice.
5. An original model for surgical simulation training with great practical importance is offered.

The abstract is written according to the requirements of the relevant regulations, and reflects the main results achieved in the dissertation.

Critical remarks and recommendations - in the "Results" chapter, the description of epidemiological studies can be reduced by transferring part of it into the "Materials and methods" chapter.

CONCLUSION

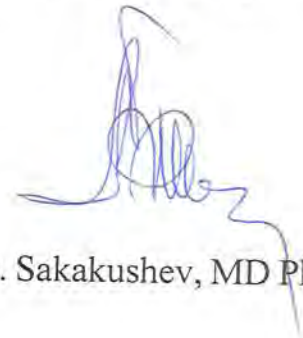
The presented dissertation is an in-depth scientific study of the modern diagnostics and surgical treatment of breast cancer. The clinical material and the academic author's approach reveal his theoretical knowledge, qualities and skills for independent research.

Based on these findings, I believe that the study presented by the above reviewed dissertation, abstract, results and contributions is an original research with practical implementation, which meets the necessary requirements, so I confidently give my positive assessment "Yes".

I propose to the esteemed Scientific Jury to award the educational and scientific degree "DOCTOR"/PhD/ to Dr. VALENTIN IVANOV in the doctoral program of "General Surgery".

Plovdiv, March 4, 2022

Prepared by:



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