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DOCTORAL SCHOOL OF MEDICINE AND PHARMACY

PhD THESIS SUMMARY

# **Assessment of Sentinel Lymph Node Biopsy in Endometrial and Cervical Cancer**

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## Introduction

Sentinel lymph node (SLN) biopsy has become, over the past two decades, a central strategy for the staging of malignant tumors, particularly breast cancer and melanoma. In gynecologic oncology, the method has proven its usefulness in cervical and endometrial cancer, two entities in which lymph node status represents the most important prognostic factor and a key element in choosing the therapeutic approach. Compared with systematic lymphadenectomy, which entails significant morbidity, SLN identification and selective excision allow for accurate evaluation through the detection of micrometastases using ultrastaging techniques, while simultaneously reducing invasiveness and complications.

Data from the multicenter SENTICOL, FIRES, and SENTIX trials have validated the method, with sensitivity and negative predictive value (NPV) above 90% when bilateral detection is achieved. Its inclusion in ESGO and NCCN guidelines confirms SLN biopsy as a viable alternative to conventional lymphadenectomy in early-stage disease. However, in resource-limited countries, access to fluorescent tracers or nuclear infrastructure is restricted, necessitating adaptation of the technique to accessible dyes and rigorous evaluation of the method's performance in these conditions.

## Objectives

The primary aim of this research was to evaluate the feasibility and accuracy of SLN biopsy in cervical and endometrial cancer in a resource-limited center, using primarily methylene blue, complemented in some cases by the combined technique with radiocolloid. Secondary objectives included analyzing clinico-pathological factors that may influence the performance of the method, such as age, tumor size, depth of stromal invasion, and presence of LVI; assessing the role of SLN biopsy in the context of fertility-sparing treatment in cervical cancer; and exploring the limitations of the method in endometrial cancer staging, with particular focus on the difficulty of identifying paraaortic drainage.

## Methodology

The thesis comprised three prospective observational studies conducted between 2019 and 2025, with a total of 71 patients: 42 with cervical cancer, of whom 4 underwent fertility-sparing treatment through abdominal radical trachelectomy, and 29 with endometrial cancer. In all cases, intracervical injection of methylene blue was used, sometimes in association with radiocolloid ( $Tc-99m$ ), and the identified nodes were excised and subjected to conventional histopathological examination and ultrastaging with serial sectioning and immunohistochemistry.

Sensitivity and NPV were calculated only in patients who underwent systematic pelvic  $\pm$  paraaortic lymphadenectomy, according to standard surgical guidelines, which allowed direct comparison between the true status of the lymphatic chains and the SLN biopsy results.

## Study 1 – Cervical cancer

In this cohort, SLN biopsy demonstrated a satisfactory overall detection rate with methylene blue, with performance improving significantly when the combined technique was applied. Comparative analysis with complete lymphadenectomy showed that the method could identify most cases with nodal dissemination, with a high NPV. However,

false negatives were observed, particularly in patients with bulky tumors, deep stromal invasion, or positive LVSI, confirming international observations that these biological features can alter lymphatic drainage and compromise the accuracy of simple dye-based mapping.

A notable finding was the presence of metastases exclusively in parametrial nodes, highlighting the importance of thorough exploration of this territory. Age-stratified analysis revealed higher bilateral detection rates in younger women, suggesting that the integrity of the lymphatic network may directly influence mapping success.

## Study 2 – Abdominal radical trachelectomy

In young patients eligible for fertility preservation, SLN biopsy provided complete and reliable nodal staging, with no false negatives compared with lymphadenectomy performed according to guidelines. Even when only simple dyes were used, the method consistently achieved bilateral detection, identifying micrometastases that influenced therapeutic management. Oncologic outcomes were favorable in all cases, and fertility was preserved in most. This study demonstrates that integrating SLN biopsy into fertility-sparing cervical cancer surgery is feasible and can reliably support patient selection for conservative treatment.

## Study 3 – Endometrial cancer

The results showed that the method is reproducible and accurate when detection is complete. Sensitivity in hemipelvises with identified SLNs was 100%, confirming the predictive value of the technique. Major limitations were related to unilateral detection and the inability to visualize paraaortic drainage with exclusively intracervical injection. In such cases, applying the algorithm (additional lymphadenectomy on the undetected side) reduced the risk of understaging. Compared with fluorescent techniques, the performance of methylene blue remained more modest, but the study demonstrates that even in resource-limited conditions, accurate staging with tangible clinical impact can be achieved.

## Conclusions

This thesis demonstrates that SLN biopsy is feasible and safe for detecting nodal metastasis in early-stage cervical and endometrial cancer, even in a center with limited infrastructure. The method can reduce the need for systematic lymphadenectomy, thereby lowering postoperative morbidity while still enabling the detection of low-volume metastases through ultrastaging. In cervical cancer, accuracy is highest in small tumors and younger patients, and the method is indispensable for fertility-sparing treatment. In endometrial cancer, SLN biopsy is a validated alternative to extensive dissection when the completion algorithm is applied.

The originality of this study lies in validating the method in a Romanian center with limited resources, through prospective analysis and reporting of results in line with international standards. These findings may form the basis for expanding the implementation of SLN biopsy nationwide and for consolidating a modern, less invasive, yet oncologically safe practice.