



UMEÅ UNIVERSITET

Umeå University Medical Dissertations, New Series No 2240

---

# Tumour stromal and demographical factors affecting the metastatic aggressiveness of small differentiated papillary thyroid cancers in Sweden

**Haytham Bayadsi**

## Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorexamen framläggs till offentligt försvar i Hörsalen, Östersunds Sjukhus, fredagen den 10e november 2023, kl. 09:00.

Avhandlingen kommer att försvaras på svenska.

Fakultetsopponent: Docent Robert Bränström, institutionen för molekylär medicin och kirurgi/Endokrinkirurgi, Karolinska Institutet, Stockholm, Sweden

## Organization

Umeå University  
Department of Surgical and  
Perioperative Sciences

## Document type

Doctoral thesis

## Date of publication

20 October 2023

## Author

Haytham Bayadsi

## Title

Tumour stromal and demographical factors affecting the metastatic aggressiveness of small differentiated papillary thyroid cancers in Sweden.

## Abstract

**Background:** The incidence of papillary thyroid cancer (PTC) has been increasing over the recent decades, especially that of small papillary thyroid cancers (sPTCs) ( $\leq 20$ mm in size). sPTCs are generally classified as low risk cancers with a very favourable diagnosis, yet some of these cancers still cause locoregional and distant metastasis, recurrence and even death.

**Aims:** To investigate the role of tumour stromal, environmental and demographical factors affecting the metastatic aggressiveness of sPTCs in Sweden.

**Material & Methods:** Selected tumour stromal proteins (Types I (Col1) and IV (Col4) collagens, alpha smooth muscle actin ( $\alpha$ -SMA) and matrix metalloproteinase 9 (MMP-9)) were analysed for their role in metastatic disease (Paper I). Demographic and clinicopathological differences regarding recurrence between metastasized vs. non-metastasized sPTCs in Sweden were studied in 2 registry-based retrospective observational cohort studies (Papers II & III). The geographic distribution of patients with sPTC in Sweden was pinpointed and layered with maps of gamma radiation deposits of radionuclides Caesium-137 (Cs-137), Thorium-232 (Th-232), Uranium-238 (U-238) and Potassium-40 (K-40) using different spatial analysis methods (Paper IV).

**Results:** Col1 and Col4 were significantly more expressed in the non-metastatic tumours compared with metastatic ones. Patients with N1b disease were younger, had a smaller tumour size and higher recurrence rates compared to patients with N0 and N1a disease. The mean number of metastatic LNs at initial surgery was higher in the N1b group than the N1a group and correlated with more recurrent disease. The prevalence of metastatic sPTC was associated with significantly higher levels of gamma radiation from Th-232, U-238 and K-40.

**Conclusions:** The higher expression of Col1 and Col4 in the non-metastasized tumours indicates a potential protective role in tumour progression. LN stage N1b at diagnosis, and having five or more metastatic nodes, are strong risk factors for cancer recurrence and decreased disease-free survival in sPTC. Environmental factors such as gamma radiation are believed to play a major role in the pathogenesis of the PTC. These findings altogether underscore the importance of LN evaluation, tumour biological as well as environmental factors in sPTC patients, suggesting that the management of these patients should be based on an individual risk stratification instead of a "one size fits all" approach.

## Keywords

Papillary thyroid cancer, tumour stroma, lymph node metastasis, ionizing radiation, GIS.

## Language

English

## ISBN

print: 978-91-8070-049-8  
PDF: 978-91-8070-050-4

## ISSN

0346-6612

## Number of pages

71 + 4 papers