

THYROID DISEASES	
GENERAL INFORMATION	
Course coordinator	Prof. Ivica Mihaljević, MD, PhD
Assistant(s)/Associate(s)	Assoc. Prof. Biljana Pauzar, MD, PhD Asst. Prof. Tomislav Kizivat, MD, PhD Ivana Marić, MD, PhD Vlado Wagenhofer, MD, PhD Katica Mijatović, MD, assistant Hrvoje Delalić, MD Marija Kordić Brandić, MD Dunja Mudri, MD, PhD
Study Programme	Integrated Undergraduate and Graduate University Study of Medicine
Status of the course	Elective course
Year of study, semester	4 th year, 8 th semester
ECTS	2
Course delivery methods (workload in hours)	Lectures (7), seminars (6), exercises (12)
Expected number of students	30
COURSE DESCRIPTION	
Course objectives	
<p>Elective course Thyroid Diseases has been designed with a view of offering students the possibility to gain knowledge and skills in the use of nuclear medicine diagnostic methods and therapeutic procedures in thyroid diseases.</p> <p>The course enables the acquisition of theoretical knowledge about thyroid diseases, testing the thyroid by using radionuclides, thyroid scintigraphy and <i>in vitro</i> thyroid function tests (radioimmunological assays). Ultrasound examinations and ultrasound-guided fine needle aspiration complement the radionuclide tests. A portion of the course is dedicated to thyroid disease treatment by medications, surgery and radioiodine and to monitoring the progress of non-neoplastic and neoplastic diseases of the thyroid, which account much of the clinical practice in nuclear medicine. Special attention is paid to new approaches in diagnostics, treatment and follow-up of differentiated and non-differentiated thyroid cancers and changes in thyroid cancer epidemiology. This elective course gives students an opportunity to expand their knowledge and skills in thyroidology. Particular emphasis lies on clinical approach to diagnostics, treatment and follow-up of non-neoplastic and neoplastic diseases of the thyroid, which are covered by seminars and clinical exercises.</p>	
Enrolment requirements and entry competencies	
<p>General competencies:</p> <ul style="list-style-type: none"> - principles of medical ethics and deontology and the duty to protect patient privacy and dignity - communication skills (conduct around patients, colleagues and other professionals) - ability to identify and properly document relevant information about the patient - principles of managing one's own medical practice and career management - understanding the importance of a science-based approach to the profession - preparing papers for publication - principles of evidence-based medicine - basic sciences applied in nuclear medicine (anatomy, physiology, biochemistry, pathophysiology). <p>Special competencies:</p> <ul style="list-style-type: none"> - basic knowledge in radiochemistry (<i>in vitro</i> radioimmunological assay of thyroid hormones and antibodies and of other biochemically important substances in the serum and in urine) 	

- radionuclides and radiopharmaceuticals for *in vivo* diagnostics of thyroid functional disorder
- clinical examination of a patient suspected of suffering from thyroid disease
- diagnostic and therapeutic procedures with benign and malignant thyroid diseases
- use of ^{131}I in treating autonomous and autoimmune forms of hyperthyroidism and thyroid cancer
- treating thyroid cancer with other radiopharmaceuticals based on the protocols for specific nuclear medicine procedures
- clinical follow-up of patients being treated for thyroid disease
- diagnostic procedures and treatment of thyroid-associated orbitopathy (TAO)
- diagnostics and types of diseases of the parathyroid glands
- ultrasound examination of the thyroid, parathyroid glands and the anterior neck region with ultrasound-guided fine needle aspiration

Learning outcomes at programme level

1.2., 2.1., 2.2., 2.3., 3.1., 3.2., 3.3., 3.4., 3.5., 4.1., 4.2.

Learning outcomes (5-10)

After passing the exam in Thyroid Diseases, students will:

- 1 be familiar with methods of laboratory measurement of concentrations of thyroid hormones, enzymes, antibodies and tumour markers for thyroid cancers
- 2 know about work methods of a thyroid disease clinic
- 3 be familiar with and describe the nuclear medicine diagnostic procedures used in diagnosing thyroid disease: thyroid scintigraphy using $^{99\text{m}}\text{Tc}$ -pertechnetate, ^{131}I sodium iodide and whole-body scintigraphy using ^{131}I sodium iodide
- 4 be familiar with treatment methods for benign thyroid disease
- 5 understand the use of ^{131}I in treating autonomous and autoimmune forms of hyperthyroidism and thyroid cancer
- 7 be familiar with treatment methods for malignant thyroid disease
- 8 be able to describe clinical follow-up of patients being treated for thyroid disease
- 9 be familiar with diagnostic procedures and treatment of thyroid-associated orbitopathy (TAO)
- 10 be able to describe diagnostic procedures used in follow-up and in and evaluation of success of radioiodine ablation in treating differentiated thyroid cancers, performing whole-body scintigraphy using ^{131}I and achieving exogenous TSH elevation by injecting recombinant human thyrotropin (rhTSH)

Course content

Thyroid disease diagnostics. Imaging and radionuclide diagnostic methods. Ultrasound, ultrasound-guided fine needle aspiration, cytodiagnosics. Rational diagnostics of thyroid disease and diagnostic algorithms.

Thyroid disease diagnostics based on *in vitro* tests Laboratory measurement of thyroid hormone concentration (FT4, FT3, TSH) and TRH, autoantibodies and tumour markers. Biosynthesis, serum transport, distribution of thyroid hormones and hypothalamic-pituitary axis. Total and free T3 and T4. Thyroid autoantibodies (TPOAt, TRAb, TgAt): epidemiology, functional, clinical and pathological significance, their role in diagnostics and prognostics of thyroid disease. Tumour markers in thyroidology: thyroglobulin, calcitonin and their role in follow-up. Immunoanalysis and non-radioimmunoassay - non-RIA in determining hormone concentration, antibodies and thyroid tumour markers. History, concept and principles of radioimmunoassays. Classification of radioimmunoassay (RIA) methods. Competitive and non-competitive RIA with derivatives and comparison with competing methods. Sources of variability and quality control. Reference ranges and medical report interpretation. Rational use of laboratory hormone analysis, antibodies and tumour markers in diagnosing thyroid disease.

Radionuclide thyroid function testing and thyroid scintigraphy Radiopharmaceutical accumulation

measurement devices: structure, selection and application of radionuclide and indications. Measuring points and radioiodine accumulation measurement. Thyroid scintigraphy using ^{131}I and $^{99\text{m}}\text{Tc}$ -pertechnetate: indications, contraindications, image acquisition and dosimetry. Iodine 131 therapeutic activity monitoring methods in benign and malignant thyroid disease.

Thyroid cancer diagnostics. Simple nontoxic nodular goiter. Multinodular toxic goiter: symptoms and laboratory test results. Toxic adenoma: clinical presentation and laboratory test results.

Benign thyroid tumours. Thyroid nodule evaluation. Types of cysts. Thyroid suppression test in differentiating autonomously functioning thyroid nodule from a non-autonomously functioning one. Follicular and Hürthle cell adenomas.

Role of scintigraphy in nodular thyroid disease. Toxic and non-toxic nodules, laboratory values and scintigraphy results. Role of scintigraphy in differential diagnosis and screening for cytological verification and in therapy approach for "hot" and "cold" nodules. Measurement of radioiodine accumulation in preparation for radioiodine treatment of decompensated autonomous nodule.

Thyroid ultrasound and cytology. Ultrasound-guided fine needle aspiration of the thyroid: device demonstration and examination techniques. B-mode ultrasound and ultrasound probes. Doppler effect and its use. Fundamentals of ultrasound imaging of the anatomical structures in the neck and image interpretation. Ultrasound image of a normal thyroid, diffuse disease and nodular thyroid disease. Images of enlarged, pathological lymph nodes. Images of enlarged parathyroid glands. Cytology test results indicating degenerative changes (colloid, haemorrhagic and complex cysts), inflammatory changes (acute, subacute inflammation, lymphocytic thyroiditis, chronic inflammation, fibrosing thyroiditis), functional changes (hyper and hypoactivity), proliferative changes (benign: adenomas, nodular hyperplasia, and malignant: primary and metastatic thyroid tumours). Sonographic differentiation of solid nodules and cysts. Role of ultrasound in rational thyroid and parathyroid gland disease diagnosis.

Cyodiagnosics of thyroid disease and immunocytochemical methods. Ultrasound-guided fine needle aspiration: aspiration techniques, indications for fine needle aspiration and nodule screening, complications and treatment. Cytological smear preparation, method of processing fine-needle aspiration material. Determination of aspiration-acquired analyte. Interpretation of test results, indications for follow-up fine-needle aspiration. Cytology test results and indications for histopathological verification. Normal thyroid tissue, degenerative changes (colloid, haemorrhagic and complex cysts), inflammatory changes (acute, subacute inflammation, lymphocytic thyroiditis, chronic inflammation, fibrosing thyroiditis), functional changes in epithelial cells (hyper and hypoactivity), proliferative changes (benign: adenomas, nodular hyperplasia, and malignant: primary and metastatic thyroid tumours). Immunocytochemical markers in differential diagnosis of primary and metastatic tumours of the anterior neck.

Ultrasound image of diffuse and nodular thyroid disease. Imaging of a diffuse goiter, lymphomatous goiter, Graves' disease and subacute thyroiditis. Imaging of nodular disease: hypoechoic, isoechoic, calcified nodules, cysts. Imaging of malignant tumours and metastases in the neck.

Non-neoplastic thyroid cancers. Classification of hyperthyroid diseases and most common causes. Thyrotoxicosis with hyperthyroidism. Basedow's disease: clinical presentations, objective signs, laboratory test results, differential diagnosis and epidemiological characteristics. Hyperthyroid syndrome – clinical presentation, laboratory test results and organ manifestations. Trophoblastic disease. Hyperthyroidism with elevated TSH. Basedow's disease. Multinodular toxic goiter and toxic adenoma. Clinical presentation, laboratory, scintigraphy and ultrasound test results. Classification and aetiology of hypothyroid diseases, clinical presentation, differential diagnosis, laboratory test results: primary idiopathic, subclinical, post-radiation, post-ablation hypothyroid disease, sporadic congenital hypothyroidism, hypothalamic-pituitary-adrenal (HPA) axis dysfunction and myxoedema.

Diffuse and multinodular nontoxic goiter. Diffuse goiter. Medication-induced goiter. Endemic goiter. Epidemiology, pathogenesis and evolution of goiter. Clinical presentation, elements and epidemiological characteristics of diffuse and nodular euthyroid goiter. Laboratory test results,

scintigraphy and sonography results. Differential diagnosis and treatment.

Hyperthyroidism, hypothyroidism and goiter treatment. Hypothyroidism hormonal replacement therapy. Pharmacological and radical treatment of immunohyperthyroidism. Surgical treatment of thyroid disease and radioiodine therapy. Indications and guidelines for selection of treatment. Radioiodine treatment of toxic adenoma and toxic multinodular goiter. Iodine 131 therapeutic activity monitoring methods in benign and malignant thyroid disease. Administration technique, standard operating procedure in radionuclide therapy and hospital discharge requirements. Diffuse and nontoxic goiter and endemic goiter. Salt iodization. Diagnostic algorithms for evaluation of multinodular goiter, indications for radical treatment and histopathological verification. Surgical resection principles, extent of resection, and perioperative complications.

Thyroid inflammation. Classification of inflammatory thyroid diseases. Autoimmune, infectious and granulomatous diseases. Epidemiology, clinical, laboratory, sonographic and cytological specificities and differential diagnosis.

Chronic Hashimoto thyroiditis and subacute De Quervain's thyroiditis. Clinical presentation, elements and epidemiological characteristics of subacute and Hashimoto thyroiditis. Laboratory test results, scintigraphy and sonography results. Differential diagnosis and treatment.

Treatment of inflammatory thyroid diseases. Suppurative thyroiditis: epidemiology, etiopathogenesis, clinical manifestations and diagnostics. Principles of treatment, including surgical treatment. Treatment of subacute thyroiditis and progression phases.

Diagnosis and treatment of dysthyroid orbitopathy. Pathogenesis, epidemiology, clinical presentation, natural progression and classification of dysthyroid orbitopathy. Diagnostic methods, computed tomography (CT) scan/ultrasound of the orbit, extraocular muscles and motility, function evaluation. Local therapy, pulse corticosteroid, radiation and decompressive surgical treatment of Graves orbitopathy.

Malignant thyroid tumours. Classification of malignant thyroid tumours. Demographic and clinical characteristics, prognosis. Diagnostic approach, scintigraphy, laboratory, sonography and cytology test results.

Treatment of thyroid cancers. Common characteristic of differentiated thyroid cancers. Principles of surgical, radioiodine and palliative treatment of thyroid cancer. Papillary thyroid cancer treatment: surgical treatment (total thyroidectomy and neck dissection), radioiodine ablation treatment and suppression treatment with L-thyroxine. Differentiated thyroid cancer follow up. Iodine-131 treatment of metastatic differentiated thyroid cancer. New approaches in thyroid cancer treatment. Diagnostics of non-¹³¹I-avid cancers. Preoperative workup and treatment of medullary thyroid cancer. Medullary thyroid cancer follow up. Treatment of anaplastic thyroid cancer. Thyroid cancer prognostic systems. TNM classification of thyroid cancers. Thyroid cancer follow up, prognosis and mortality.

Radioiodine treatment of differentiated thyroid cancers. Importance, role and techniques of residual thyroid tissue ablation with ¹³¹I after total thyroidectomy in treatment and follow up of differentiated thyroid cancers. Importance of TSH stimulation, selection of ¹³¹I activity and whole body post-ablation scintigraphy. Patient preparation, protection measures and complications. Radioiodine treatment of disseminated and recurrent differentiated thyroid cancers.

Diagnostics and treatment of medullary thyroid cancer. Clinical, sonographic and cytological characteristics of sporadic and familial medullary thyroid cancer. Pre- and postoperative staging. Tumour markers (calcitonin, CEA, NSE, chromogranin A) in diagnosing primary tumours, recurrences and metastases. Elements, differential diagnosis and cytogenetics of MEN2 syndrome. Principles of radical surgical treatment, radiotherapy, cytostatic and palliative treatment. Paraneoplastic syndromes.

Positron emission tomography/computed tomography (PET/CT) in thyroid cancer follow-up. ¹⁸F¹⁸FDG

pharmacodynamics in malignancies. Non-iodine-avid thyroid cancers and diagnostics of biochemical recurrence. Flip-flop phenomenon in differentiated cancers of the thyroid and role of ^{18}F FDG-PET/CT in postoperative/post-ablative follow up, prognosis and choice of therapy of recurrent thyroid carcinomas. ^{18}F -DOPA in diagnosing biochemical recurrence and restaging of medullary thyroid cancer.

WBS – whole body scintigraphy with ^{131}I , ^{123}I , ^{201}Tl , technetium ($^{99\text{m}}\text{Tc}$) tetrofosmin or technetium ($^{99\text{m}}\text{Tc}$) sestamibi and recombinant TSH in follow up of thyroid cancers. Whole body scintigraphy with $^{131}\text{I}/^{123}\text{I}$ under TSH stimulation in diagnosing recurrent differentiated thyroid cancers after total thyroidectomy with ablation therapy with ^{131}I ; importance and role in diagnostic algorithms, activities and instrumentation. Recombinant hTSH and diagnostics of recurrence in suppression therapy conditions. Biochemical recurrence and diagnostic localization of non-iodine-avid cancers: flip-flop phenomenon and role of ^{201}Tl , $^{99\text{m}}\text{Tc}$ -MIBI, $^{99\text{m}}\text{Tc}$ -tetrofosmin and ^{18}F FDG.

Course delivery methods

Lectures, seminars and exercises.

Students' responsibilities

Student is required to regularly attend and actively participate in all course delivery forms. In order to be able to successfully complete seminars and exercises, the student is required to prepare by reviewing the relevant chapter in the course textbook. For performing exercises and working in the laboratory, the student has to have the required work clothing (white coat).

Monitoring students' work (Connecting learning outcomes, teaching methods and evaluation)

Teaching activity	ECTS	Learning outcome	Student activity	Assessment methods	Grade points	
					Min.	Max.
Attending classes	0.1	1-10	Attendance	Attendance records	5	10
Practical work (exercises)	0.1	1-10	Learning for the practical exam and attending classes	Completing tasks	5	10
Seminar paper	0.4	1-10	Preparing a seminar paper	Seminar paper presentation	10	20
Written exam	1	1-10	Continuous learning during the course	Written exam	20	30
Oral exam	0.4	1-10	Continuous learning during the course	Oral exam	10	30
Total	2				50	100

Attending classes

Student is required to attend at least 70% of all forms of course delivery (lectures, seminars and exercises). Student who has been absent from more than 30% of each form of course delivery may be instructed to take a makeup midterm exam to make up for such absence. The makeup examination will be taken with the teacher who referred the student to take the makeup exam. In order to be able to take the final exam, the student requires the teacher's signature in the student record book as proof of regular attendance.

Students' work is evaluated during classes and in the final exam. Students are given numerical and descriptive grades: insufficient (1), sufficient (2), good (3), very good (4) and excellent (5). During each block of courses, the student will be able to earn a maximum of 100 grade points. In various form of course delivery (Table 1) students will be able to earn a maximum of 40 points. Student has

to pass a written essay to be able to attend the oral part of the exam. Final grade is based on the sum of grade points earned during classes and in the final exam.

Practical work (exercises):

During classes there will be 12 clinical exercises, in the context of which the student may earn a maximum of 10 grade points. At each individual clinical exercise the student may earn 0.8 grade points. Assessment of practical work involves an individual clinical exercise for which the student attendance record is kept.

Seminars:

During classes there will be 6 seminars, in the context of which the student may earn a maximum of 20 grade points, through active participation. At each individual seminar the student may earn 3.3 grade points.

Lectures:

By attending lectures the student may earn a maximum of 10 grade points. At each individual lecture the student may earn 1.4 grade points.

Final exam

The student who attended classes and earned a minimum of 20 grade points in total from the exercises, seminars and lectures and who has earned at least 12 grade points in the written essay, becomes entitled to take the oral part of the final exam.

Written part of the final exam comprises 20 questions with five answers offered, only one of which is correct. Minimum criteria for earning the grade points is 60% of correct answers. Points acquired in the written part of the final exam are converted in grade points according to the criteria listed in Table 1. Points earned in the final exam are added to the points achieved in classes. In the event that the student fails to satisfy the minimum criteria on the first examination date, he/she will take the exam again on the next date scheduled for that exam, and the same applies if the student fails the oral part of the exam.

Table 1 Evaluation of written part of exam

Evaluation of written part of exam - percentage (%)	Grade points
65-69.99	12
70.00-74.99	16
75-79.99	18
80-84.99	20
85-89.99	22
90.00-94.99	24
95-100	30

Evaluation of written part of final exam:

- 1 – 10 grade points: answer satisfies minimum criteria
- 11 – 16 grade points: average answer with clearly identifiable errors
- 17 – 24 grade points: very good answer with minor errors
- 25 – 30 grade points: excellent answer

Final exam is obligatory and it consists of a written part and an oral part. In the final exam a student may earn a maximum of 60 grade points, of which 30 grade points pertain to the written part and

30 to the oral part. Points earned in the written part are converted to grade points according to the criteria listed in Table 1. Points earned in the final exam are added to the points achieved in classes. In the event that the student fails to satisfy the minimum criteria on the first examination date, he/she will take the exam again on the next date scheduled for that exam.

Calculation of the final grade:

Grade points earned in the final exam are added to the grade points earned in course classes. Grading is done by absolute distribution, i.e. based on overall result. Grades are numerically expressed as follows:

- A – Excellent (5): 80-100 grade points
- B – Very good (4): 70-79 grade points
- C – Good (3): 60-69 grade points
- D – Sufficient (2): 50-59 grade points
- E – insufficient (1): less than 49 grade points

Required reading (available in the library and through other media)

	Number of copies in the library	Availability through other media
Bence-Žigman Z, Kusić Z et al. Dijagnostika i liječenje bolesti štitnjače. In: Dodig D, Kusić Z., editors. Klinička nuklearna medicina. Second revised and amended edition. Course textbook. Zagreb, Medicinska naklada, 2012., pp. 53-110.	11	

Further reading

1. Kusić Z. et al. Hipertireoza. Zagreb: Medicinska naklada; 2016.
2. Kusić Z. et al. Hipotireoza. Zagreb: Medicinska naklada; 2014.
3. Solter M. Bolesti štitnjače - klinička tireoidologija. Course textbook. Zagreb: Medicinska naklada; 2007.
4. Biersack H-J, Grünwald F, editors. Thyroid cancer, 2nd ed. Berlin-Heidelberg: Springer-Verlag; 2005.

Course evaluation procedures

The quality and success in delivery of course content is evaluated by an anonymous student survey, which includes students’ assessment of the quality of various forms of course delivery and about the teachers. The survey is performed by the Nuclear Medicine and Oncology Department of the Faculty of Medicine Osijek. Moreover, students’ acquired knowledge after the course is evaluated based on their result at the end of the course. A record is kept at classes of the students’ attendance at lectures, seminars and exercises.

In addition to that, the quality of the teaching process is also monitored based on a uniform university study, which is conducted among the students with a view of them evaluating the teachers. The survey is provided by the Senate of Josip Juraj Strossmayer University of Osijek.

Note

E-learning is not included in the class quota, but it is used in teaching and it contains links to various sites and video and audio materials available online.