



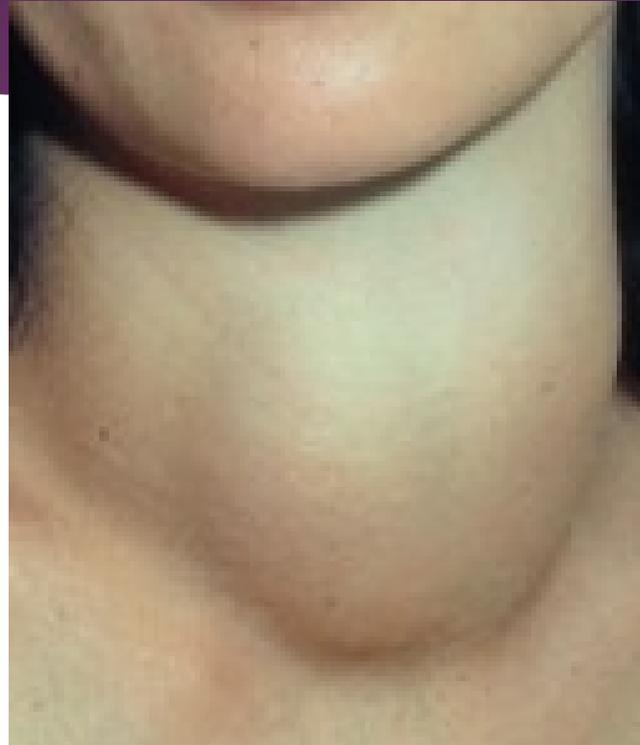
THYROID NODULES AND THYROID CANCER

DEPARTMENT OF ENDOCRINOLOGY, DIABETES AND ISOTOPE THERAPY

WROCLAW MEDICAL UNIVERSITY

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THYROID NODULES



THYROID NODULES

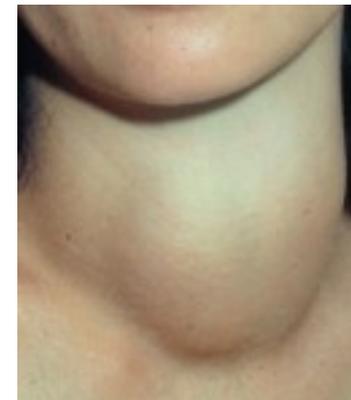
Benign

- ▶ Colloid-filled follicles
- ▶ Adenomas
- ▶ Cysts
- ▶ Lymphocytic thyroiditis
- ▶ Painful (subacute, deQuervain) thyroiditis

Malignant

- ▶ Papillary
- ▶ Follicular
- ▶ Medullary
- ▶ Anaplastic

- ▶ Lymphoma
- ▶ Metastases



Prevalence of thyroid nodules

- ▶ Clinical findings 7-15%
- ▶ US findings 30-40%
- ▶ Autopsy findings **50%**
- ▶ DTC (autopsy) 4-8%

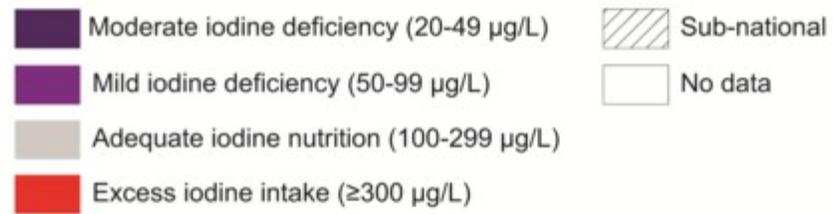
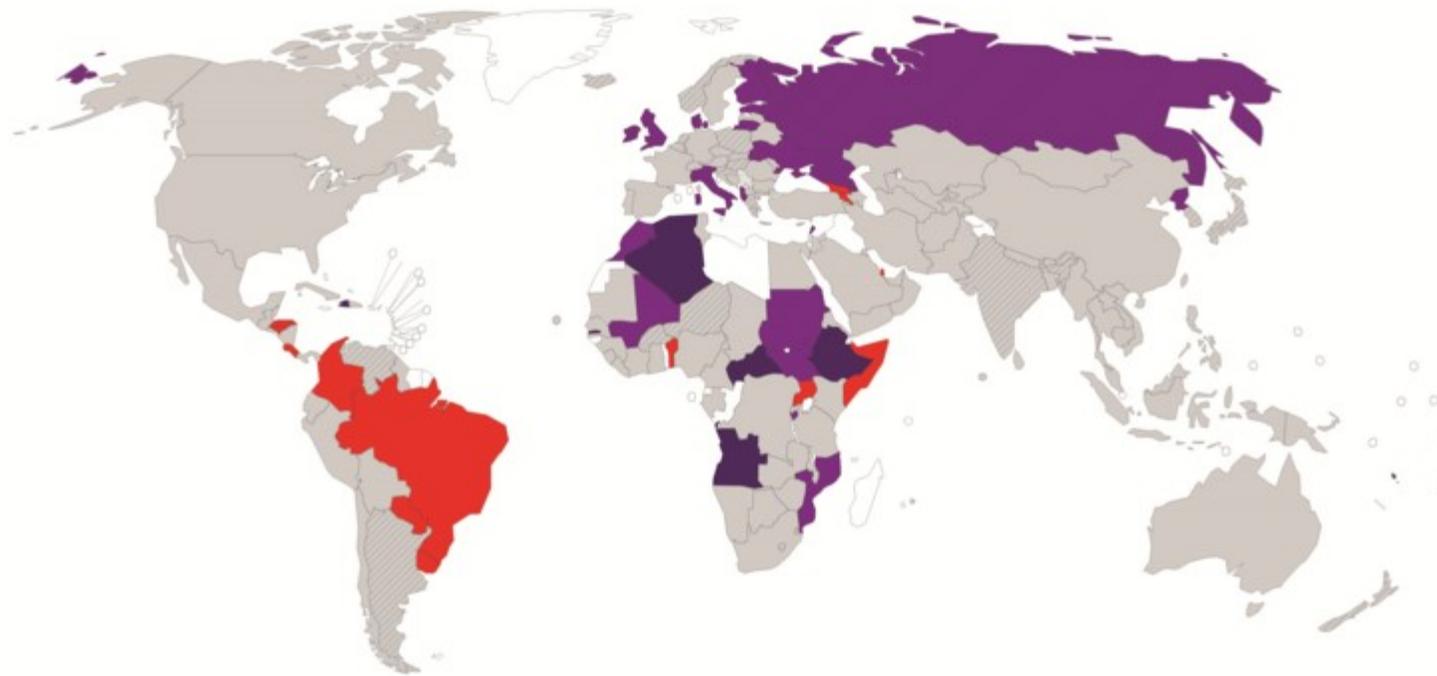
CAUSES OF TYROID NODULES

Primary factors

- ▶ Functional heterogeneity of normal follicular cells, cause unknown, possibly genetic and acquisition of new inheritable qualities by replicating epithelial cells
- ▶ Subsequent functional and structural abnormalities in growing goiters

Secondary factors (Stimuli to New Follicle Generation)

- ▶ TSH (induced by, e.g., iodine deficiency, goitrogens, inborn errors of thyroid hormone synthesis)
- ▶ Other thyroid-stimulating factors (TGF- β , EGF, IGF)



NATURAL HISTORY OF MULTINODULAR GOITER

- ▶ Usually the goiter **grows gradually** for a period of a few to many years, and then becomes stable with little tendency for further growth
- ▶ Spontaneous **reduction** in the size of the thyroid gland **is very rare**

NATURAL HISTORY OF MULTINODULAR GOITER

- ▶ Rarely, if ever, do the patients become hypothyroid and if they do, the diagnosis is more probably Hashimoto's thyroiditis than nodular goiter
- ▶ If the goiter is present for a long time, thyrotoxicosis develops in a large number of patients (8-10%)

Multinodular goiter – indications for surgical treatment

Vena cava superior syndrome – dilatation of superficial chest veins









Toxic Multinodular Goiter

- ▶ More common in places with lower iodine intake
 - ▶ Accounts for **less than 5%** of thyrotoxicosis cases in iodine-sufficient areas and **up to 50% in iodine-deficient** areas
- ▶ Evolution from sporadic diffuse goiter to toxic multinodular goiter is gradual
- ▶ **TSH receptor mutations** mutations have been found in some patients with toxic multinodular goiters
- ▶ Surgery or ^{131}I is recommended – **(radical treatment)**

SIGNS AND SYMPTOMS OF GOITER

(usually asymptomatic)

- ▶ Presence of an enlarging mass in the neck
- ▶ Dysphagia, cough, and hoarseness
- ▶ Paralysis of a recurrent laryngeal nerve (very unusual – suggesting cancer)
- ▶ Horner's syndrome (rather rare)
- ▶ Symptoms suggesting constriction of the trachea (dyspnoe)

Multinodular goiter and single nodule – management

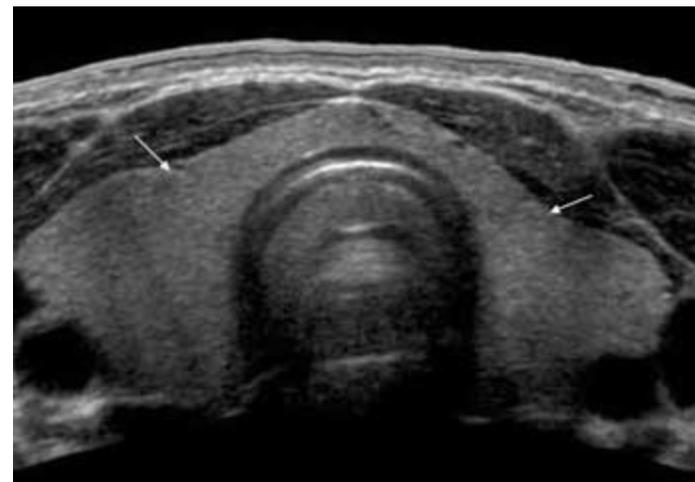
- ▶ Prophylaxis – on national level
- ▶ Exclusion of malignancy
- ▶ Follow – up
- ▶ LT4 treatment – rarely in young subjects,
efficacy not confirmed
- ▶ Thyroidectomy

DIAGNOSTIC TESTS

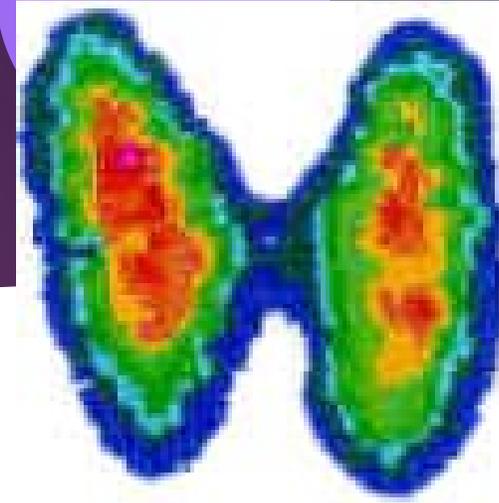
- ▶ TSH, fT4
- ▶ AntiTPO, TRab
- ▶ USG
- ▶ Isotope scintigraphy (?)
- ▶ Chest X-ray
- ▶ **FNAB**

Ultrasound of thyroid

- ▶ rapid, simple, inexpensive
- ▶ **extremely sensitive**
- ▶ thyroid and nodule measurement
(follow up)
- ▶ nodule solid or cystic
- ▶ US assisted FNAB



Thyroid scintigraphy



- ▶ ^{99m}Tc , ^{131}I
- ▶ **function** of the nodule: cold, warm, toxic
- ▶ sensitivity (cold + warm) 96%
- ▶ specificity for TC 17%



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Data badania: 2012-11-22

ID pacjenta: [REDACTED]

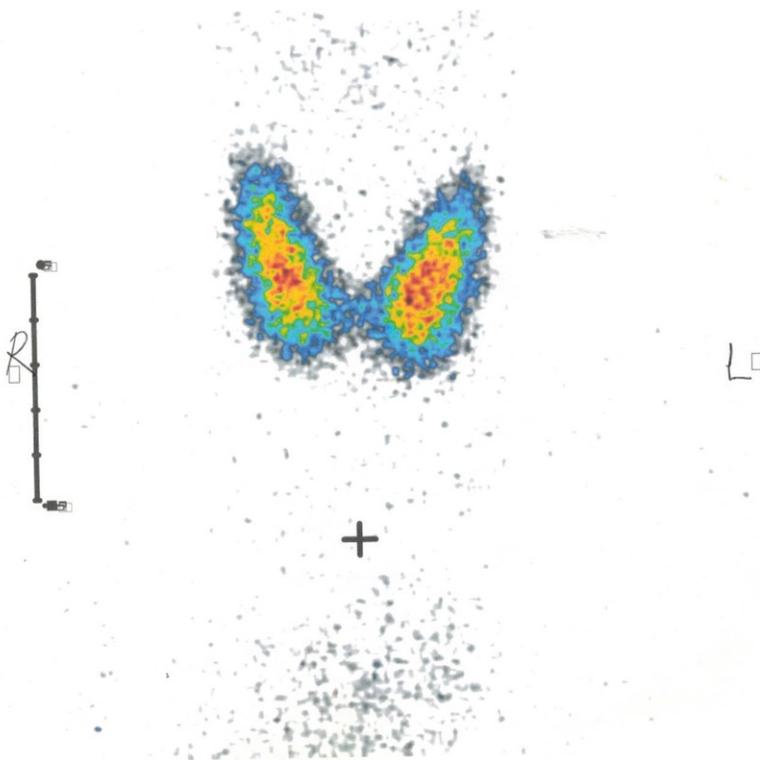
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Kierujący: DR TRZMIEL-BIRA A.

ID badania: TT121410

Wykonujący: A.ZIAJSKA 650 CPS

SCYNTYGRAFIA TARCZYCY Tc-99m





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Imię i nazwisko:

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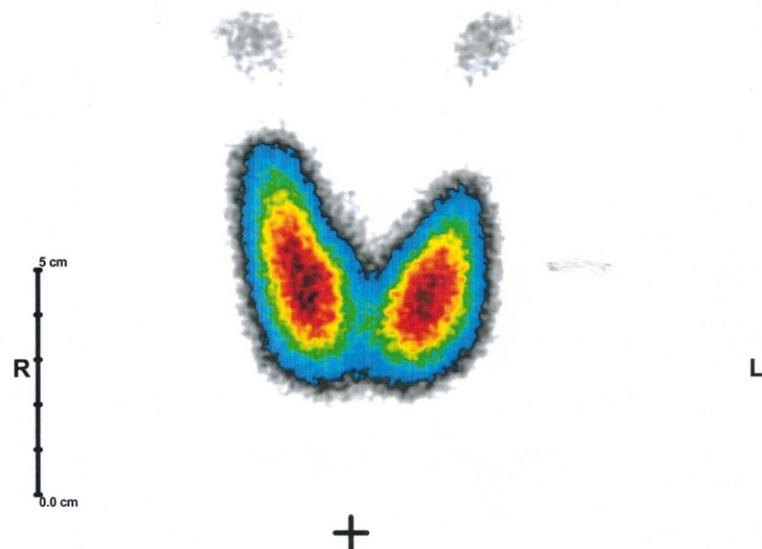
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Kierujący: DR. JEDRZEJUK D.

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SCYNTYGRAFIA TARCZYCY Tc-99m



TT AP[1]



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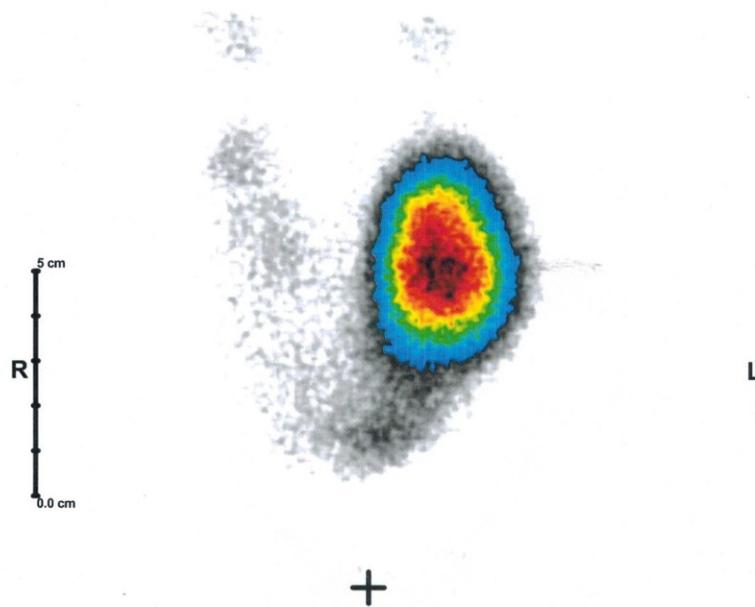
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Kierujący: DR JEDRZEJUK D.

ID badania: TT143338

Wykonujący: A.ZIAJSKA 650 CPS

SCYNTYGRAFIA TARCZYCY Tc-99m



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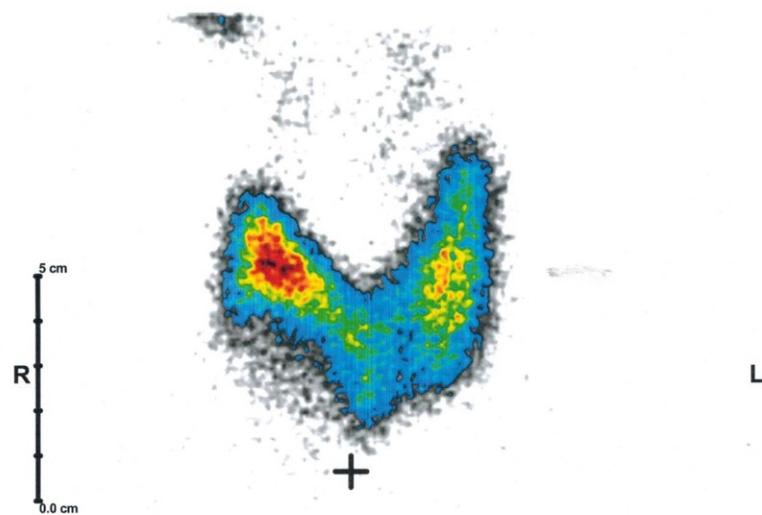
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Kierujący: DR BOHDANOWICZ-PAWLAK A.

ID badania: TT143238

Wykonujący: A.ZIAJSKA 450 CPS

SCYNTYGRAFIA TARCZYCY Tc-99m



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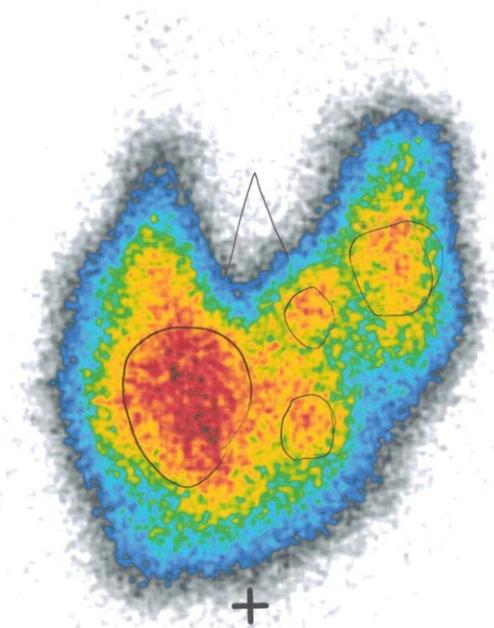
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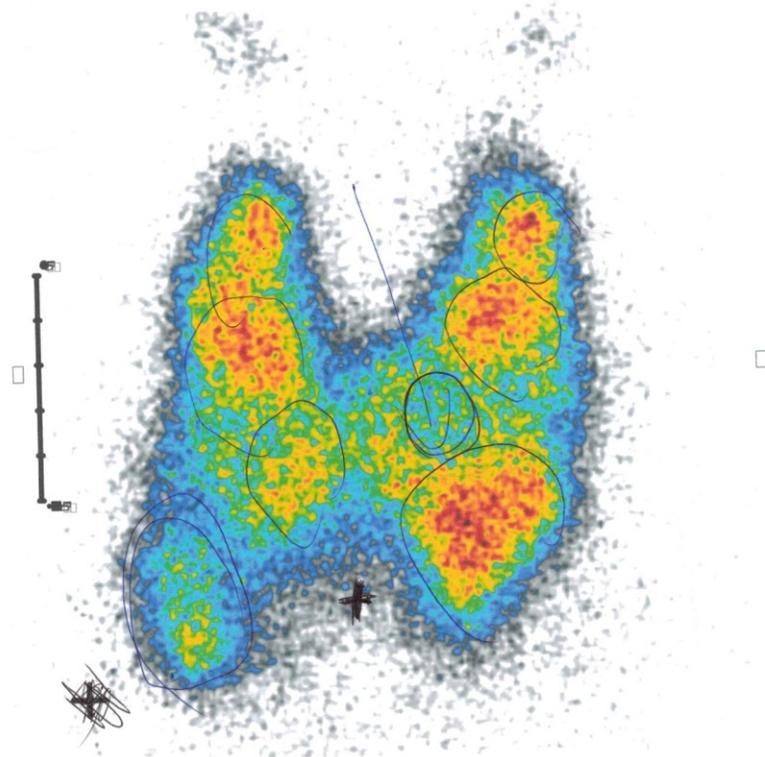
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Imię i nazwisko: BOHECKA IZABELA

Data badania: 2012-07-26

ID pacjenta: 1340

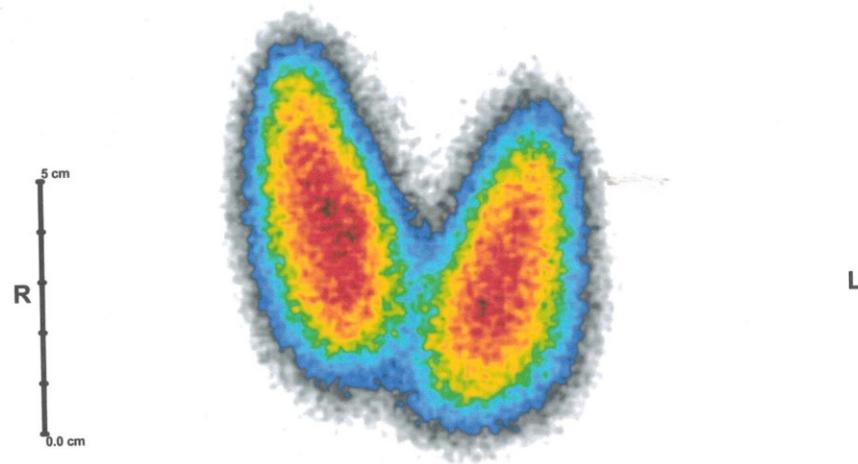
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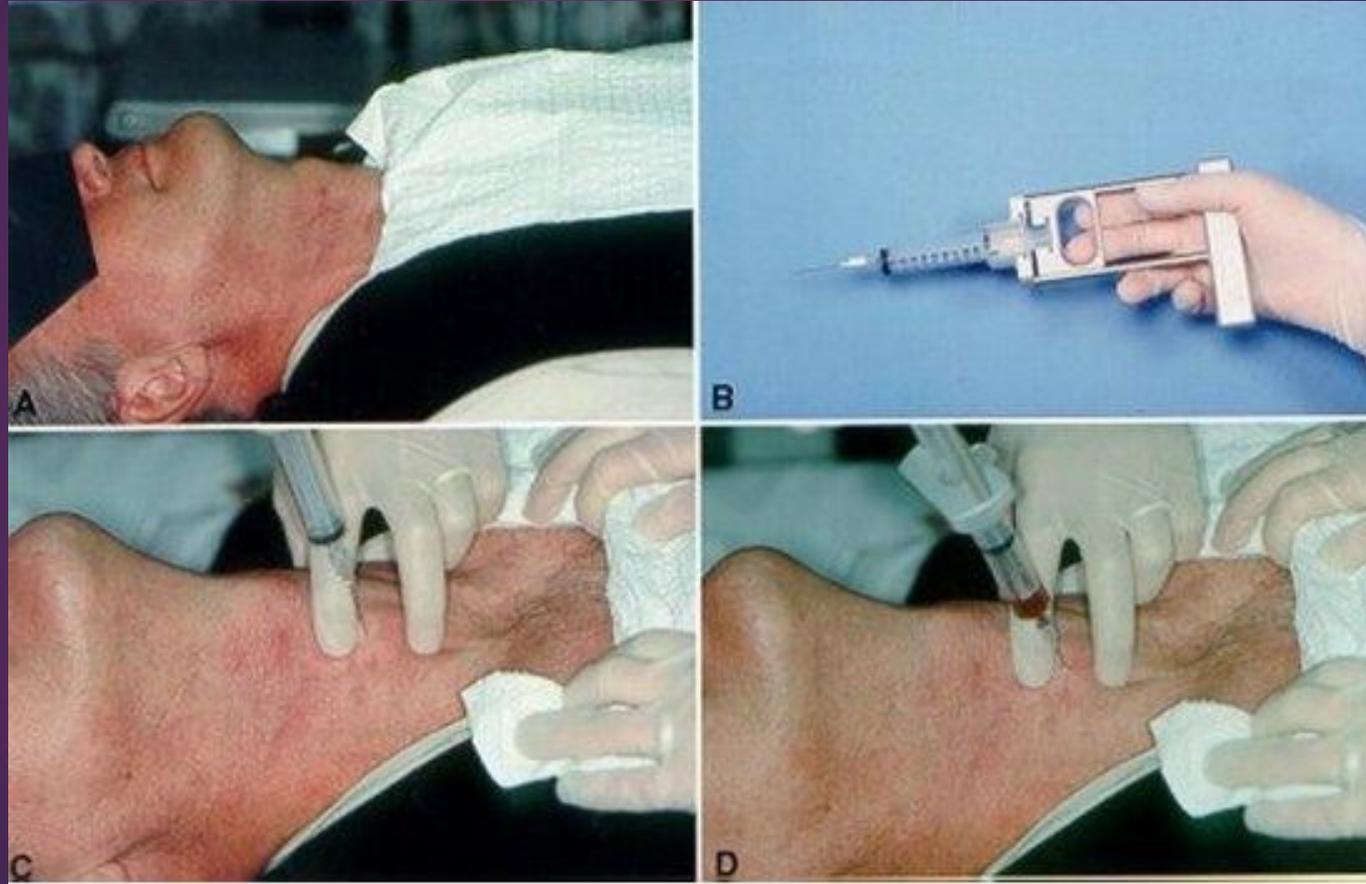
SCYNTYGRAFIA TARCZYCY Tc-99m



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FNAB



Indications for FNAB

- ▶ Single palpable tumour
- ▶ Multinodular goiter
 - solid hypoechogenic nodules,
 - microcalcifications
 - poorly defined or irregular margins
 - intranodular vascularity
 - enlarged lymph nodes on the site of the nodule
- ▶ Painful goiter or goiter of increased compactness
- ▶ Foci found on US > 1 cm (especially hypoechogenic)

Advantage of Fine Needle Aspiration Biopsy

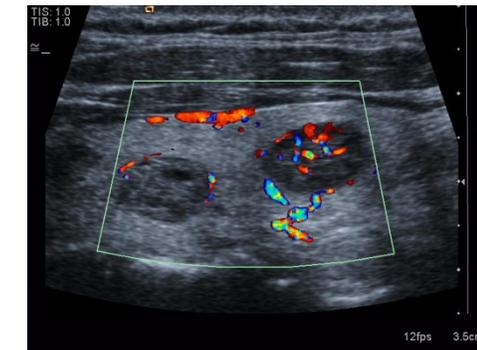
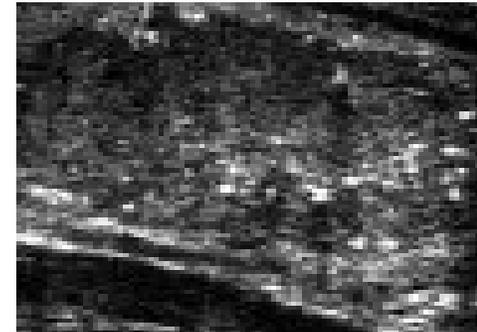
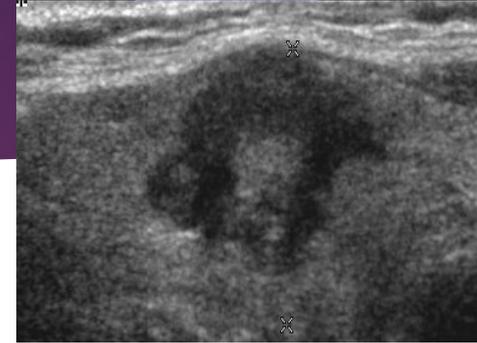
- ▶ nodules > 10 mm
- ▶ high sensitivity
- ▶ high specificity
- ▶ simple ??

Bethesda system of reporting thyroid cytopathology. Implied risk of malignancy and recommended clinical management

Diagnostic Category	Risk of Malignancy, %	Usual Management
Nondiagnostic or unsatisfactory	1-4	Repeat FNA with ultrasonographic guidance
Benign	0-3	Clinical follow-up
Atypia of undetermined significance or follicular lesion of undetermined significance	5-15	Repeat FNA
Follicular neoplasm or suspicious for a follicular neoplasm NF	15-30 5+10%	Surgical lobectomy
Suspicious for malignancy	60-75	Near-total thyroidectomy or surgical lobectomy
Malignant	97-99	Near-total thyroidectomy

Increased risk of malignancy – ultrasound

- ▶ Metastatic lymph nodes
- ▶ Infiltration of surrounding organs
- ▶ Microcalcifications
- ▶ Hypoechogenic
- ▶ Irregular margins
- ▶ More tall then wide
- ▶ Intranodular vascularisation



Decreased risk of malignancy - ultrasound

- ▶ Hyperechogenic
- ▶ Simple cyst
- ▶ Spongiform nodule
- ▶ Isolated macrocalcification
- ▶ Toxic nodule - scintigraphy

Clinical features of malignancy

- ▶ Metastases to lymph nodes or distant meta
- ▶ Familial history
- ▶ Exposition on external radiation in history
- ▶ Speed growth of a nodule
- ▶ Firm consistency
- ▶ Fixation to environment
- ▶ Diameter > 4 cm
- ▶ Age at diagnosis < 20 and > 60

Multinodular goiter – indications for surgical treatment

URGENT

- Compression of tracheae with ventilation disturbances
chest X-ray, US, CT, SPECT-CT
- Vena cava syndrome - due to compression of retrosternal goiter
- Dysphagia

Multinodular goiter – indications for surgical treatment

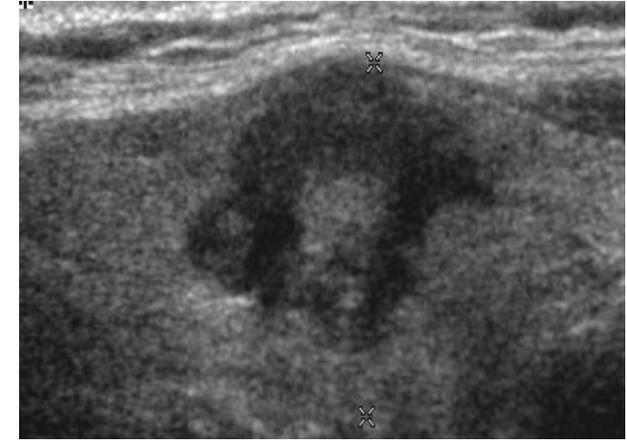
X-ray - dislocation and stenosis of trachea



Multinodular goiter – indications for surgical treatment

SCHEDULED

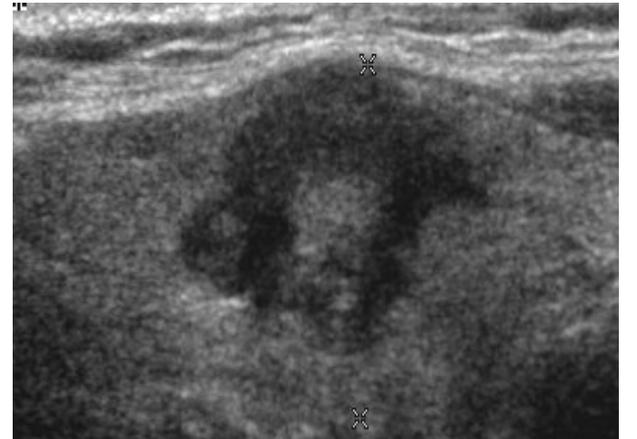
- Reasonabe suspicion of malignancy - based on clinical features and/ or FNAB
- Some risk factors of malignancy in multinodular goiter
- Retrosternal, mediastinal goiter
- High calcitonin level, MEN2 syndrome, RET mutation (molecular tests)



Multinodular goiter – indications for surgical treatment

RELATIVE

- Large goiter
- Cosmetic reasons – patient's choice



Epidemiology of thyroid cancer

- ❖ Infrequent
- ❖ 0.5-1.5% of all malignancies
- ❖ 90% of cancers in endocrinology

THYROID CANCER

- ▶ quite rare
- ▶ accounting for only 1.5% of all cancers in adults
- ▶ accounting for 3% of all cancers in children
- ▶ the rate of new cases increasing in recent decades
- ▶ in contrast to other cancers, thyroid cancer - almost always curable

THYROID CANCER

- ▶ the most common endocrine malignancy
- ▶ arising from follicular cells (adenoma, carcinoma, and follicular/papillary carcinoma) - a broad range of overlapping clinical and cytologic features
- ▶ follicular and papillary thyroid cancers - differentiated thyroid cancers
- ▶ together making up 95% of thyroid cancer cases

THYROID CANCER EPIDEMIOLOGY AND CHARACTERISTICS

- ▶ Of all thyroid cancers, 74-80% of cases are papillary cancer.
- ▶ Of all thyroid cancers, 17-20% are follicular ones.
- ▶ Follicular carcinoma incidences are higher in regions where goiter is common.
- ▶ The most common presentation of thyroid cancer is an asymptomatic thyroid mass or a nodule that can be felt in the neck.

Types of thyroid carcinoma

	Poland	USA	
❖ Papillary (PTC)	65%	80%	} DTC
❖ Follicular (FTC)	20%	>5%	
❖ Medullary (MTC)	5%	>5%	C-cells
❖ Anaplastic (ATC)	10%	<5%	

Factors influencing carcinogenesis of TC

- ❖ Log-term TSH stimulation DTC
- ❖ Ionising radiation PTC(+++) FTC(+)
- ❖ I deficiency FTC
- ❖ I excess PTC
- ❖ Genetic factors MTC
- ❖ Thyroiditis lymphoma
- ❖ neoplasms persisted
after 131-I treatment ATC

Papillary thyroid carcinoma characteristics

- ▶ most common (65%)
- ▶ mostly in young (< 45 yrs)
- ▶ multifocal
- ▶ local metastases to lymph nodes
- ▶ very good prognosis

PAPILLARY THYROID CARCINOMA CHARACTERISTICS

- ▶ - the most common form of well-differentiated thyroid cancer
- ▶ - the most common form of thyroid cancer to result from exposure to radiation
- ▶ -propensity to invade lymphatics but are less likely to invade blood vessels.

PAPILLARY THYROID CANCER PATHOGENESIS

- ▶ several chromosomal rearrangements in papillary thyroid carcinoma
- ▶ chromosomal rearrangements involving the rearranged during transfection (*RET*) proto-oncogene, which arises from a paracentric inversion of chromosome 10
- ▶ molecules that physiologically regulate the growth of the thyrocytes (interleukin-1, interleukin-8), or other cytokines (eg, insulin-like growth factor-1, transforming growth factor-beta, epidermal growth factor) could play a role in the pathogenesis of this cancer.

PAPILLARY THYROID CANCER PATHOGENESIS

- ▶ mutation in the *BRAF* gene - prominent in papillary thyroid carcinoma
- ▶ the *BRAF* V600E mutation is associated with aggressive clinicopathological characteristics of papillary thyroid carcinoma, (including lymph node metastasis, extrathyroidal invasion, and loss of radioiodine avidity)

PAPILLARY THYROID CANCER PATHOGENESIS

- ▶ a clear association between radiation exposure (from radiotherapy or fallout) and incidence of papillary thyroid carcinoma
- ▶ Port et al report:
 - ▶ papillary thyroid cancers in patients exposed to radiation from the Chernobyl accident could be completely distinguished from sporadic papillary thyroid cancers in patients with no history of radiation exposure, on the basis of gene expression patterns involving seven genes (ie, *SFRP1*, *MMP1*, *ESM1*, *KRTAP2-1*, *COL13A1*, *BAALC*, *PAGE1*)

PAPILLARY THYROID CANCER PATHOGENESIS

- ▶ Approximately 7% of individuals exposed to the atomic bombs in Japan developed thyroid cancers.
- ▶ Individuals, especially children, who lived in Ukraine during the time of the Chernobyl nuclear event may have increased risk of papillary thyroid cancer.

THYROID MICROCARCINOMA CHARACTERISTICS

- ▶ A study by Yu et al found that papillary thyroid microcarcinomas are generally associated with an excellent prognosis; however, 0.5% of patients may die.

Thyroid microca. has a perfect prognosis

AUTHOR	n	Follow-up (Yrs)	Specif. mortality
Baudin, 1998	281	7	4%
Hay, 2008	900	17	0,3%
Chow, 2003	203	8	1%
Noguchi , 1996	867	13	0,2%
Yamashita, 1999	1743	12	0,2%
Buffet, 2012	669	7	0%

SYMPTOMS OF THYROID CANCER

- ▶ The principal sign of thyroid carcinoma - a palpable nodule, usually solitary
- ▶ In the thyroid area that has the following characteristics:
 - ▶ Painless
 - ▶ Hard consistency
 - ▶ Average size of less than 5 cm
 - ▶ Ill-defined borders
 - ▶ Fixed in respect to surrounding tissues
 - ▶ Moves with the trachea at swallowing
 - ▶ Cervical lymphadenopathy (if present)
 - ▶ palpable on either the ipsilateral or contralateral
 - ▶ tight or full feeling in the neck, hoarseness, or signs of tracheal or esophageal compression.

THERAPY OF THYROID CANCER

- ▶ Surgery - the definitive management of papillary thyroid cancer
- ▶ Total thyroidectomy
- ▶ Radioiodine therapy - approximately 4-6 weeks after surgical thyroid removal
- ▶ Radioiodine therapy
 - ▶ detection and destruction of any metastasis and residual tissue in the thyroid
- ▶ A diagnostic dose of radioiodine (^{131}I or ^{123}I)
- ▶ A whole-body scintiscan
- ▶ If any normal thyroid remnant or metastatic disease is detected, a therapeutic dose of ^{131}I is administered to ablate the tissue.
- ▶ Thyroid hormone replacement (levothyroxine) therapy.
- ▶ Lifelong thyroid hormone replacement therapy, especially after total thyroidectomy

Treatment and follow-up of DTC- summary

- ▶ Primary surgery - (near) total thyroidectomy lobe + isthmus
- ▶ Secondary surgery
- ▶ Radioiodine therapy – ^{131}I
- ▶ TSH suppression with LT_4
- ▶ Thyroglobulin (TG) is a marker in follow-up

Follicular thyroid carcinoma

- ▶ 20% of all thyroid cancers
- ▶ TSH-dependent
- ▶ all ages
- ▶ blood vessels invasion
- ▶ distant metastases: lungs, bone
- ▶ mean survival ca. 10 – 15 yrs.

FOLLICULAR THYROID CANCER CHARACTERISTICS

- ▶ Follicular thyroid carcinoma (FTC)
- ▶ a well-differentiated tumor
- ▶ resembles the normal microscopic pattern of the thyroid
- ▶ originates in follicular cells
- ▶ the second most common cancer of the thyroid, after papillary carcinoma.
- ▶ may be overtly or minimally invasive

FOLLICULAR CANCER PATHOGENESIS

- ▶ Activating point mutations in the *ras* oncogene
- ▶ Especially in poorly differentiated (55%) and anaplastic carcinoma (52%)

FOLLICULAR CANCER PATHOGENESIS

- ▶ Several reports have shown a relationship between iodine deficiency and the incidence of thyroid carcinoma.
- ▶ Incidence of FTC has decreased in geographic areas of endemic goiter after iodized salt was introduced.

Medullary thyroid carcinoma characteristics

- ▶ derives from parafollicular C cells
- ▶ 5-10% thyroid malignancies
- ▶ 10% familial (autosomal dominant) - MEN IIA, MEN IIB
isolated
- ▶ calcitonin (CT) - marker of MTC
(basal and after pentagstrin, Ca, or omeprozol stimulation)
- ▶ Thyroid surgery with adenectomy
- ▶ Teleradiotherapy

MEDULLARY CARCINOMA EPIDEMIOLOGY

- ▶ Medullary carcinoma of the thyroid (MTC)
- ▶ a distinct thyroid carcinoma
- ▶ originates in the parafollicular C cells of the thyroid gland
- ▶ C cells - calcitonin
- ▶ Sporadic, or isolated, MTC accounts for 75% of cases
- ▶ inherited MTC constitutes the rest
- ▶ Inherited MTC occurs in association with multiple endocrine neoplasia (MEN) type 2A and 2B syndromes, but non-MEN familial MTC also occur.

MEDULLARY CARCINOMA SYMPTOMS

- ▶ Medullary thyroid cancer (MTC)
- ▶ on physical examination - a solitary neck nodule
- ▶ common - early spread to regional lymph nodes
- ▶ distant metastases in the liver, lung, bone, and brain
- ▶ Sporadic MTC usually unilateral
- ▶ In association with multiple endocrine neoplasia (MEN) syndromes always bilateral and multicentric

MEDULLARY CANCER PATHOGENESIS

- ▶ Mutations in the *RET* (REarranged during Transfection) proto-oncogene
- ▶ A receptor protein tyrosine kinase encoded on chromosome 10
- ▶ Prophylactic thyroidectomy can now be offered to specific types of patients with this genetic abnormality.

MEDULLARY CANCER CLINICAL FEATURES

- ▶ A specific constellation of symptoms of medullary thyroid carcinoma (MTC) is not usually noted; however, one or more of the following symptoms may be observed:
- ▶ Patients may describe a lump at the base of the neck, which may interfere with or become more prominent during swallowing
- ▶ Patients with locally advanced disease may present with hoarseness, dysphagia, and respiratory difficulty
- ▶ Physical examination may demonstrate a dominant thyroid nodule at the base of the neck.
- ▶ Palpable cervical lymphadenopathy signifies disease that has progressed locally.

MEDULLARY CANCER MANAGEMENT

- ▶ Perform a total thyroidectomy and central neck dissection for cases of symptomatic (clinically detected) MTC.
- ▶ Prophylactic thyroidectomy is indicated for carriers of *RET* mutations who have no apparent disease but are at risk for aggressive MTC.

Anaplastic thyroid carcinoma characteristics

- ▶ older age (over 60 yrs)
- ▶ rapid local invasion, distant metastases - lungs
- ▶ survival 4-6 months after diagnosis
- ▶ 5-10% of thyroid cancers
- ▶ Surgery, chemotherapy – not effective

Thyroid Carcinoma Summary

Type	%	Age	Spread	Prognosis
Papillary	65	Young <45 y	Lymph	Excellent
Follicular	20	Middle age	B.V.	Good
Anaplastic	10	Elderly	Local	Poor
Medullary	5	Elderly, familial	All	Variable