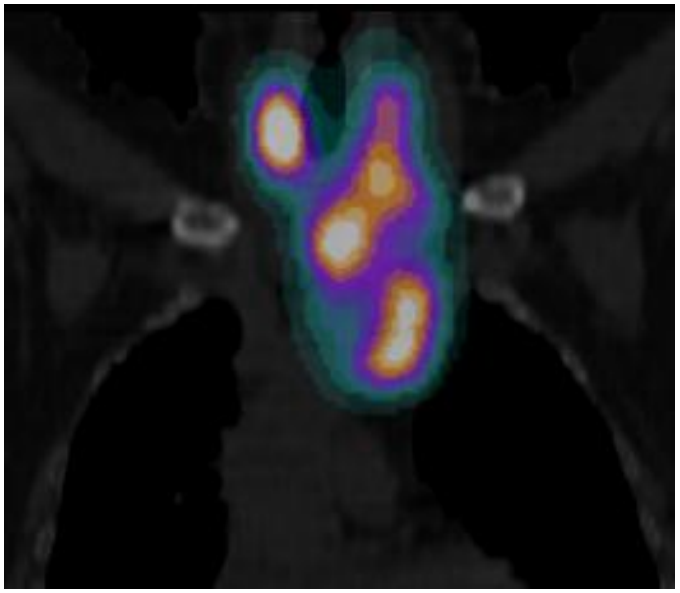
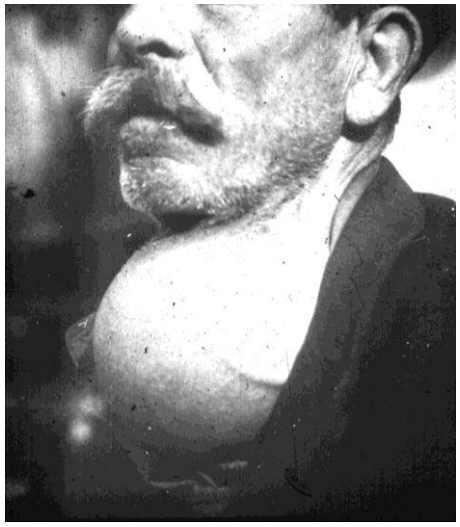
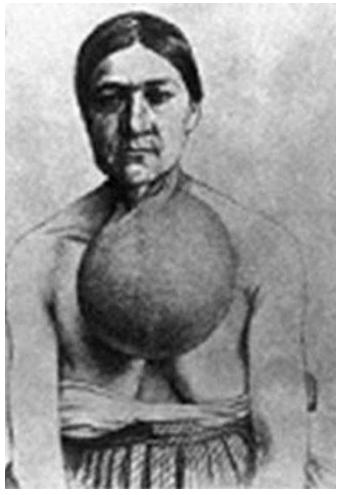
THYROID GOITER



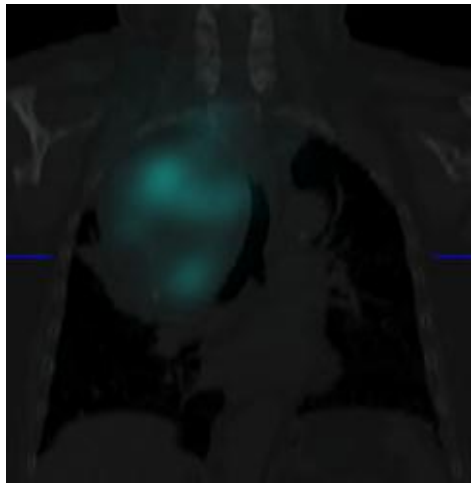




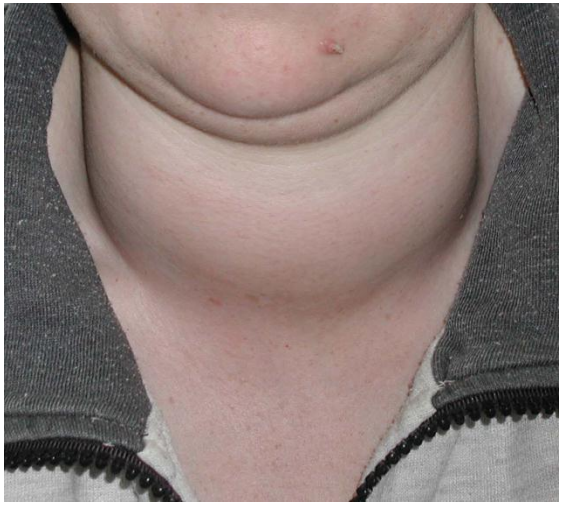
Assoc. prof. V. Marković, MD, PhD

Assoc. prof. A. Punda,MD, PhD

S. Gračan, MD, nucl. med. spec.



THYROID GOITER



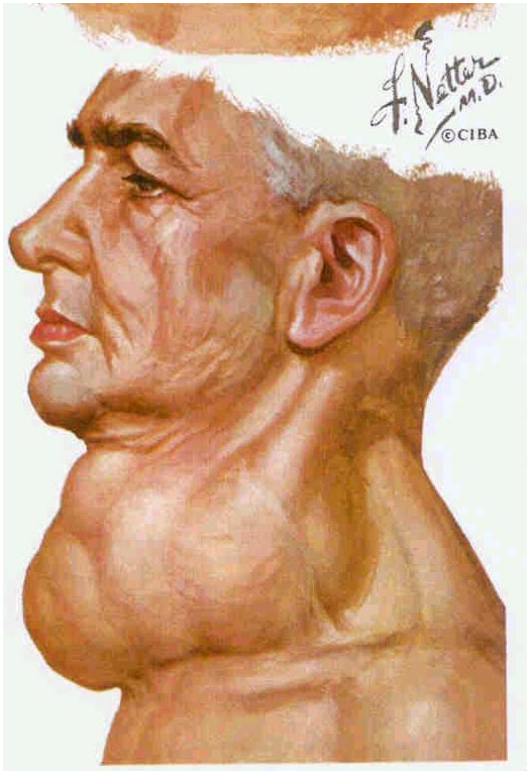
Diffuse goiter

Nodular goiter

Multinodular (polynodose)goiter

DIFFUSE GOITER

UNINODULAR GOITER



MULTINODULAR GOITER

Goiter – World Health Organisation Division (WHO)

- **Grade 0:** No goiter: hardly palpable and visible (or unpalpabile or unvisible)
- **Grade IA**: clearly palpable, but unvisible with neck extension
- **Grade IB**: clearly palpable and visible with complete neck extension (head thrown). This grade involves nodular goiter, even if the thyroid itself isn't enlarged
- **Grade II**: clearly visible when the head is in normal position (palpation isn't neccesery for diagnosis)
- **Grade III**: thyroid seen from the distance (palpation isn't neccesery for diagnosis)

Revised goiter division

Grade 0 Thyroid not enlarged by inspection or palpation

Grade 1 Goiter palpable, but not seen when head and neck are in normal position (thyroid isn't enlarged visualy). This category includes nodules in normal sized thyroid

Grade 2 Thyroid visible when head is in normal position, and palpatory enlarged

WHO, UNICEF, and ICCIDD. 2001. Assessment of the Iodine Deficiency Disorders and monitoring their elimination. Geneva: WHO publ. WHO/NHD/01.1. 1-107 pp.

What is a nodule?

- Inspection: thyroid thickening, asimetry.
- Palpation: part of the thyroid with different consistency.
- Ultrasonography: tumor of different echostructure or separated echostructure inside the thyroid.
- Scintigram: tumor of different function.

THYROID NODULES

- The most common thyroid disease (frequency 20-50%)

- Important clinical problem (thyroid cancer ~ 5%)

THE MOST COMMON CAUSES FOR THYROID NODULES

Benigne

- Folliculare adenoma
  - Macrofolliculare adenoma
  - Microfolliculare (fetale)
  - Trabecullare
  - Hürthle cell
- Multinodular goiter
- Cysts (colloid and hemorrhagic)
- Thyroiditis Hashimoto

THE MOST COMMON CAUSES FOR THYROID NODULES

Malignant

- Papillary and follicular carcinoma.
- Medullar carcinoma.
- Poorly differenciated and anaplastic carcinoma.
- Primary thyroid lymphoma.
- Metastatic carcinoma: melanoma, brest carcinoma and kidney carcinoma

Prevalence of thyroid nodules

1. * around 5% (3%–8%) **by palpation**

2. * 10 - 76% **by ultrasonography**

3. * 50% by patohistologic findings in autopsy in older people (Mortensen et al.J Clin Endocrinol Metab; 1955)

*** Increase with age**
*** More often in women**

DIFFERENTIAL DIAGNOSIS OF THYROID NODES

- 42-77% colloid nodes
- 15-40% adenomas
- 8-17% carcinomas

Mazzaferri EL. N Engl J Med 1993; 328:553-559.

THYROID NODULE'S INCIDENCE (by palpation)

- Incidence of palpable nodes
  (in areas with iodine deficit)

  ~ 5% in female

  ~ 1% in men

THYROID NODULE'S INCIDENCE (by palpation)

State	Nodule incidence	Author
SAD (Salt Lake City)	**2.3%** (young adults) **0.46%** (school children)	Rallison ML, 1991
England (Whickham)	**3.2%**	Turnbridge WMG, 1977
SAD (Massachusets)	**4.2%**	Vander JB, 1968
Italy (Sicily)	**5.1%**	Belfiore A, 1987
Denmark	**6.5%** (middle age women)	Christensen SB, 1984

THYROID NODULE'S INCIDENCE (by ultrasonography)

State	Nodule incidence	Author
SAD (Stanford)	**13.4%**	Caroll et al.; 1982
Japan (Tokushima)	**19.7%**	Miki et al.; 1993
Finland (Hyvinkaa)	**21.3%**	Brander et al.; 1991
Germany	**23.4%** (18-65 years)	Reiners et al.; 2004
Italy (Pescopagano)	**28.5%** (56-65 years)	Aghini-Lombardi et al.; 1999
Danmark (Copenhagen)	**32%** (41-71 years)	Knudsen et al.; 2000
Italy (Palermo)	**33%**	Bartolotta et al.; 2006
SAD (San Francisco)	**40**% (patients with hyperparathyroidisam)	Stark et al.; 1983
SAD	**46%**	Horlocker et al.; 1985

THYROID NODULE'S INCIDENCE (by autopsy)

State	Nodule incidence	Author
SAD	**13%** (solders age 18-39 years)	Oertel, Klinck 1965
Hungary	**27.1%** suficient iodine intake **44.6%** insuficient iodine intake	Kovacs et al. 2005
SAD	**50.5%**	Mortensen JD et al. 1955 (Mayo clinic)
Belarussia	**60%**	Furmanchuk et al. 1993

DIAGNOSIS AND TREATMENT OF PATIENTS WITH THYROID NODES

- Inspection and palpation
- TSH serum level
- Ultrasonography of the thyroid
- Thyroid scintigraphy ($^{99m}TcO_4^-$, ^{123}I, ^{131}I)
- Fine needle aspiration citology and Tg and Ct in aspirate
- RTG, CT, MR

Inspection and palpation

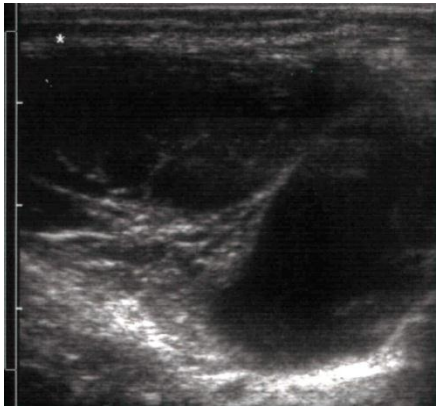
ULTRASONOGRAPHY

- Introduced in 1967. by Fujimoto as thyroid imaging method
- The most precise method for detection of thyroid nodes
- Detection of nodes larger then 2 mm
- Mandatory in palpable nodes.
- Ultrasound guided fine needle aspiration.

NODUlAR CHANGES: **Number, size, echostructure, position in the thyroid**

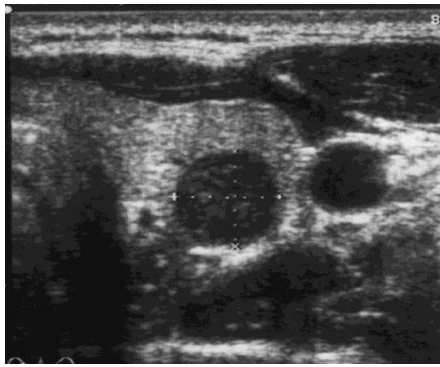
1. Cysts and cystic - degenerative noduleses
2. Single nodul - isoechogenic, hypoechogenic, degenerativly changed (benigne goiter)
3. Multinodular (polynodular) goiter
4. Nodul in lymphatic goiter

1.



2.

3.



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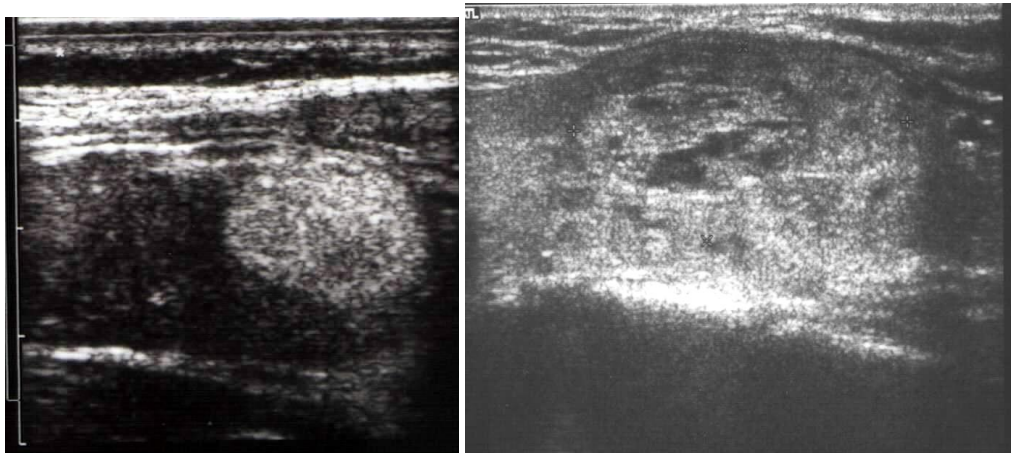
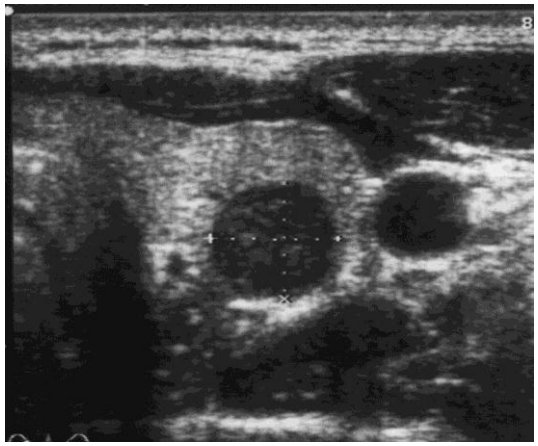
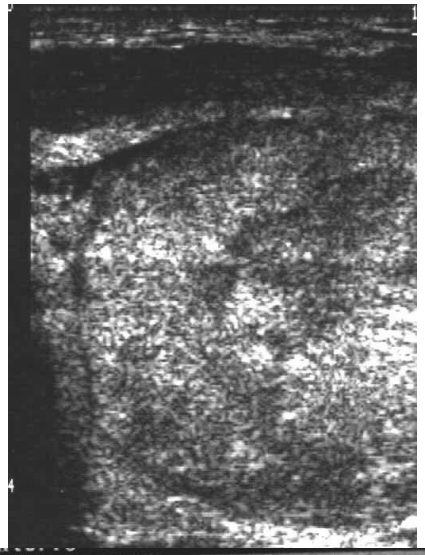
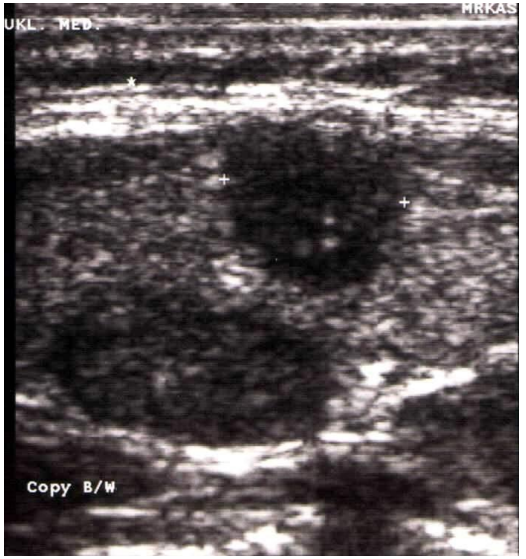
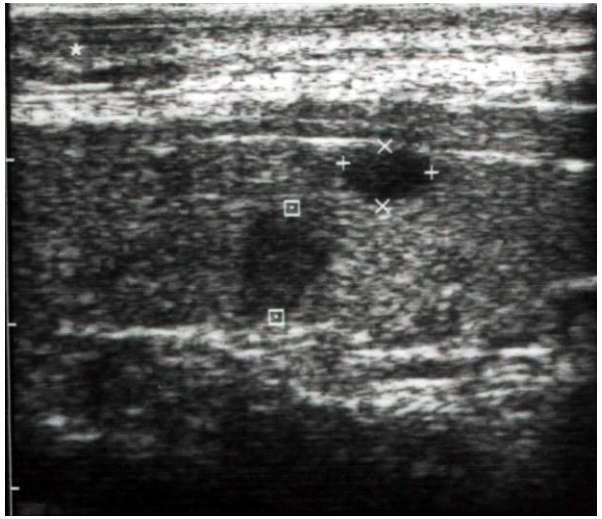


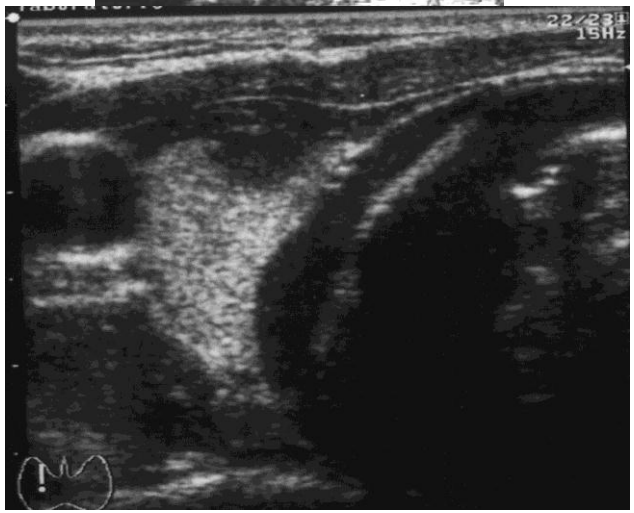
5. tumors- adenomas, cancers

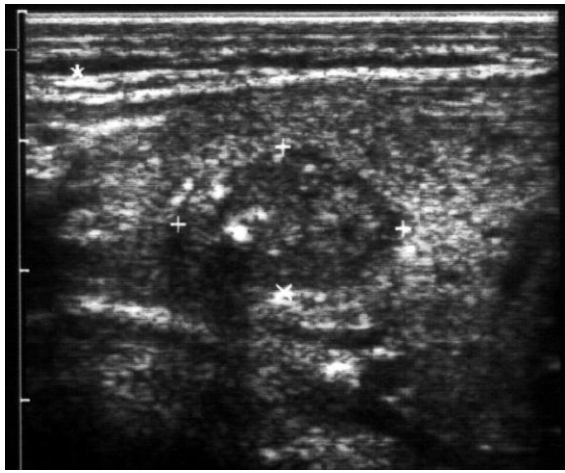


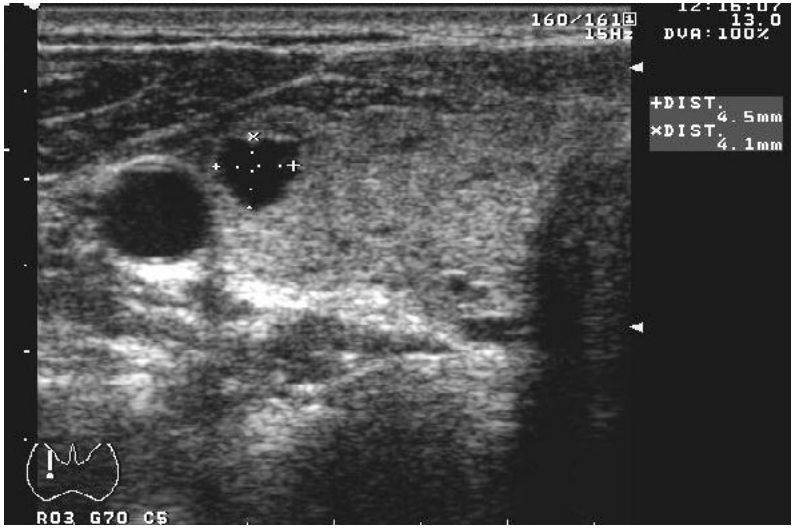


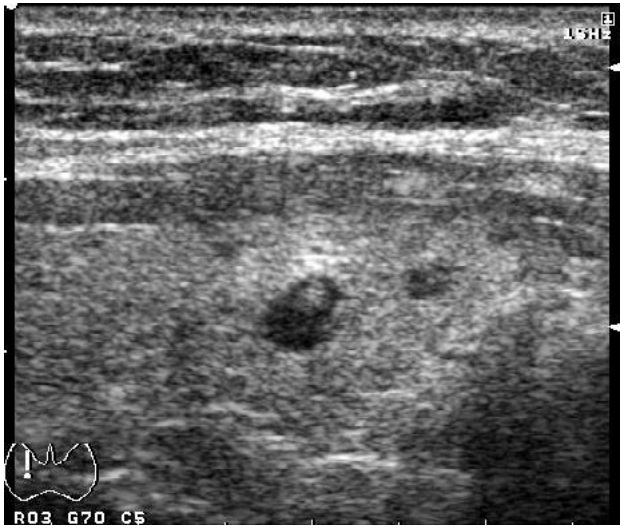


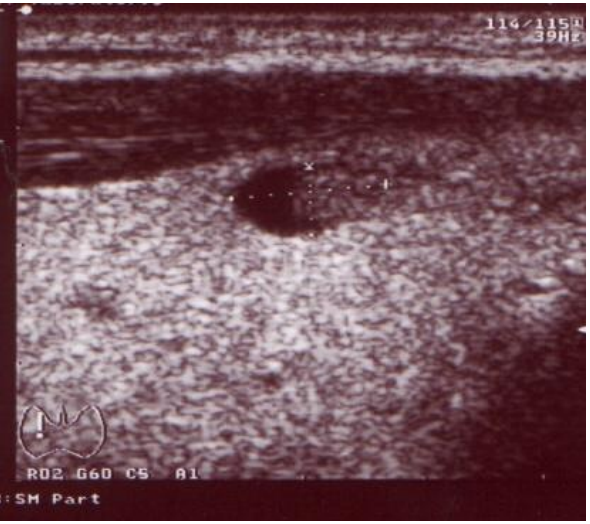


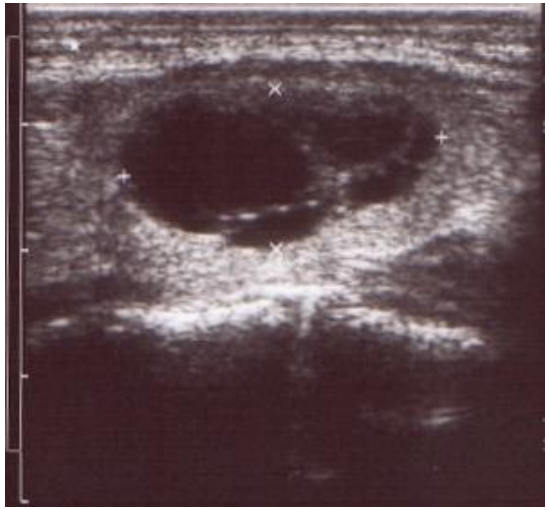


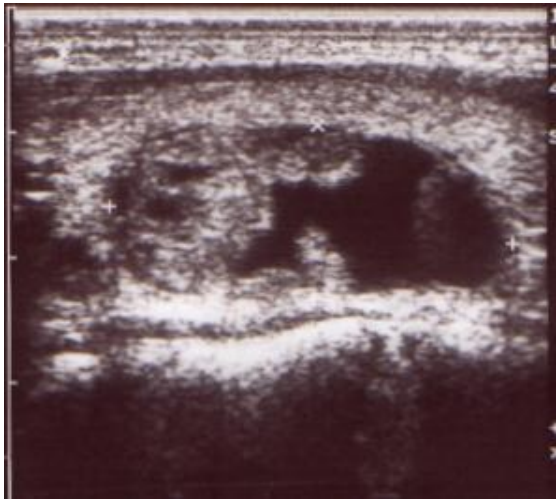



160/161
15Hz
13.0
DVA:100%
+DIST.
4.5mm
×DIST.
4.1mm
R03 G70 C5

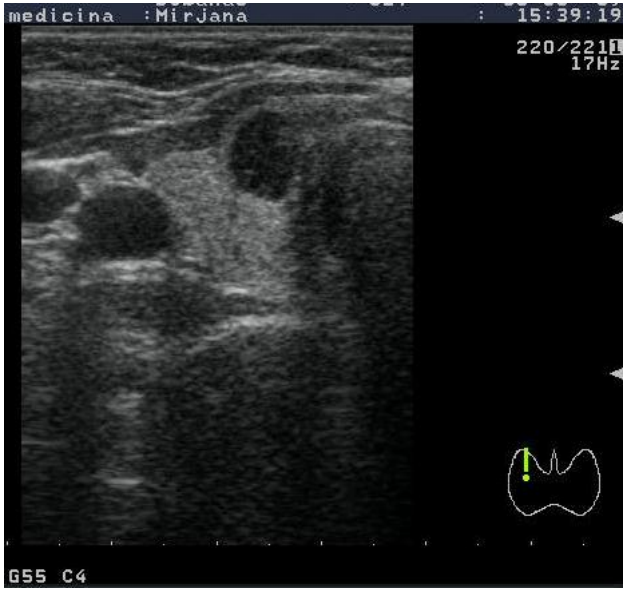

15Hz
R03 G70 C5

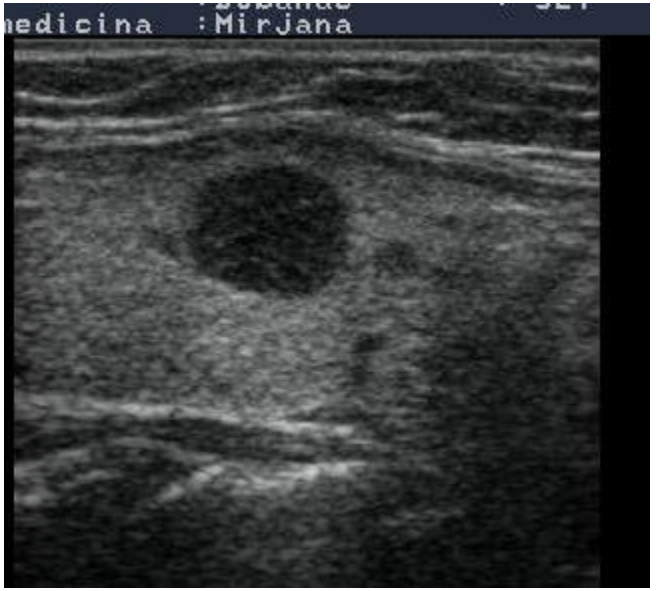

114/115
39Hz
R02 G60 C5 A1
SM Part

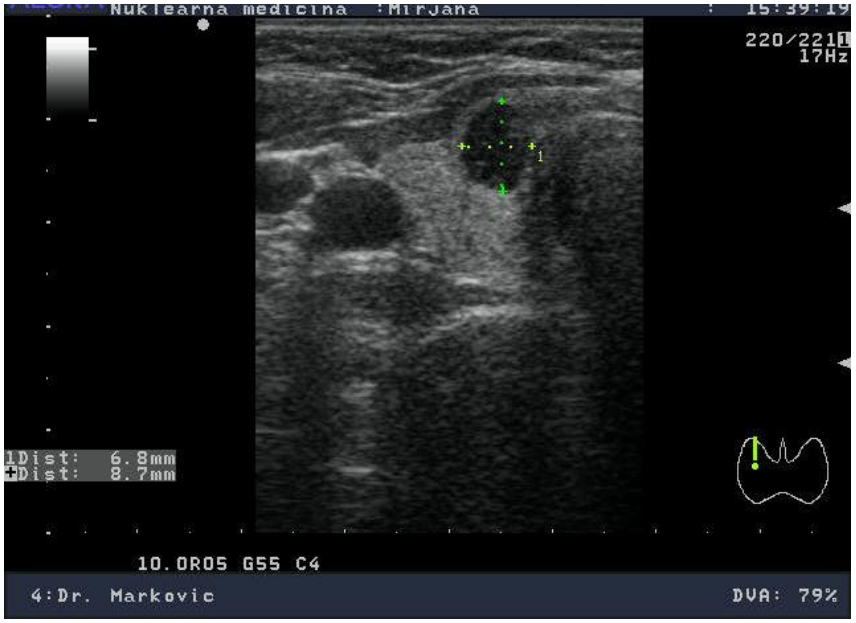


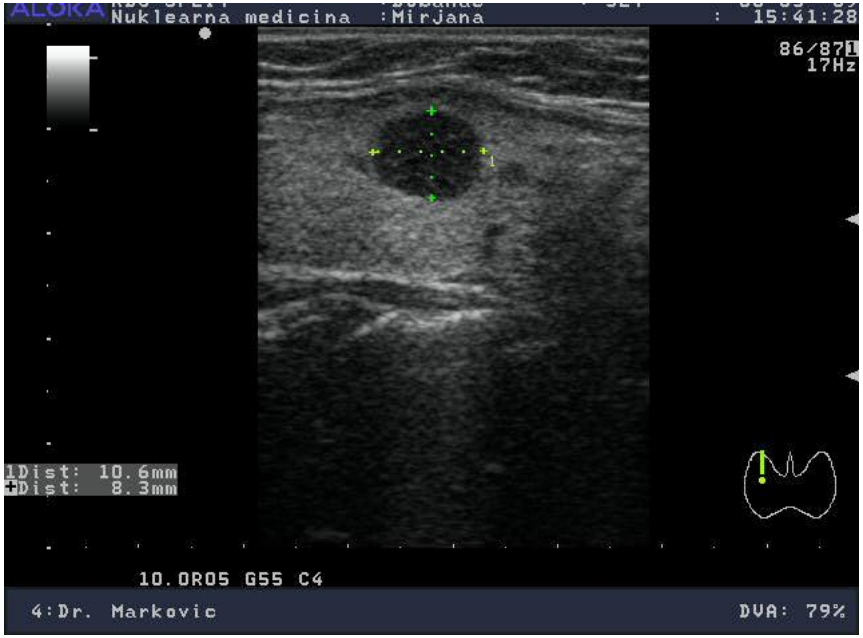


Ca. papillare

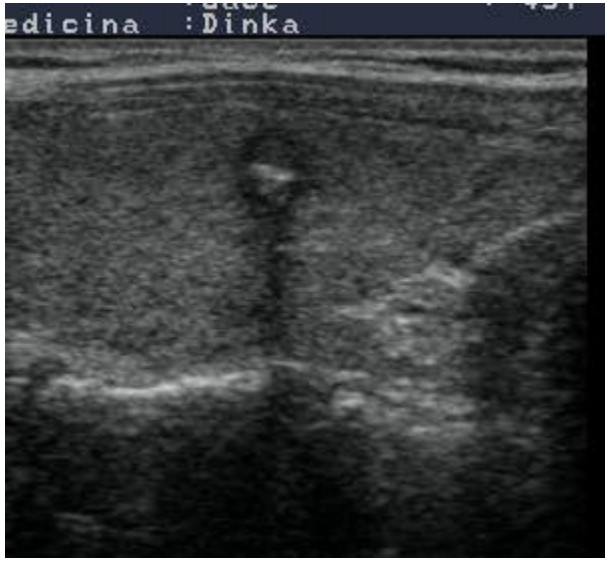


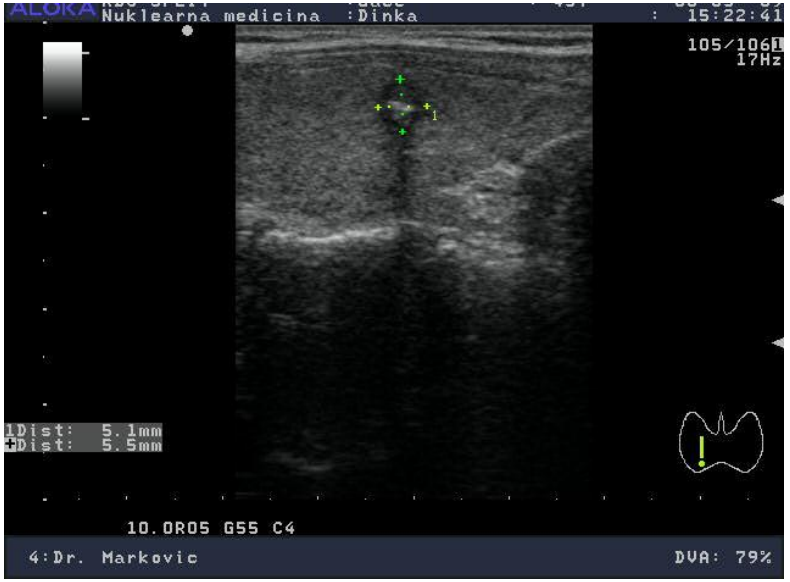


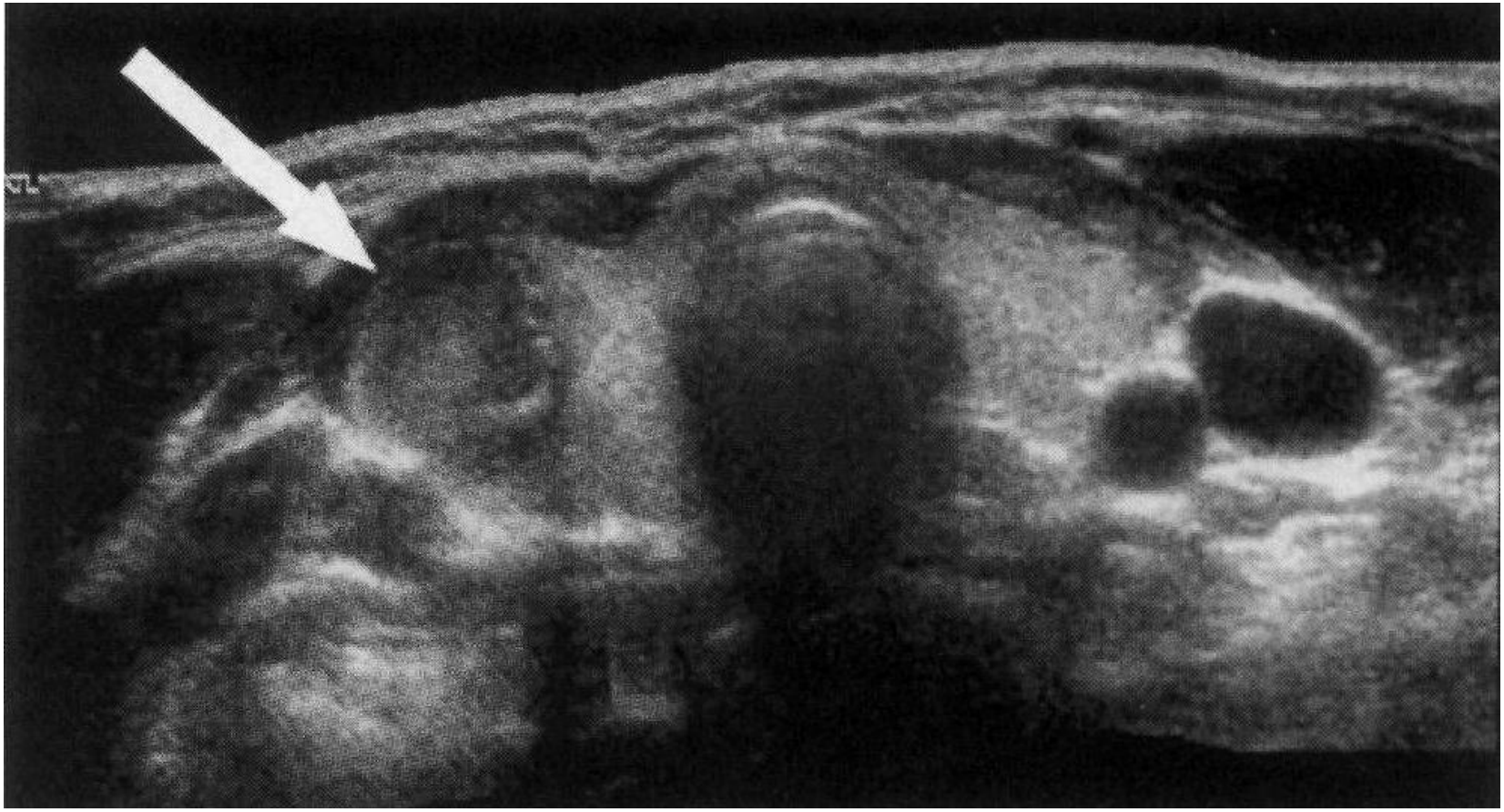




Ca. papillare

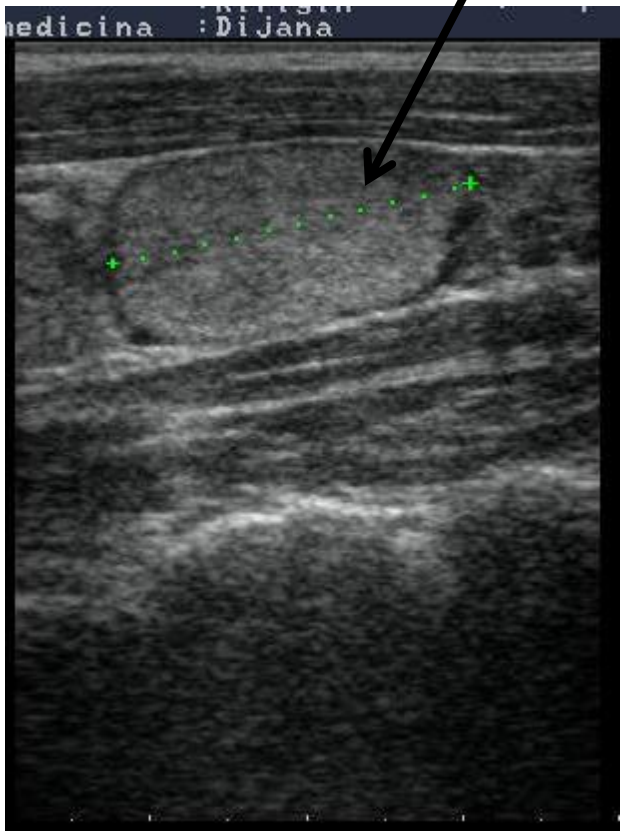


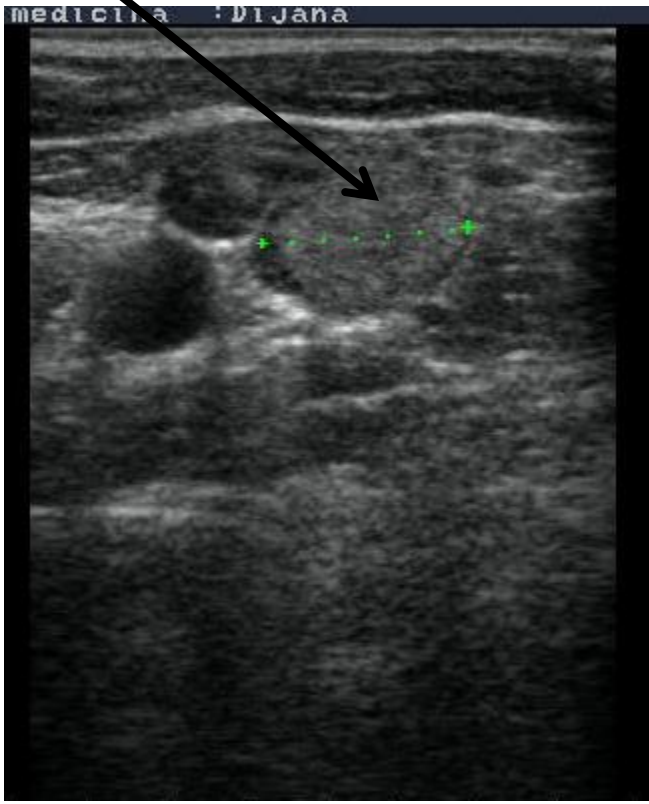




Panoramic US image, coronal section: solitary nodule in the right lobe

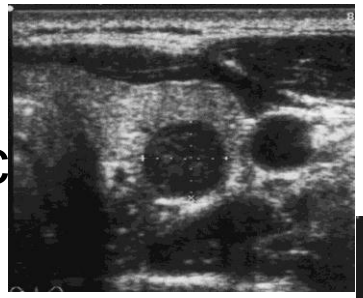
Metastatic lymph nodes



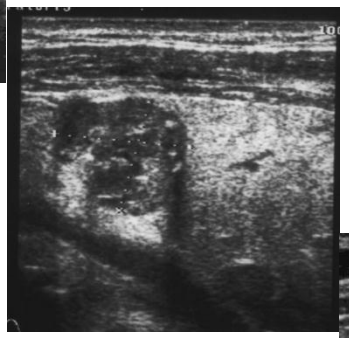


Echographic criterion of malignancy

Hypoechogenic

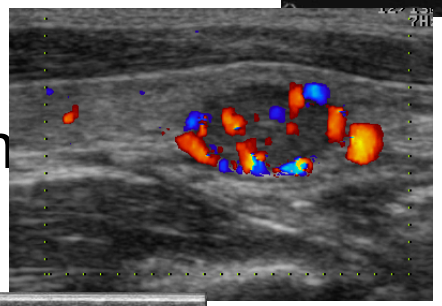


Microcalcification



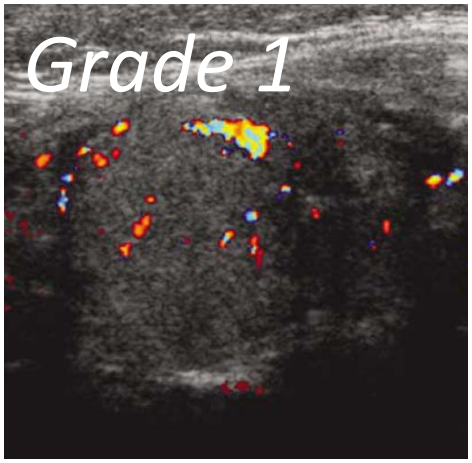
Abscense of hypoechogenic edge, irregular borders

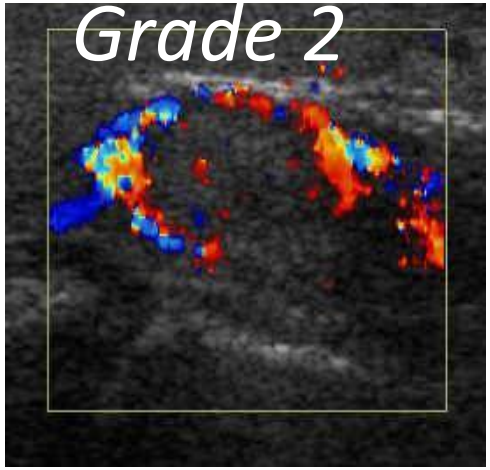
Intranodular vascularisation

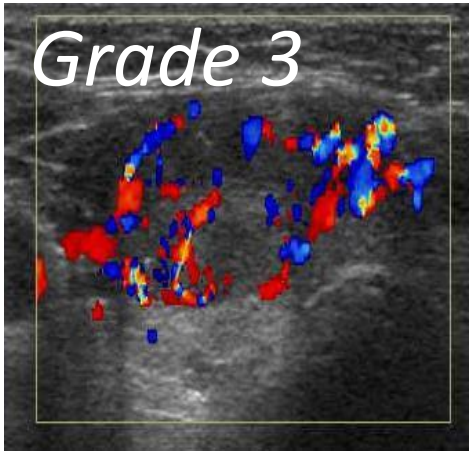


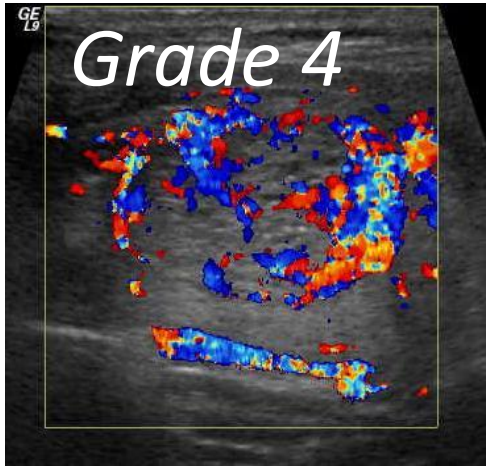
Regional lymphadenopathy

Flow grades in CD (Color Doppler)



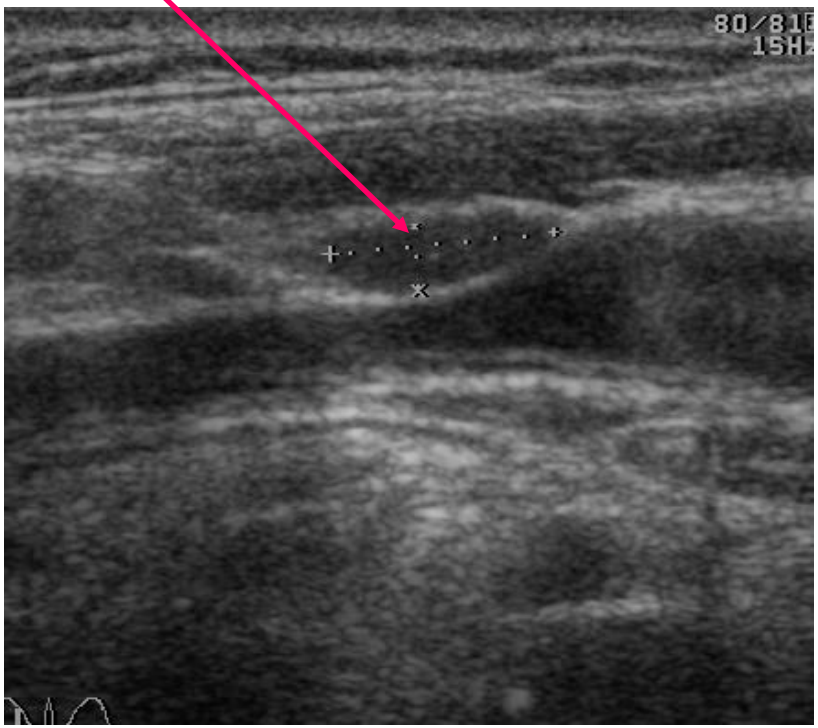




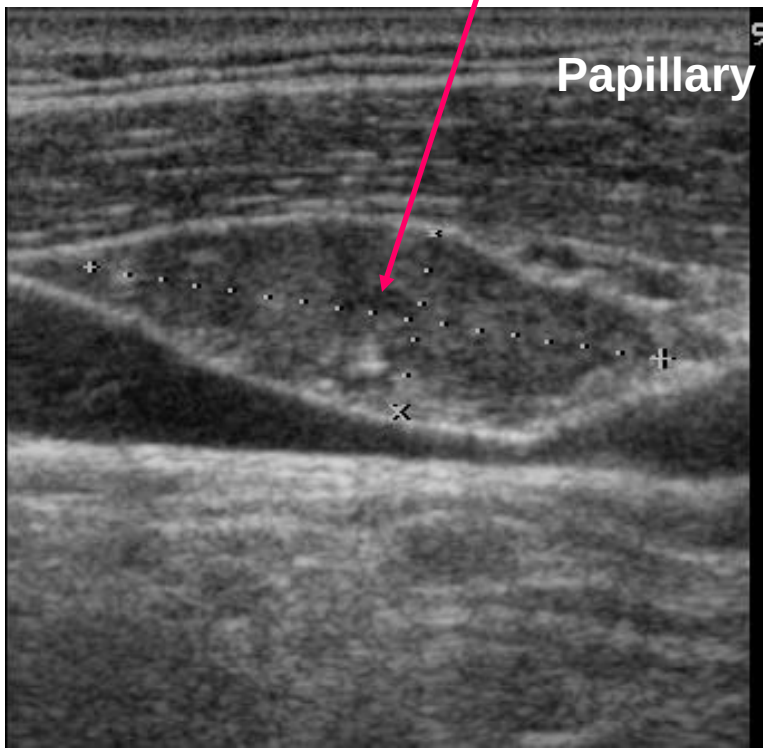


***Color Doppler can help to determine which nodules require FNAC**

Neck examination

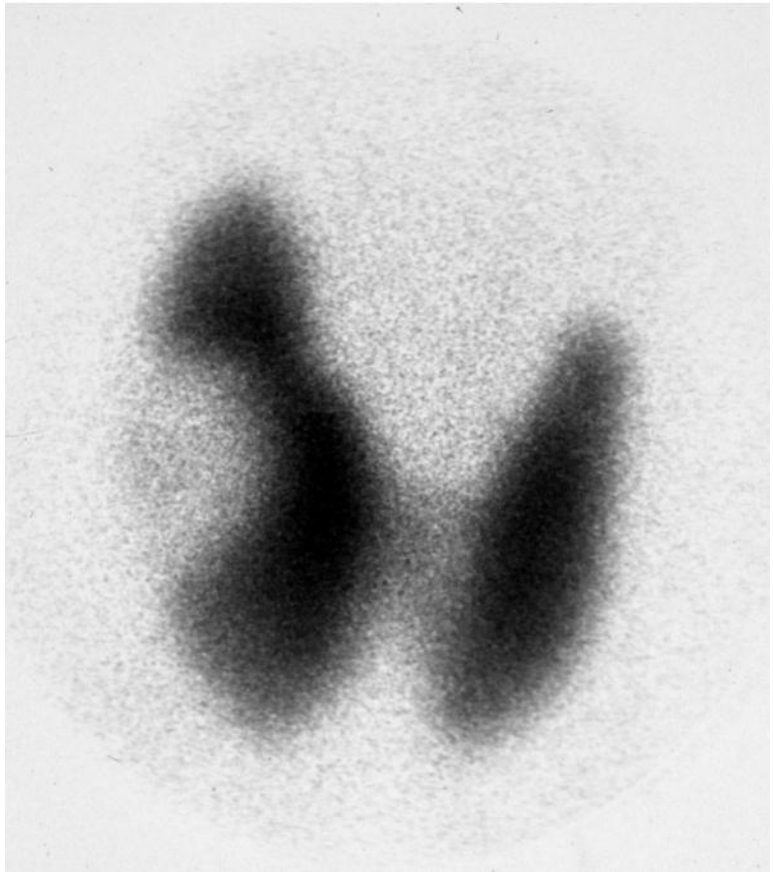


Reactive lymph node

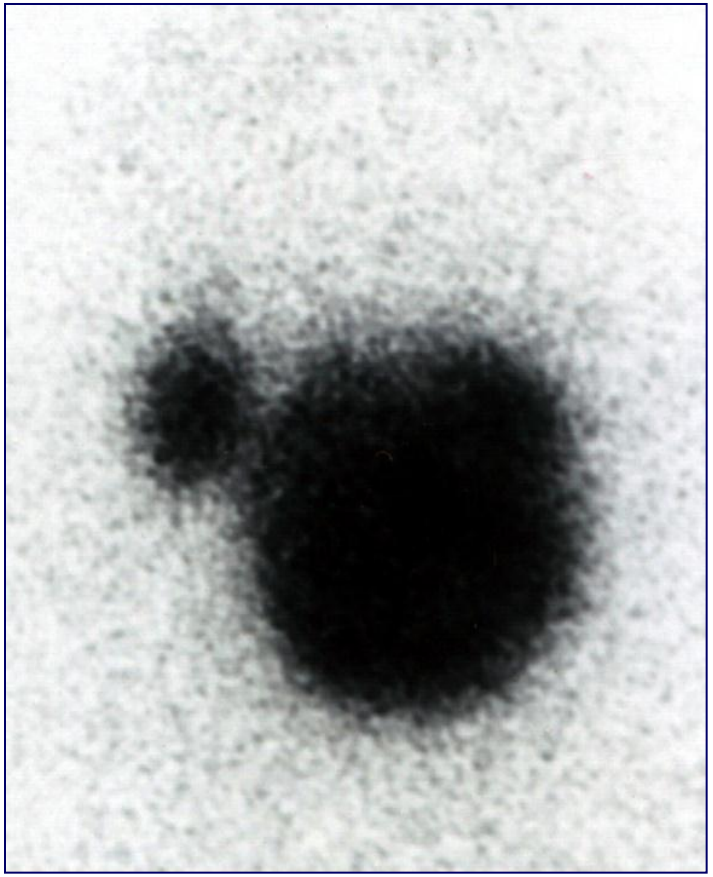


Metastatic lymph node

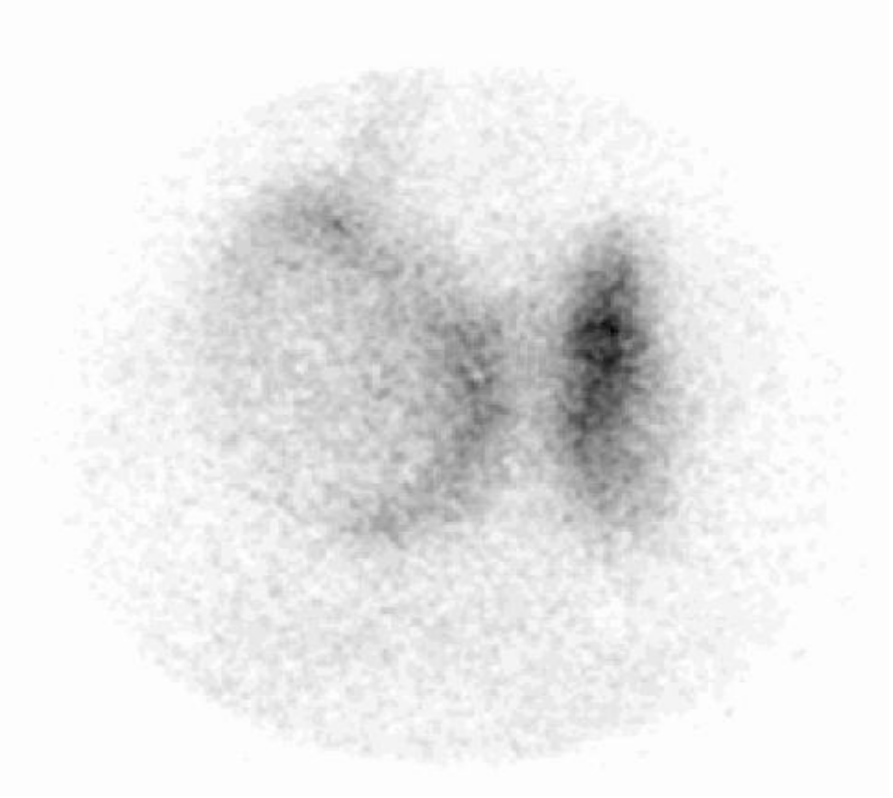
Scintigraphy



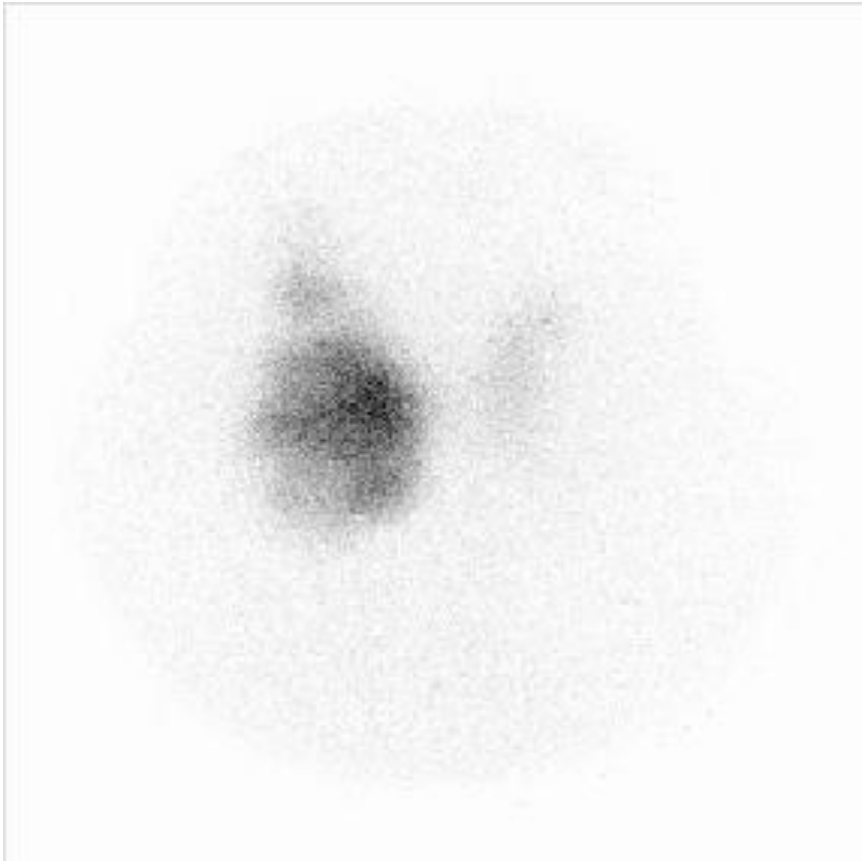
Scintigraphic “cold” node



Scintigraphic “hot” node

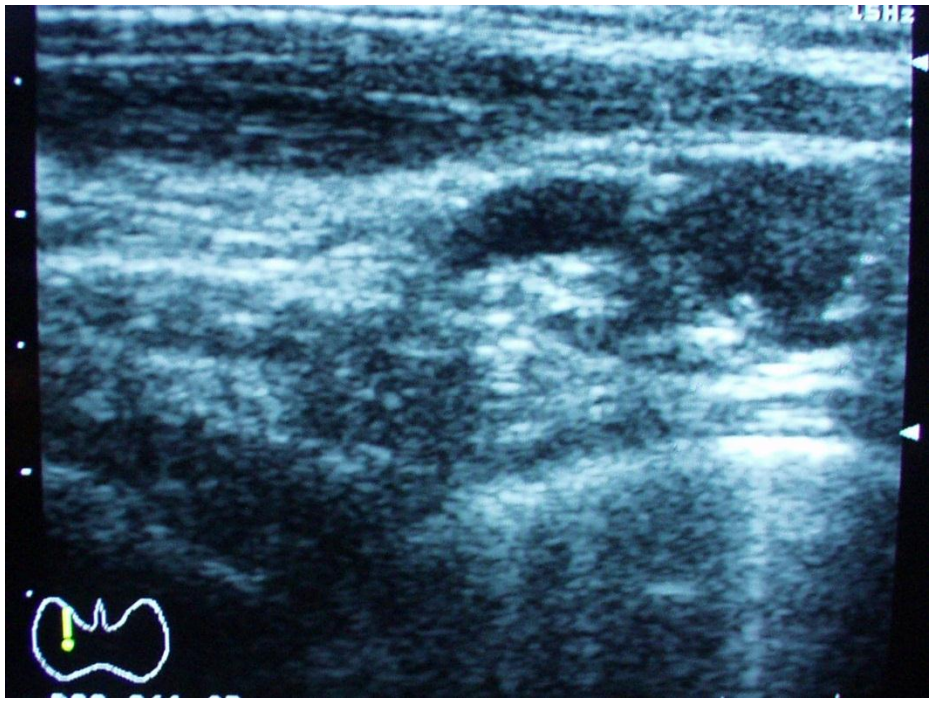


Scintigraphic “cold” node



Scintigraphic “warm” node

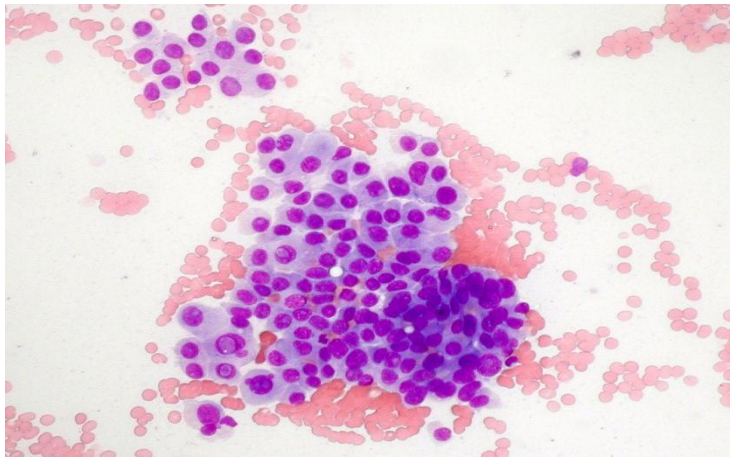
Ultrasound guided fine needle aspiration citology (FNAC)



CARCINOMA RISK IN THE NODULE

~5% solitary nodule

~5% nodes in multinodular goiter

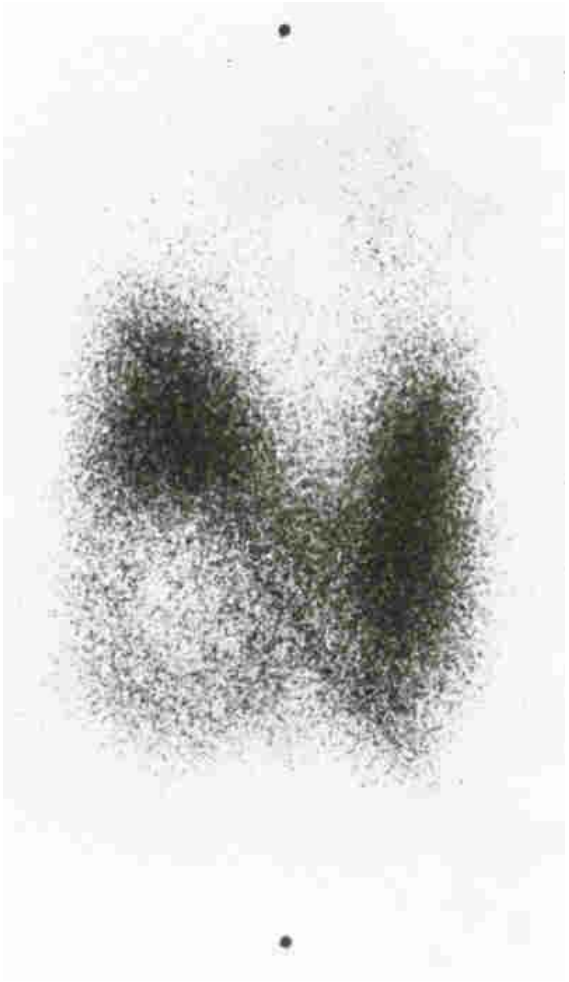


~5% small unpalpable nodes detected by ultrasound

CARCINOMA RISK IN THE NODULE

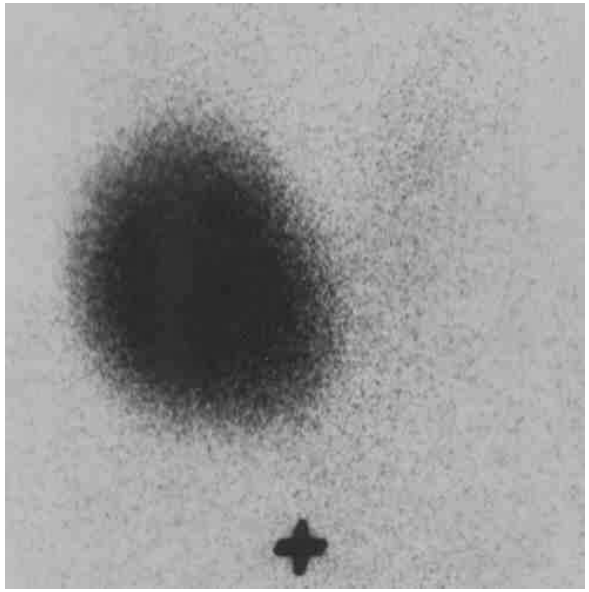
***Risk factors*:**

- Age < 20 years.
- children < 14 years – around 50% nodes are cancer
- Male gender (2 times more often)
- Scintigraphic nonfunctional “cold” nodes
- Quick growth of the nodule
- Nodes > 4 cm



Clinical findings sugesting thyroid carcinoma:

1. Quick growth of the nodul,
2. Hard and irregular by palpation,
3. Vocal cord paralysis,
4. Enlarged neck lymph nodes,
5. Family history for medullary carcinoma,
6. Distant metastasis.



Scintigraphicly “warm” or “hot” nodules (Autonomously functioning thyroid nodule-AFTN) have very low malignancy risk (0,2-0,5%),

Fine needle aspiration citology is indicated only in those nodules with clinicaly (quick grow, hard consistency) and ultrasound characteristics suspected for malignacy

Importance of thyroid nodule detection

***** Most of the patients don’t have any simptoms

* Most are euthyroid

* Some patients have palpable nodule, neck pressure or other discomfort

*** For thyroid carcinoma detection (5% of all nodes)**

* Carcinoma risk is similar in solitar nodules and inside multinodular goiter

• Cancer are found equally in small and large nodes

• Microcancer can be agressive

• **Aim** of diagnostic procedure is to reduce number of unnessesery operations of benigne thyroid diseases and early diagnosis of malignant tumors

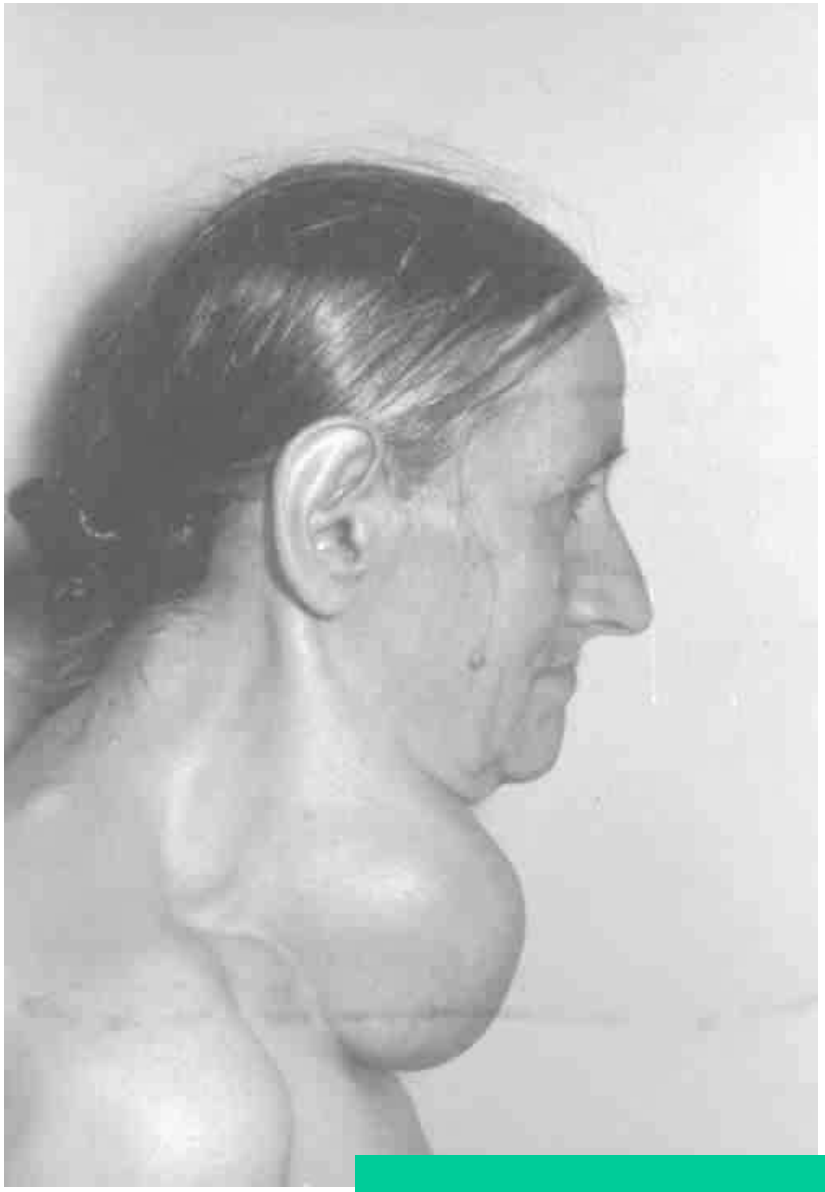
Microcarcinoma < 1 cm

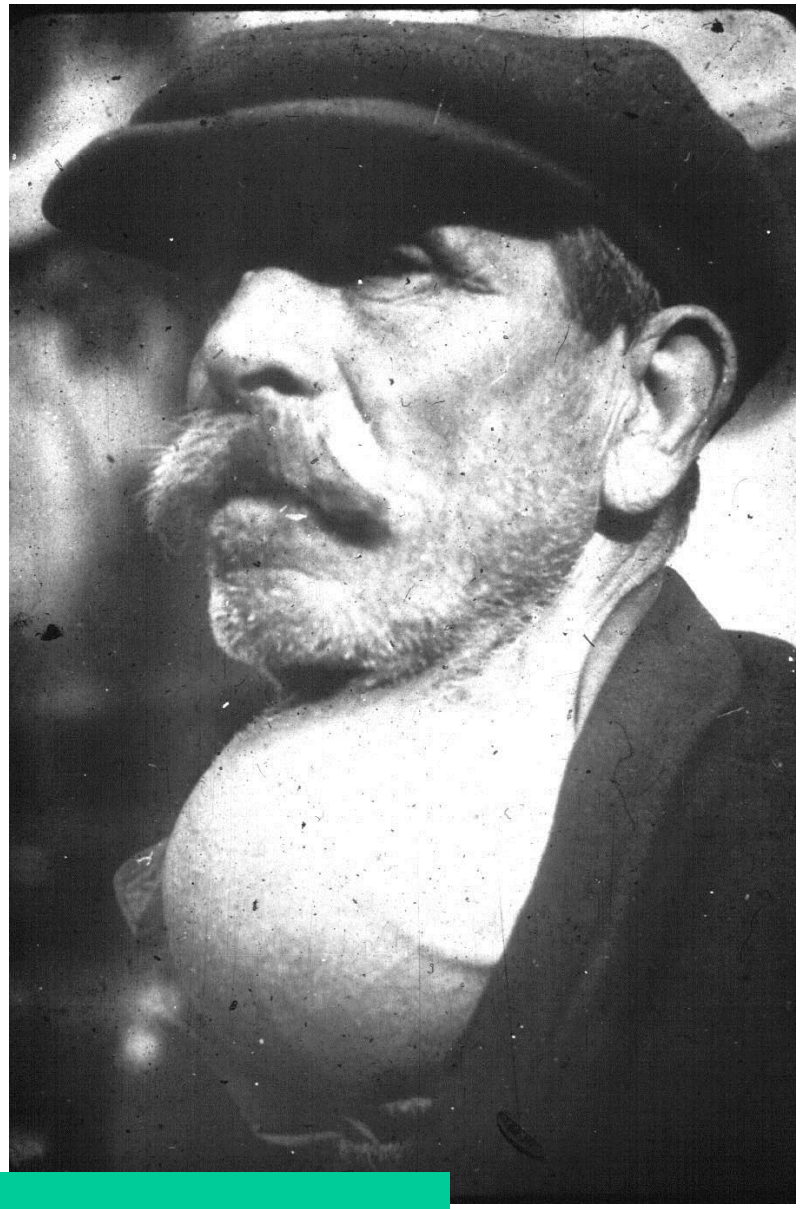
- Thanks to ultrasound significant number of detected thyroid cancers today are less then 1 cm in diameter
- **Occult m**icrocarcinomas can be found as source of neck lymphnode metastasis or distant metastasis
- **Incidental** papillary microcarcinomas are detected as patohistological finding in thyroid tissue after surgery for other reasons
- **Latent** microcarcinomas which are incidental finding in autopsy

Goiter

1. **endemic goiter:** more then 5 % of habitants or shchool children have goiter.
2. **sporadic goiter**: diffuse and nodular (multinodular) goiter.

Endemic stands for expansion in the population, because clinical manifestation, patohistological finding and biochemical parameters are same in endemic and sporadic goiter.

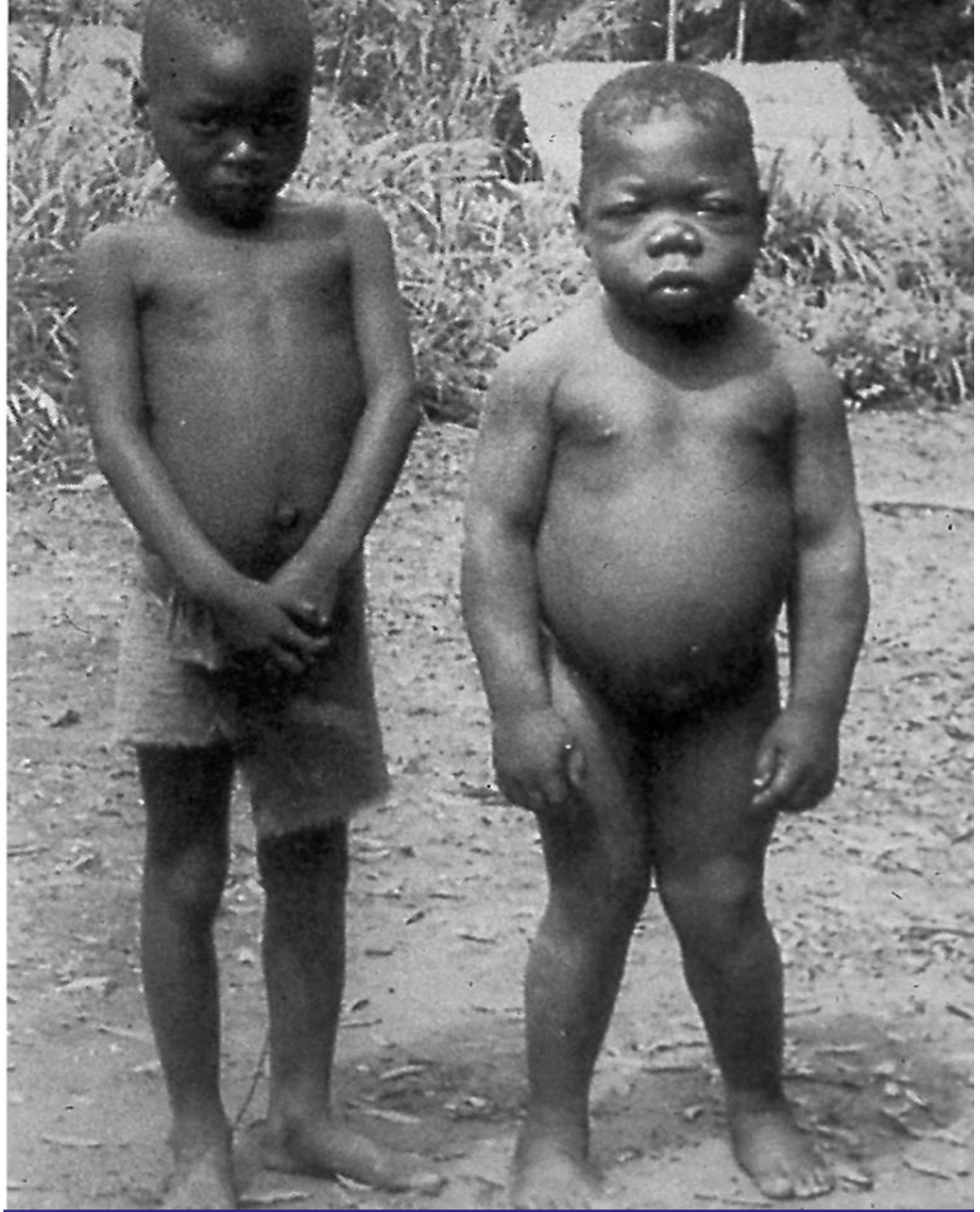




Endemic goiter

Endemic goiter

Endemic cretinism



Croatia-1950.

- 2 000 000 people with goiter
- frequency 10 - 90 %
- 20 000 endemic cretinism
- 2 - 4 000 deaf-mute
- male to female children with ratio was 1:1

Home of the family with goiter, Rude, 1950'

Cretin and his mother

Cretin’s destiny was closely related with their mother’s life...

IODINE PROPHYLAXIS IN CROATIA

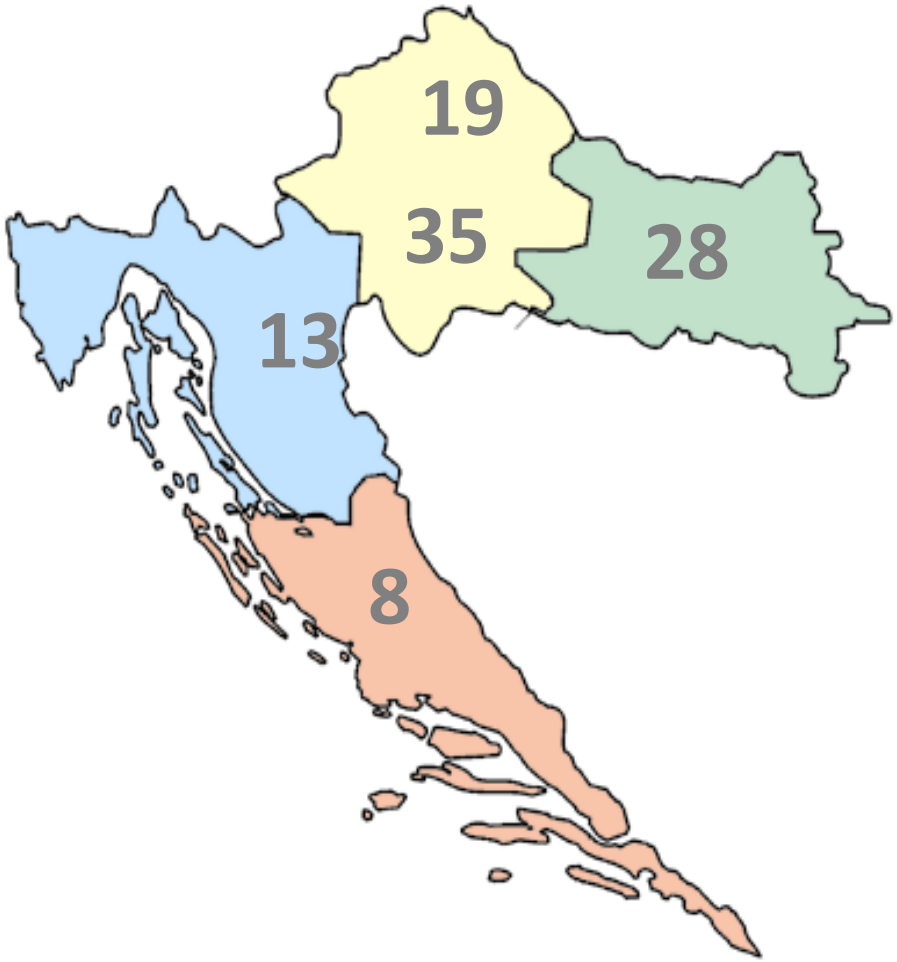
- 1930. – 1941. sporadic iodine prophylaxis

- **1953.** First low about mandatory table salt iodination

  10 mg KI/kg NaCl

- Ten years later three times reduction in goiter frequency in Croatia with loss of cretinism

In the begining of the 1990's goiter freqency in Croatia was 8%-35%



1996.

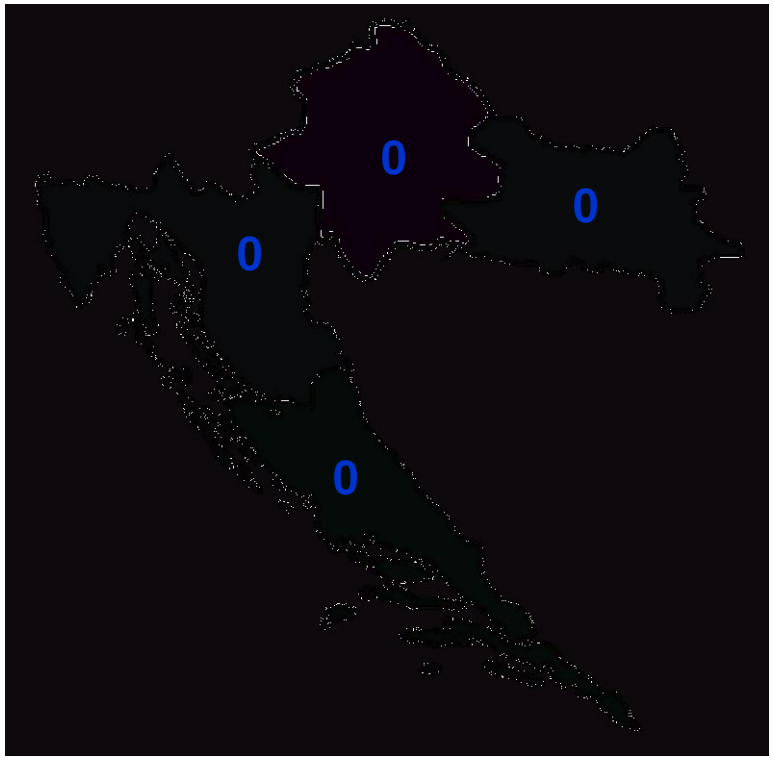
MILD TO MODERATE IODINE DEFICIENCE IN SPITE SALT IODINATION WITH

10 mg KI/kg NaCl

1996.
NEW LEGISLATION ABOUT SALT IODINATION
25 mg KI/kg NaCl

RESULTS:

Thyroid volumes measured in four main geographic regions were within normal range for school children who recive sufficient amount of iodine



Goiter frequency in four main regions in Croatia, % above upper borders – USG, 2002.

WHO/ICCIDD, 2001

THYROID VOLUME, age 13, 1991.

ZAGREB_____7,2 mL

STOCKHOLM_____ 4 mL

MÜNCHEN_____ 9 mL

THYROID VOLUME, age 12, 2002.

ZAGREB_____ 4,8 mL

Iodine intake in Europe, based on the iodine urine excretion (µg/L)			
Satisfactory (≥100 µg/L)	**Probably sufficient**	**unsatisfactory (<100 µg/L)**	**Probably unsatisfactory**
Austria	Island	Belgium	Albania
Bosna and Hercegovina	Luxemburg	Denmark	
Croatia	Norway	France	
Cyprus	Sweden	Germany	
Czech Republic		Greek	
Finland		Hungary	
Macedonia		Italy	
Netherlands		Irland	
Poland		Montenegro	
Portugal		Romania	
Slovakia		Slovenia	
Srbia		Spain	
Switzerland		Turky	
United Kingdom			

Lancet, 2003; 361: 1226

Recommended daily intake of iodine

- 90 µg for preschool children (0 to 59 months) ;
- 120 µg for schoolchildren (6 to 12 years) ;
- 150 µg for adults (above 12 years) ; and
- 200 250µg for pregnant and lactating women

From WHO/UNICEF/ICCIDD (2), WHO

Epidemiological criteria for assessing iodine nutrition based on median urinary iodine concentrations in school-aged children

Median urinary iodine	Iodine intake(µg/L)	Iodine nutrition
< 20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Mild iodine deficiency
100-199	Adequate	Optimal
200-299	More than adequate	Risk of iodine-induced hyperthyroidism within 5-10 years following introduction of iodized salt in susceptible
> 300	Excessive	Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid diseases)

WHO, UNICEF, and ICCIDD. 2001. Assessment of the Iodine Deficiency Disorders and monitoring their elimination. Geneva: WHO publ. WHO/NHD/01.1. 1-107 pp.

The natural course of multinodular goiter's development

- Gradual growth of the goiter and nodules.
- Development of multiple nodes with age.
- Variation in size and architecture of the nodes.
- Appearance of cysts, fibrosis, necrosis, hemorrhage, calcifications.
- Variable growth flow – possible longtime phases of inaction.
- Appearance of autonomic nodes with TSH supression – transit to multinodular toxic goiter (common form of hyperthyroidism in insuffitient iodine intake).

Clinical manifestation

- **Asimptomatic small goiter**
- **Large multinodular, retrosternal or intrathoracic goiter with symptoms of compression: in 10-20% patients**
  - **Dysphagia**
  - **Dyspnea**
  - **Dysphonia**
  - **Stridor**
  - **Pemberton's sign**
  - **Syndroma Horner**
- **Pain (nodule hemorrhage)**
- **Thyreotoxic symptoms**

Frequency of multinodular goiter

- **High frequency in areas with iodine deficit (endemic goiter) up to 30%.**
- **Eradication of endemic goiter in countries which implemented mandatory iodine prophylaxis.**
- **In areas with sufficient iodine intake goiter frequency is around 4% (sporadic goiter).**
- **Increase of thyroid nodule frequency with age**

Causes of nontoxic goiter

1. Iodine deficit (compensatory thyroid enlargement)
2. Strumogenic substance (tiocionats, thyreostatic preparations, lithium, different vegatables)
3. Enzymatic disorders

Multinodular goiter: Clinical problem

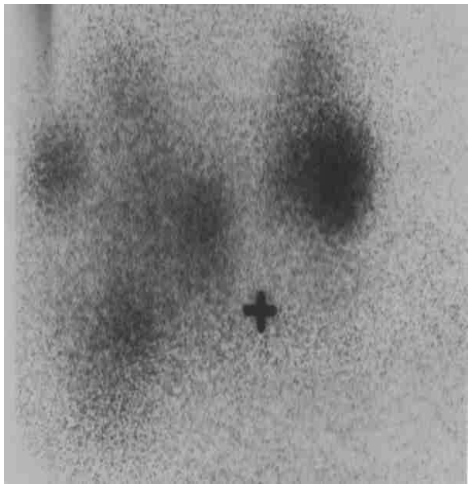
1. Compression

2. Hyperthyroidism, hypothyroidism

3. Malignancy

Dioagnostic treatment

- Inspection and palpation
- TSH
- Thyroid ultrasonography
- Thyroid scinitgraphy
- Fine needle aspiration citology
- RTG, CT, MR, SPECT



TSH

- Inversly relationship between goiter size and serum TSH level.
- Longtime goiter – development of autonomic nodes with TSH suprresion.
- Suppressed TSH: determination of FT3, FT4.
- Antibodies.

Thyroid ultrasonography

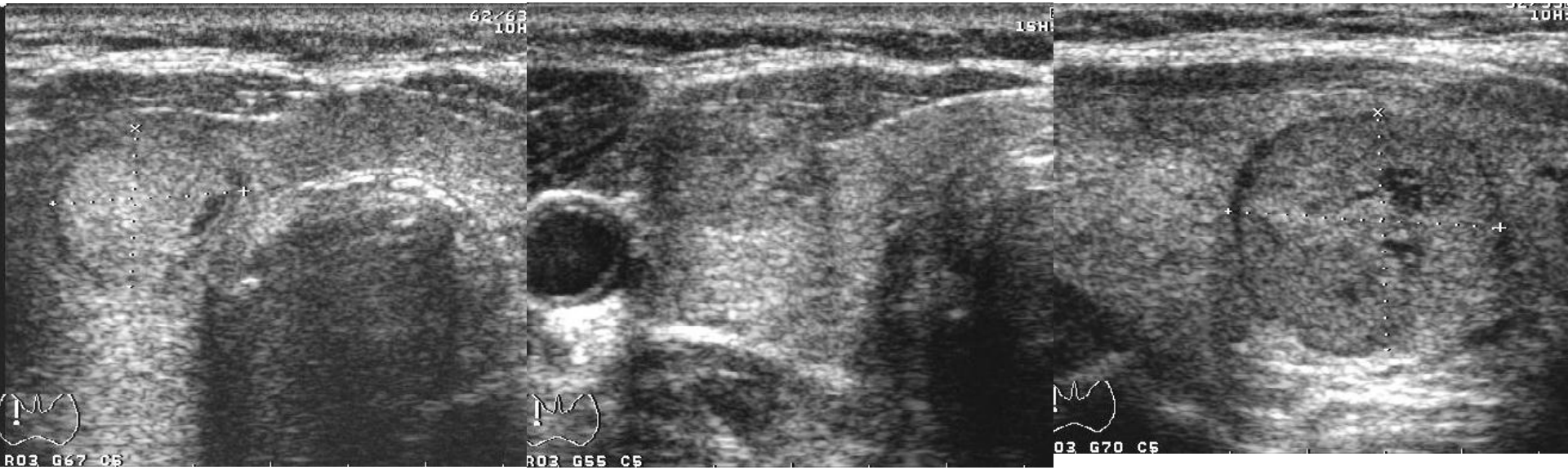
- Nodule frequency (US):

  - Up to 50 % population has multiple noduls which aren't palpable

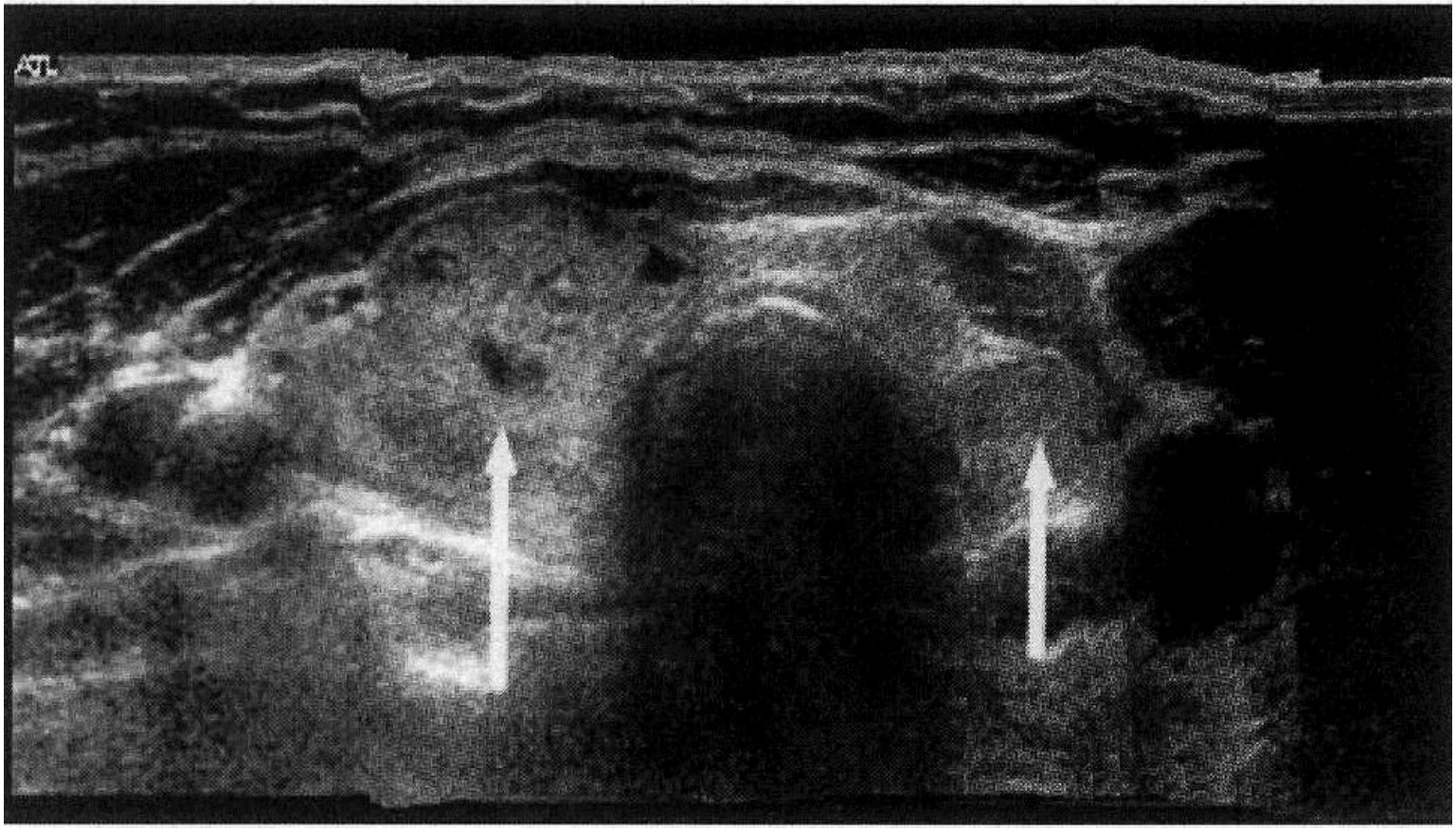
  - Up to 50% persons with single palpable nodule have multiple nodes registrated on ultrasound

- Ultrasound guided fine needle aspiration citology

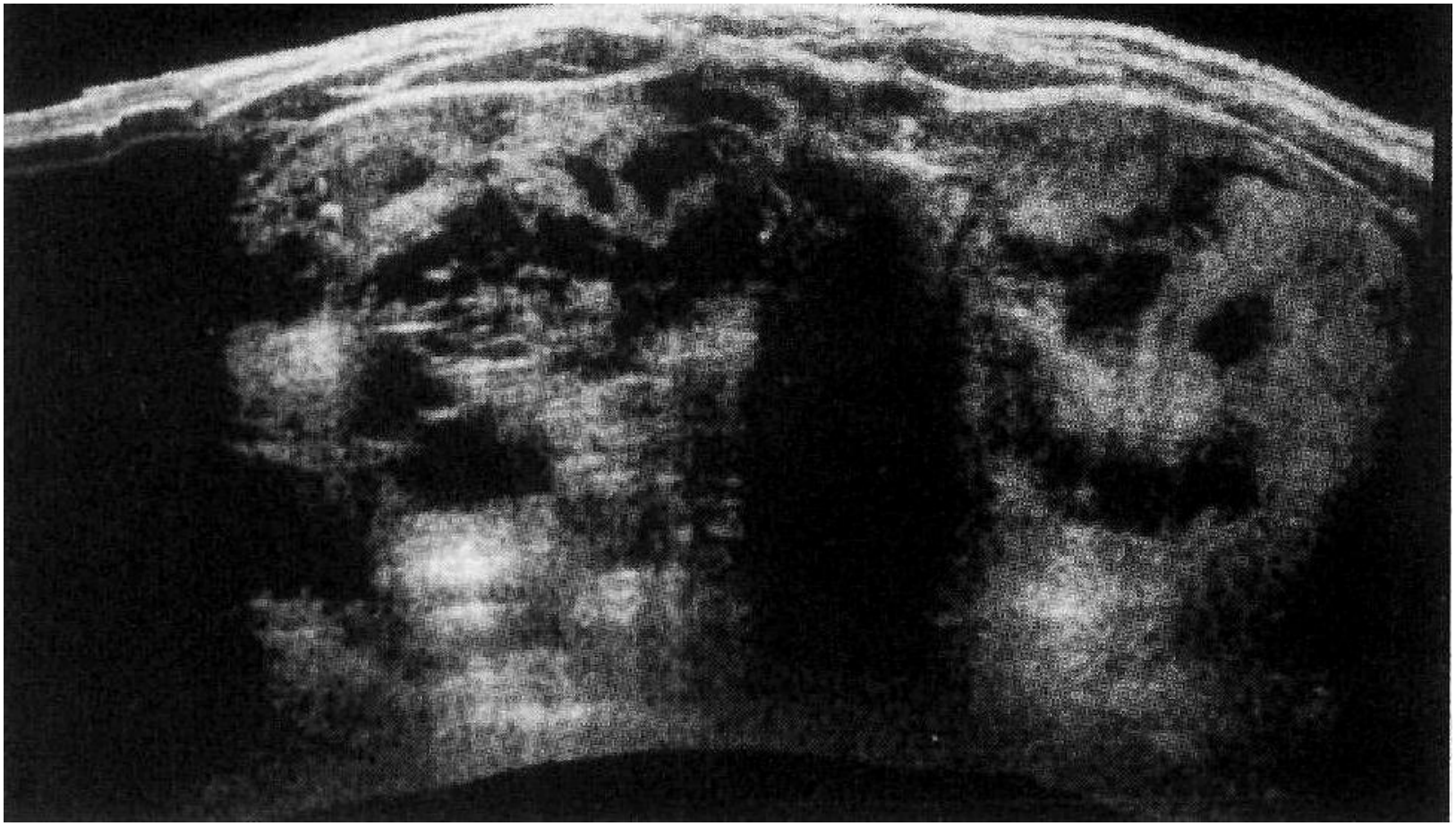
- Objective follow up of goiter and nodule size



Multinodular goiter: multiple nodes in the thyroid



Multinodular goiter: panoramic US image, cross section, multiple nodes in the thyroid



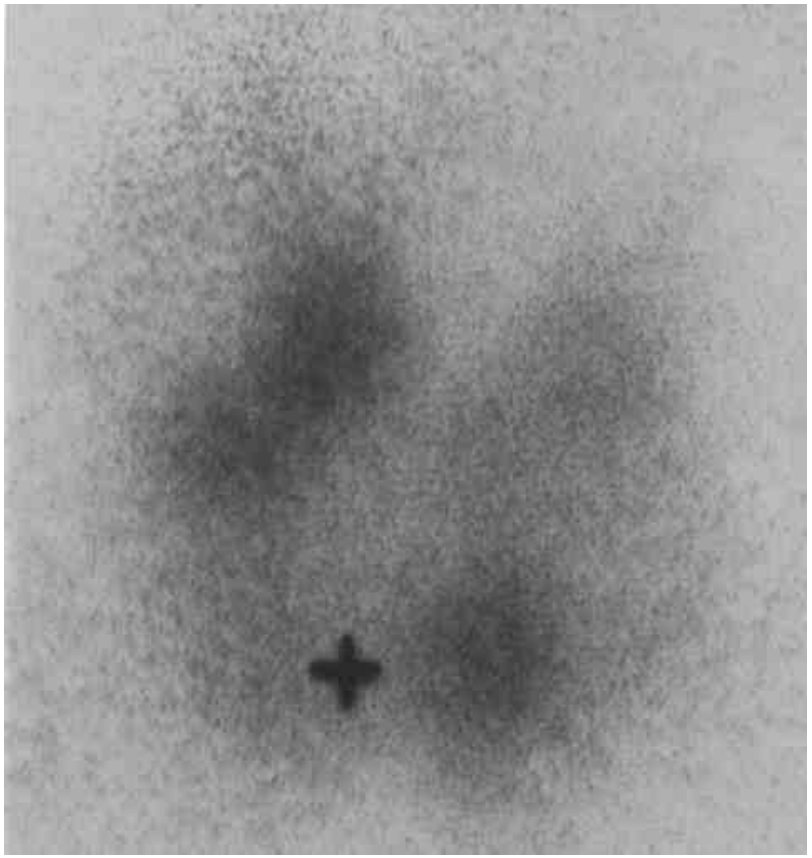
Multinodular goiter: panoramic US image, cross section, enlarged thyroid with multiple nodes

Fine needle aspiration citology (FNAC)

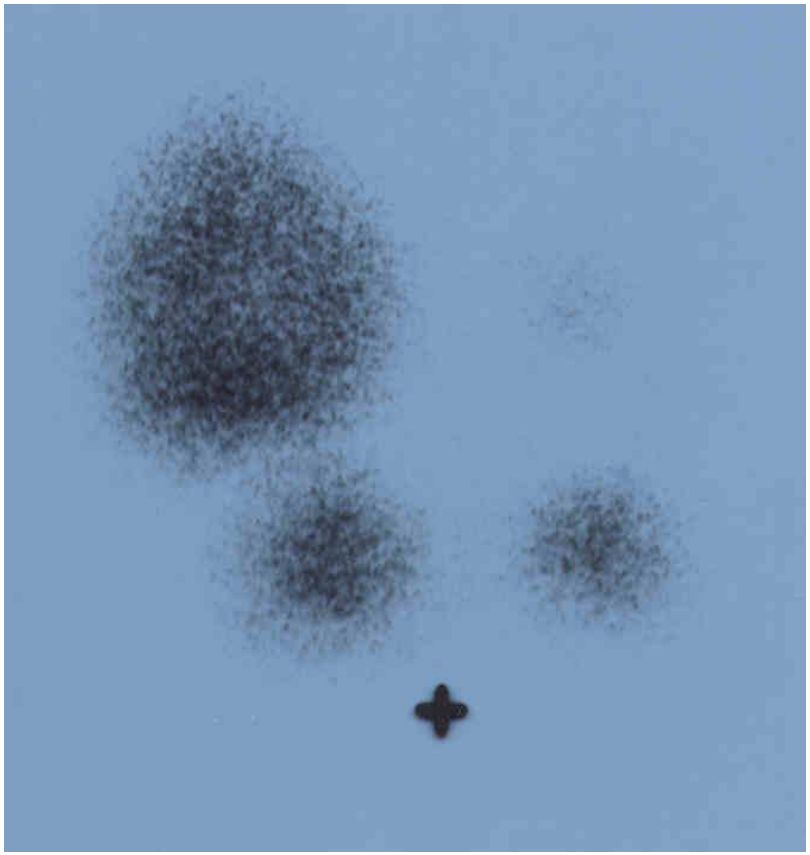
- Indicated in:
  - fast growing goiter with dominant nodule
  - clinicaly suspected nodes
  - ultrasound suspected nodes
  - unpalpable nodes larger then 1 cm – guided by ultrasound (4-6% malignant)

- Risk for carcinoma development in nodes smaller then 1 cm is same as in large nodes - around 5%
- Not routinely indicated

Thyroid scintigraphy

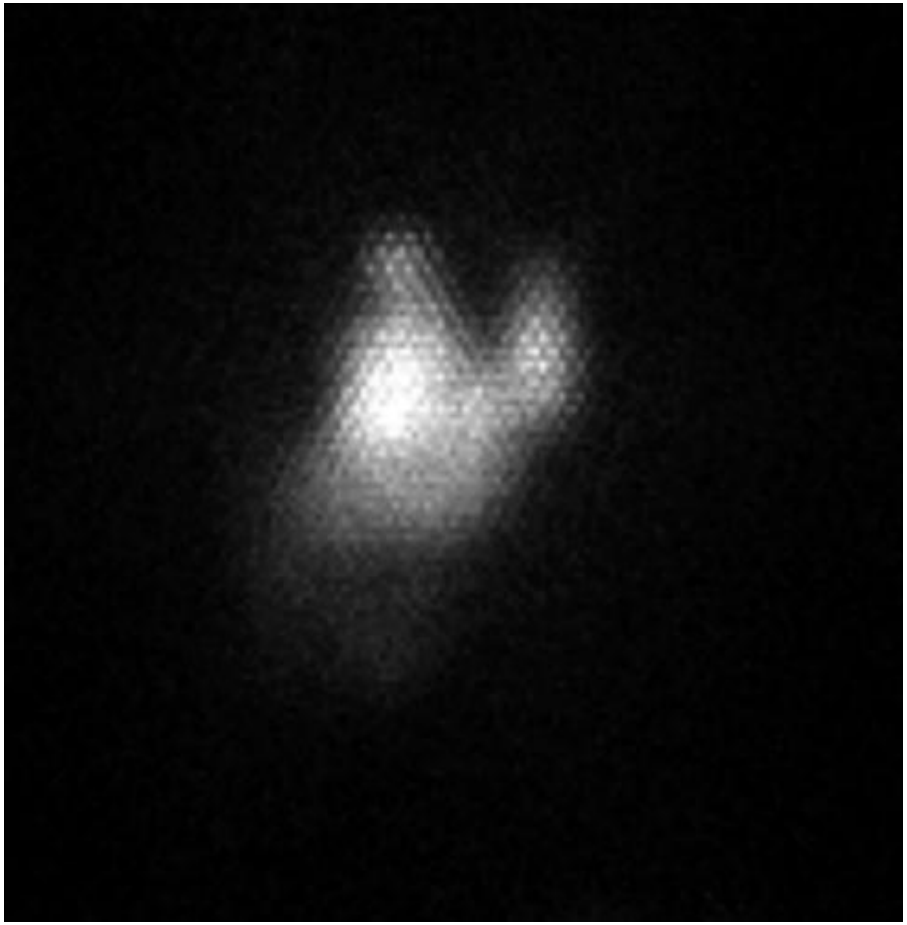


Multinodular goiter
Scintigraphy with ^{99m} Tc-pertechnetate



Multinodular toxic goiter
Scintigraphy with ^{131}I

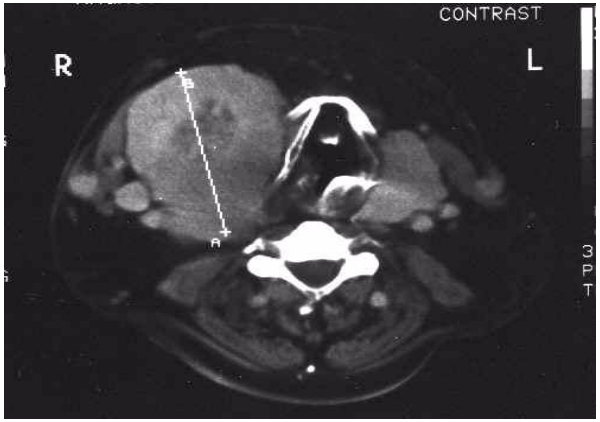
Intrathoracic goiter-planar scintigraphy with I-131-



Pemberton’s sign

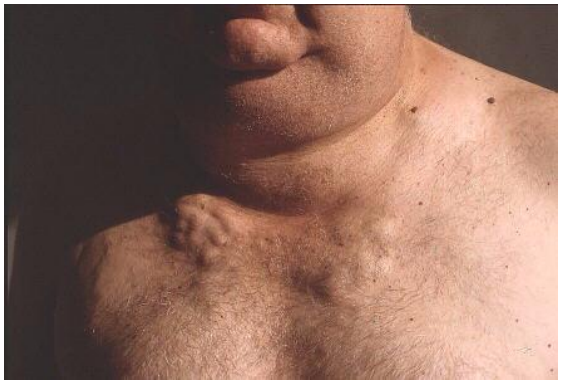
Radiological examinations

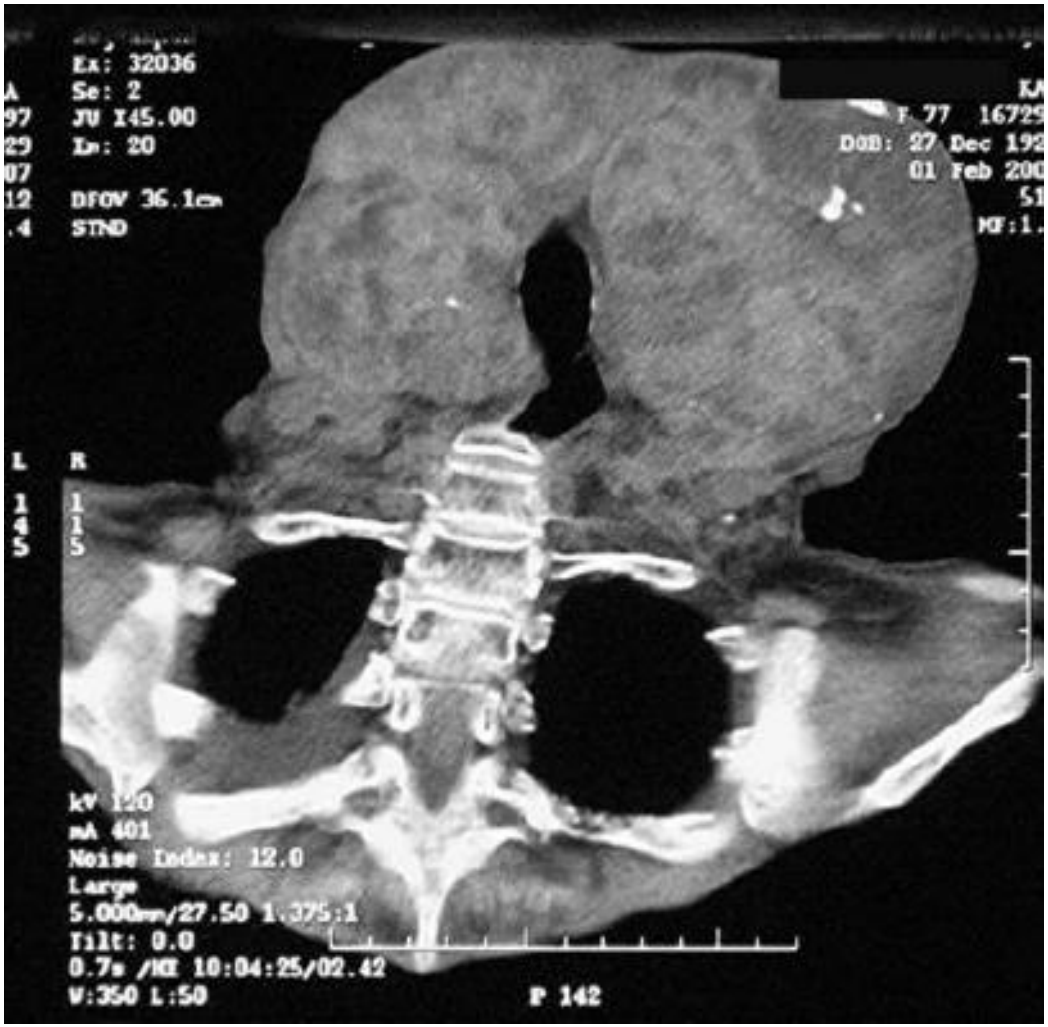
- X-ray of thorax
- X-ray of trachea and esophagus
- CT
- MR



- Indications:

- large multinodular goiter
- retrosternal goiter
- intrathoracic goiter

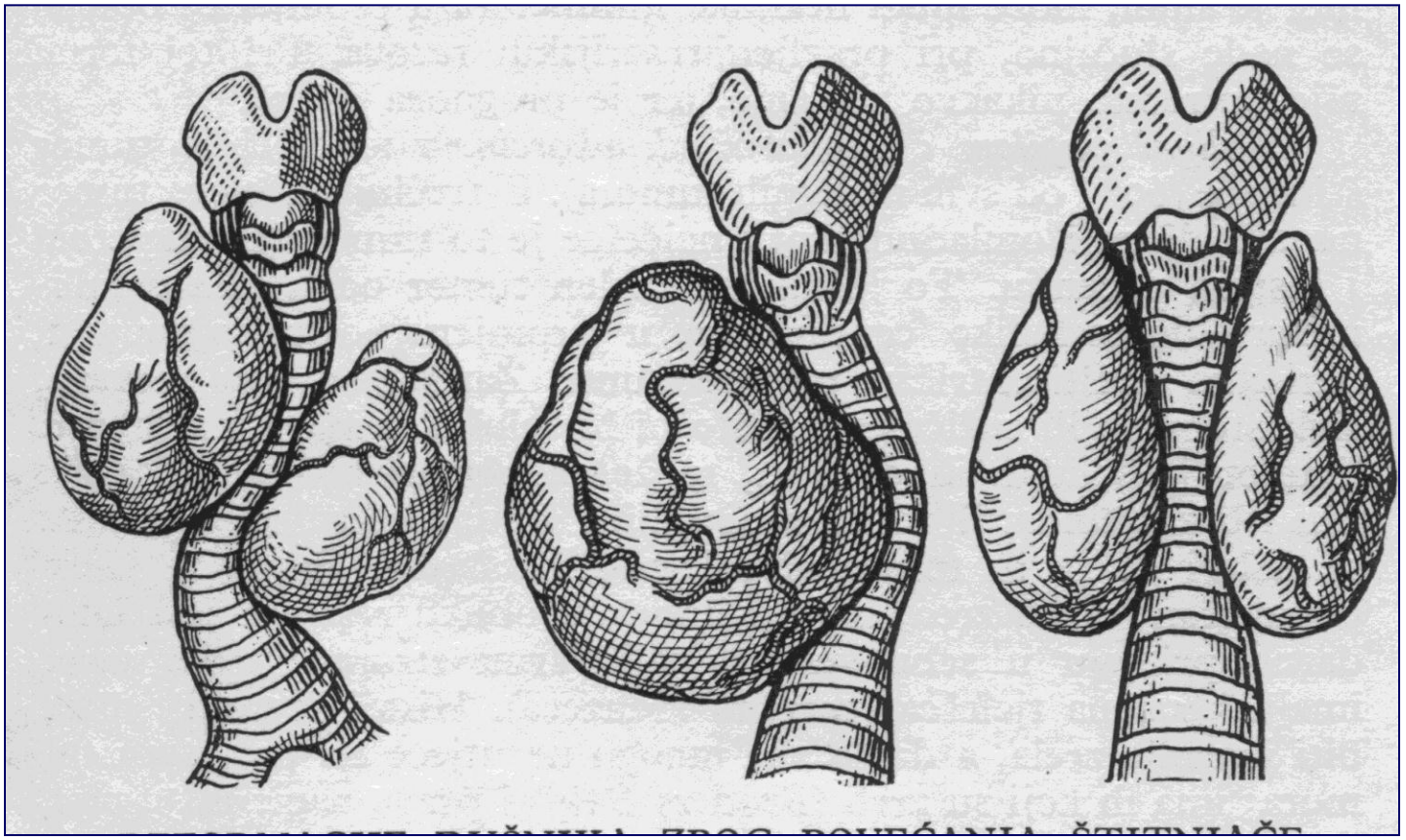


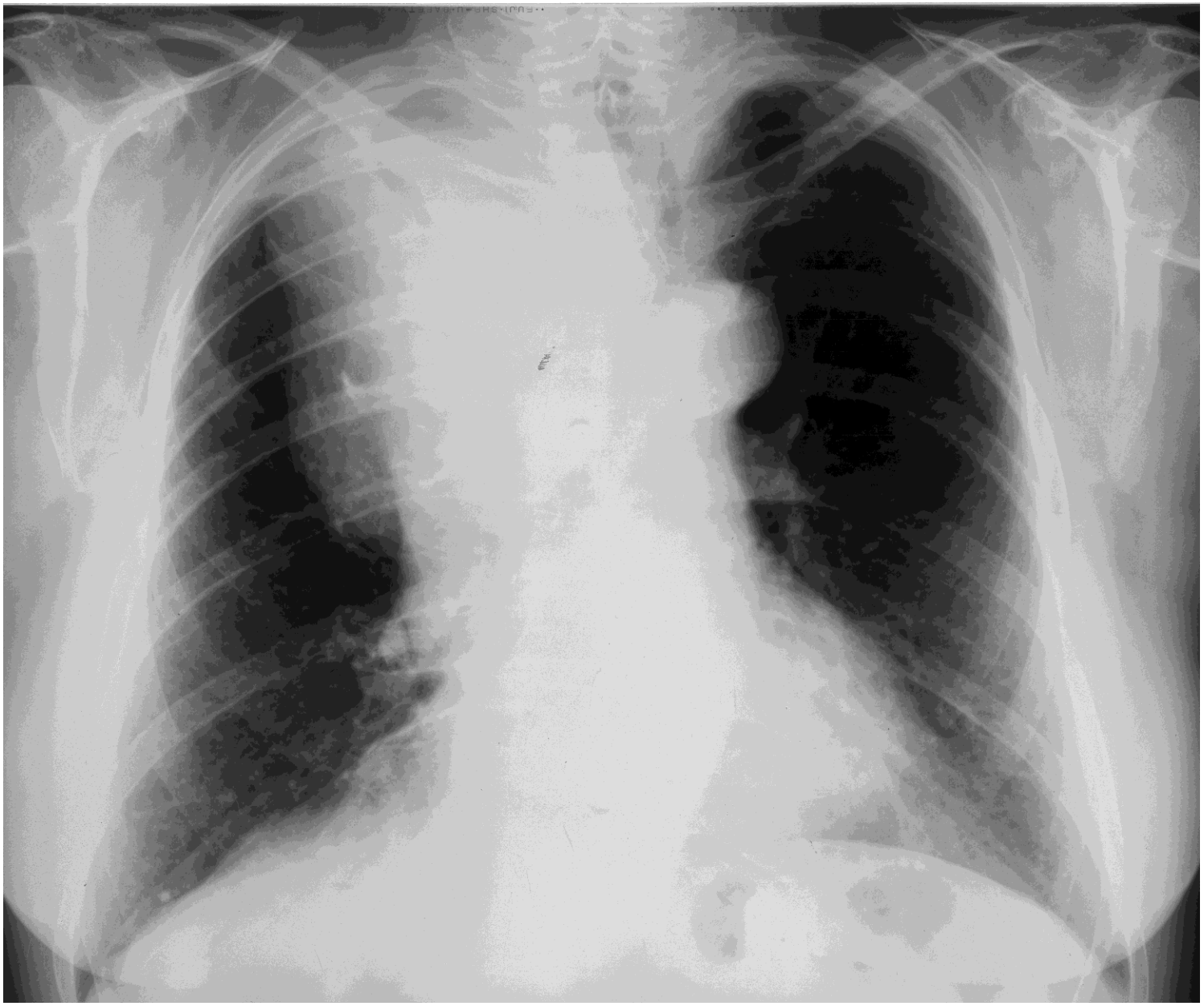

Ex: 32036
Se: 2
JU I45.00
In: 20
DFOV 36.1cm
STND
F 77
DOB: 27 Dec 192
01 Feb 200
L R
kV 120
mA 401
Noise Index: 12.0
Large
Tilt: 0.0
0.7s /HE 10:04:25/02.42
W:350 L:50
P 142

X-ray of the trachea and neck soft tissue

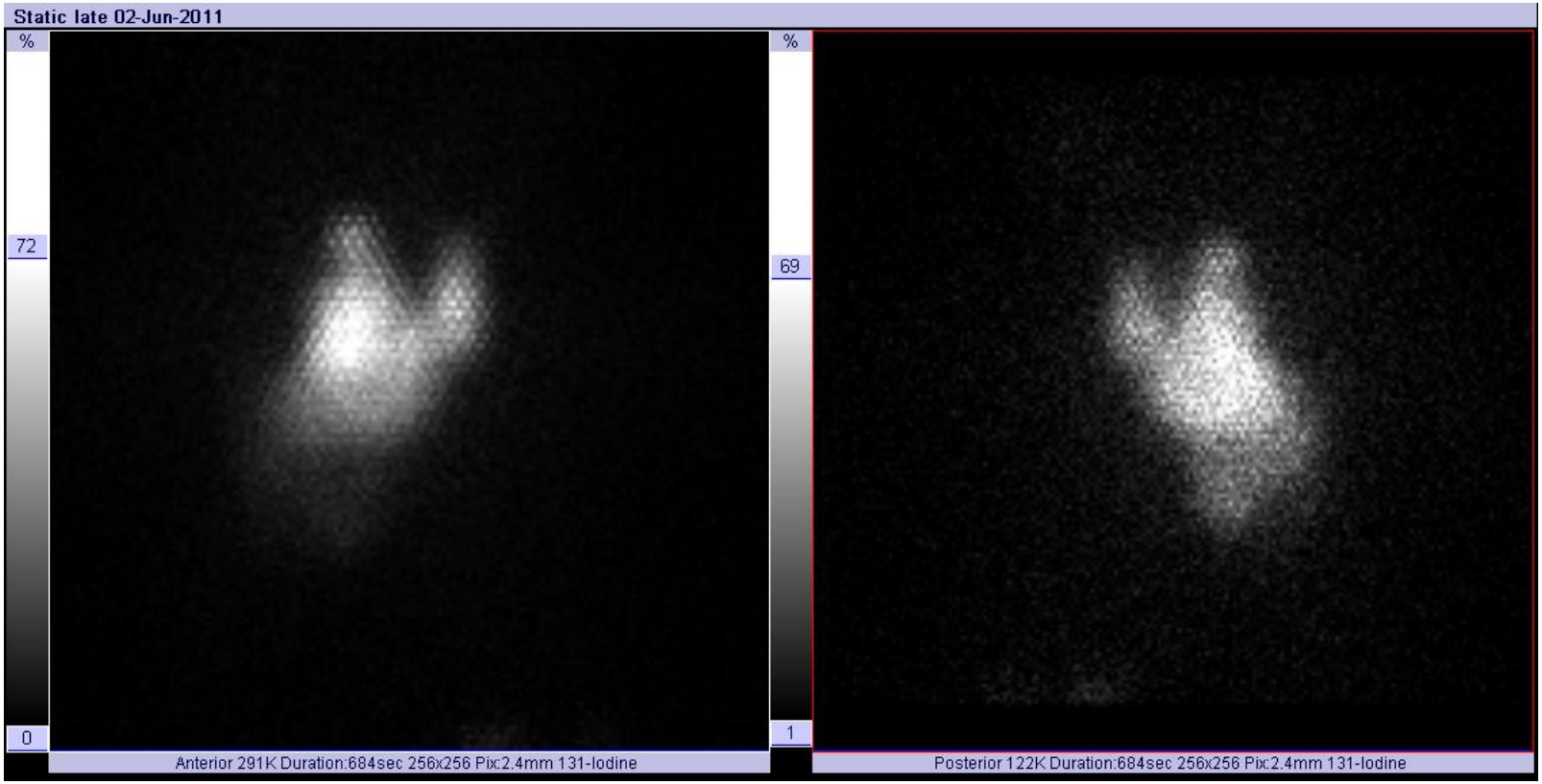
- deviation and/or compression of the trachae, tracheomalatia

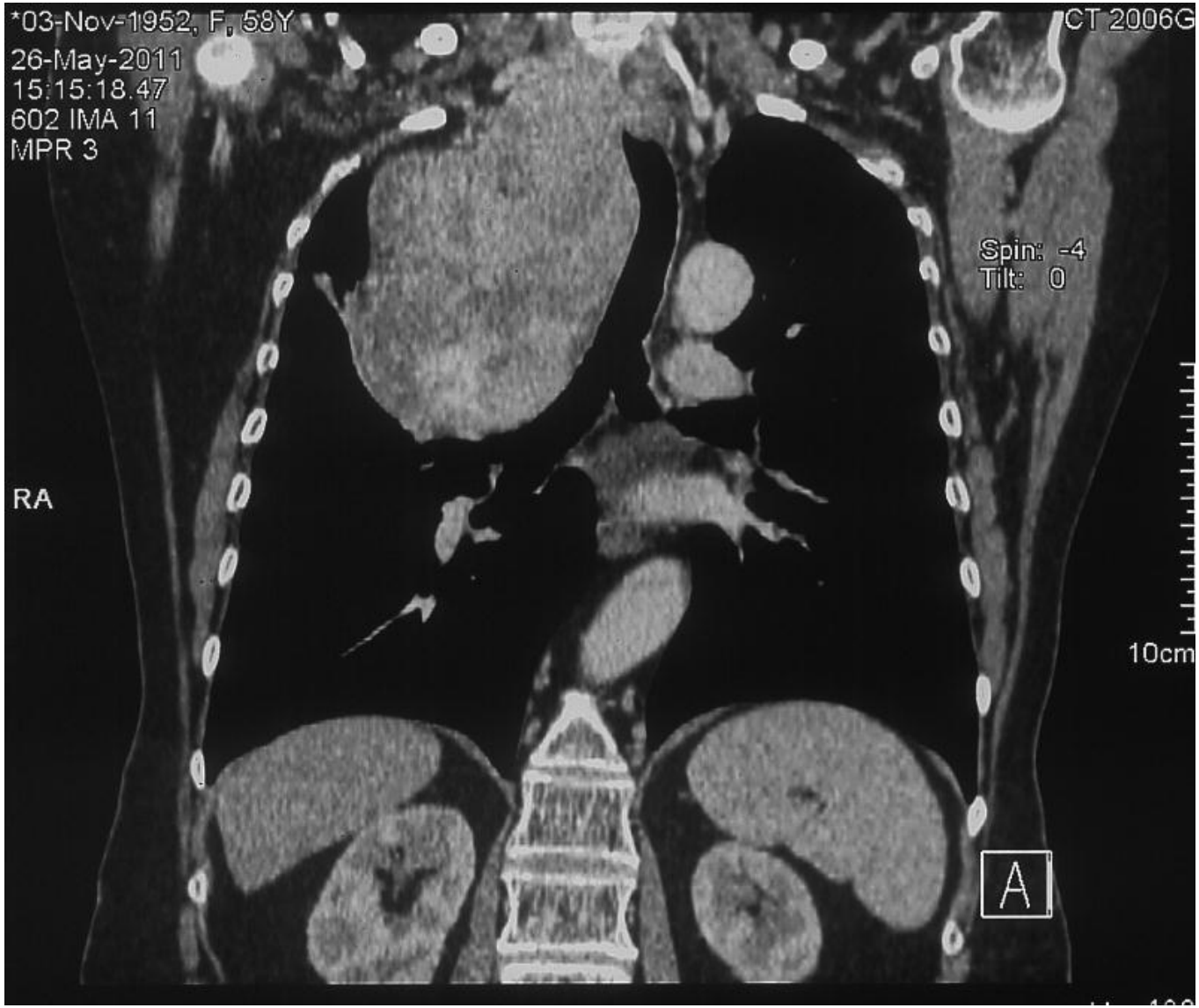
- thyroid calcification





Planar scintigraphy with I-131-intrathoracic goiter

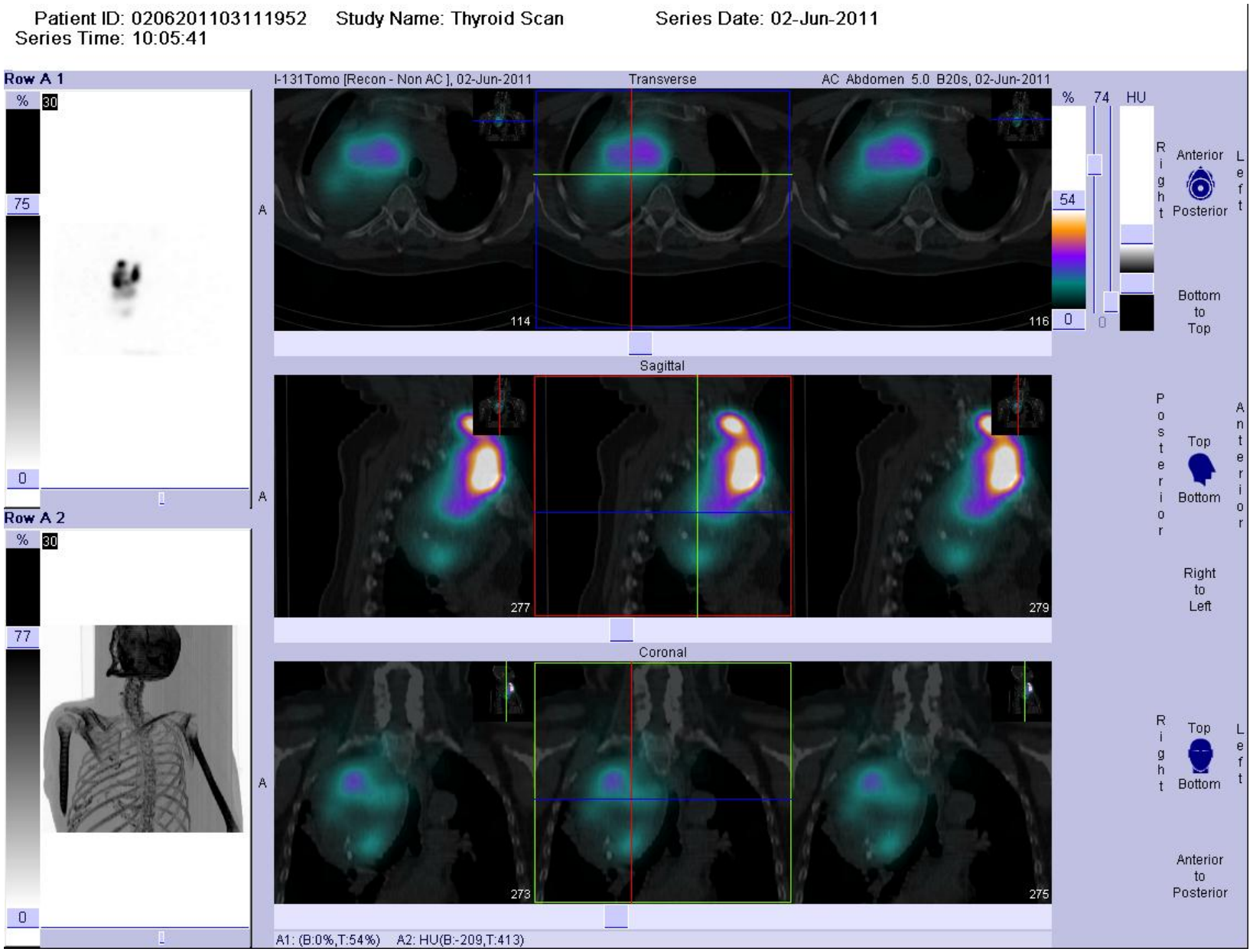



*03-Nov-1952, F, 58Y
26-May-2011
15:15:18.47
602 IMA 11
MPR 3
CT 2006G
Spin: -4
Tilt: 0
RA
10cm
A

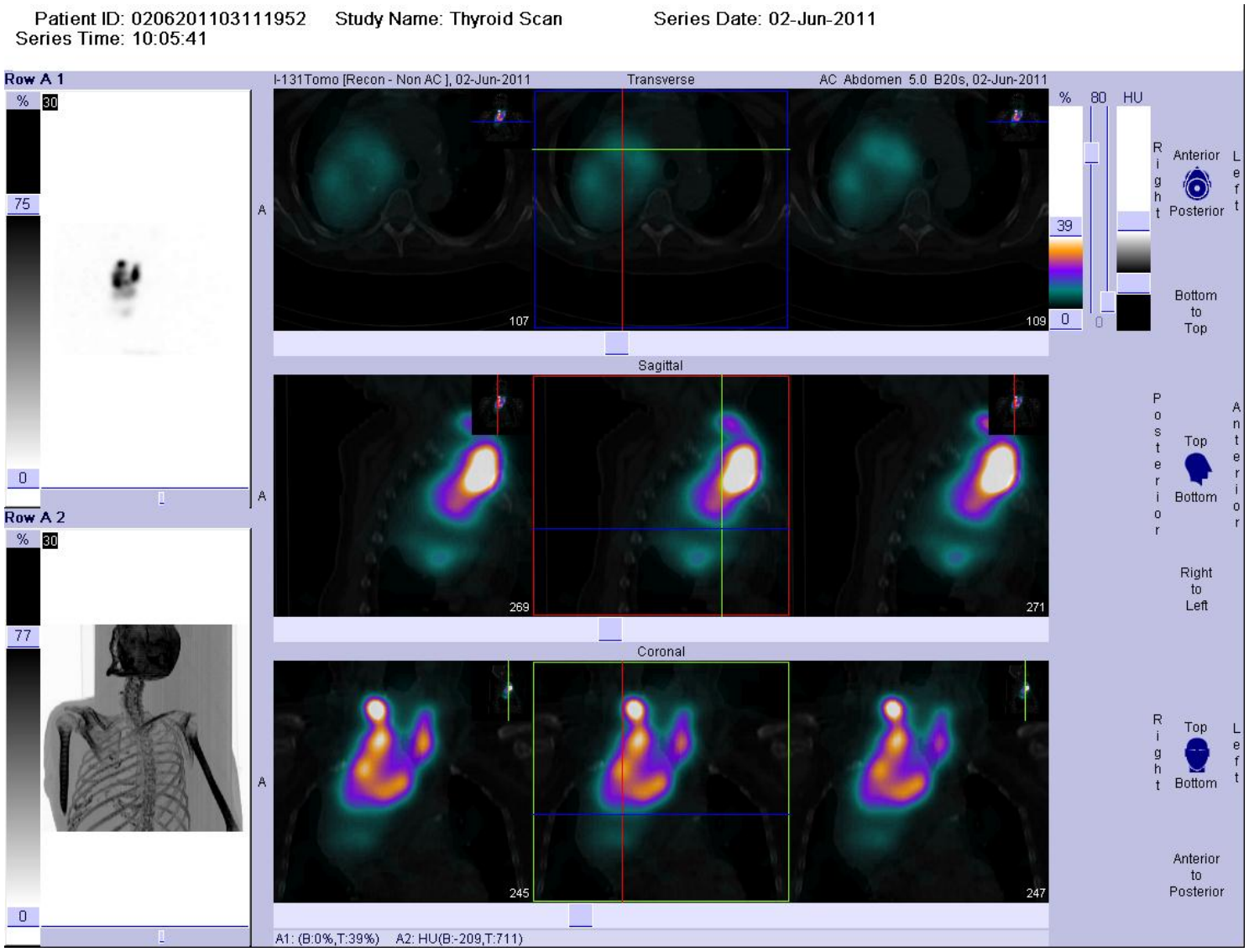

03-Nov-1952, F. 58Y
26-May-2011
15:15:18.47
603 IMA 10
MPR 3
CT 200
Spin: -100
Tilt: 0
AL
L


2 Distance: 6.38 cm
1 Distance: 11.98 cm
1
2
10cm
W 400

SPECT/CT

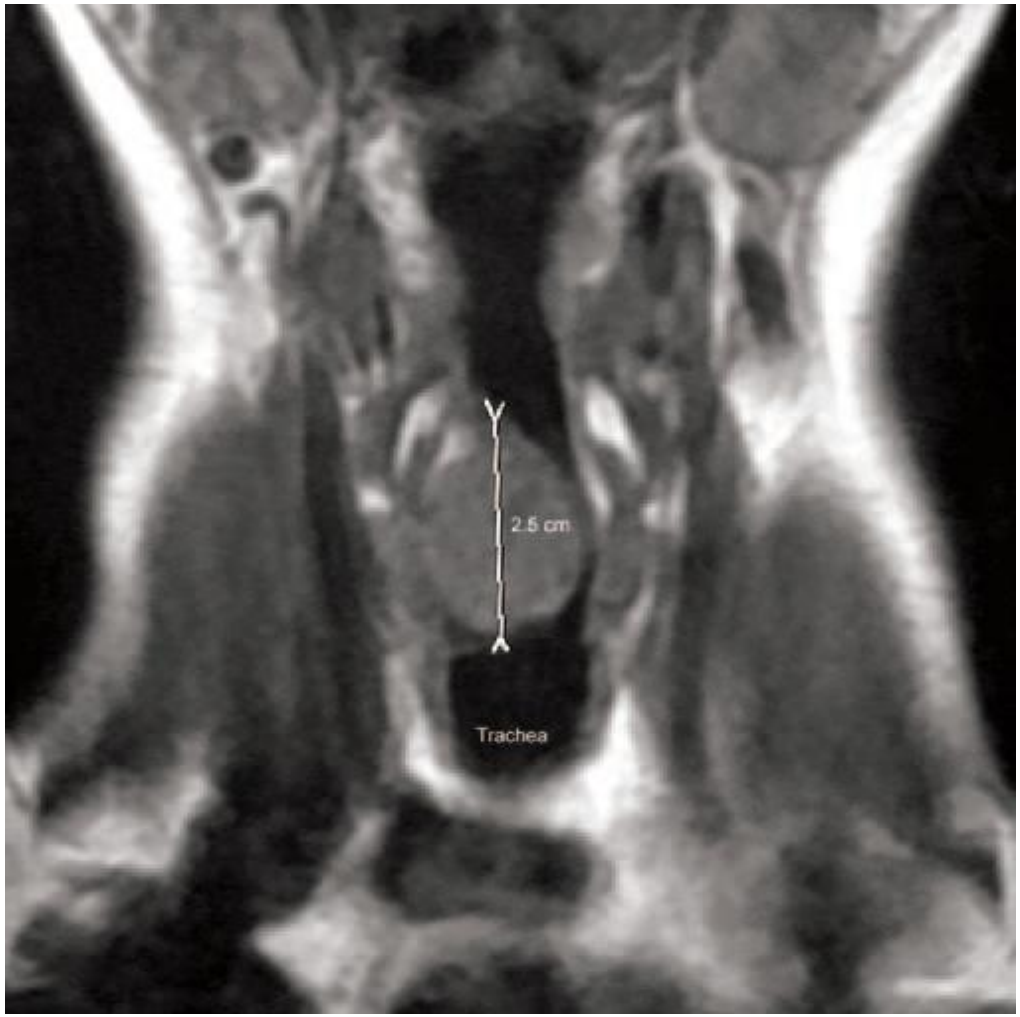

Patient ID: 0206201103111952 Study Name: Thyroid Scan Series Date: 02-Jun-2011
Series Time: 10:05:41
Row A 1
I-131Tomo [Recon - Non AC], 02-Jun-2011
Transverse
AC Abdomen 5.0 B20s, 02-Jun-2011
Sagittal
Coronal
Row A 2
A1: (B:0%,T:54%) A2: HU(B:-209,T:413)

SPECT/CT


Patient ID: 0206201103111952 Study Name: Thyroid Scan Series Date: 02-Jun-2011
Series Time: 10:05:41
Row A 1
I-131Tomo [Recon - Non AC], 02-Jun-2011
Transverse
AC Abdomen 5.0 B20s, 02-Jun-2011
%
30
75
0
A
107
109
%
80
HU
39
0
Right
Anterior
Posterior
Left
Bottom to Top
Sagittal
269
271
Posterior
Anterior
Top
Bottom
Right to Left
Row A 2
%
30
77
0
Coronal
245
247
Right
Left
Top
Bottom
Anterior to Posterior
A1: (B:0%,T:39%) A2: HU(B:-209,T:711)

CT, MR

Ectopic- intratracheal thyroid



Clinical problem: Carcinoma in multinodular goiter

- 4 - 17% cancer are found in the surgicly removed multinodular goiters.
- 4 - 24% thyroids on the autopsy have carcinoma.

- Incidentaly found unpalpable nodes have 4-6% cancer on US guided fine needle aspiration.

- Higher risk:

  - in patient who had head and neck area radiated during childhood.

Cancer problem

- Up to 5% nodes have carcinoma regardless whether they are solitar nodul or multinodular thyroid

- 4% of population have solitar nodule (40 000 per 1 000 000)
- 4% persons with nodule have carcinoma (1600 per 40 000)
- 1 600 cancers per 1 000 000 habitants
- 30 - 60 cancers a year per 1 000 000 habitants
- 6 patients die per 1 000 000 habitants

- Clinical treatment of dominant and/or suspected nodes in multinodular goiter

Treatment of multinodular goiter

- There is no simple or optimal therapy – individual approach
- Follow up without therapy
- Surgery
- Radioiodine therapy
- Suppression therapy with thyroxine

- Percutane injection of ethanol
- Laser therapy

Surgical treatment of multinodular goiter

- Indications:
  - Carcinoma finding by FNAC
  - Goiter and nodes growth with symptoms of compresion
  - Cosmetic large goiter
  - Hyperthyroidism

- Therapy of choice in young patients
- Subtotal thyroidectomia
- Near total or total thyroidectomia (relapse in up to 60%)

Therapy with I-131

- **Indications:**

  - Scintigraphic “hot” nodes – multinodular toxic goiter or just suppressed TSH, especially in elderly patients

  - malignant tumor excluded

  - large and/or retrosternal goiter

  - older patients with increased risk for surgery – especially cardiopaths

Radioiodine therapy of euthyroid goiter

- 40% reduction in goiter size during the first year, and 60% reduction during 3–5 years period
- Weaker effect in large goiters
- Recombinant hTSH.

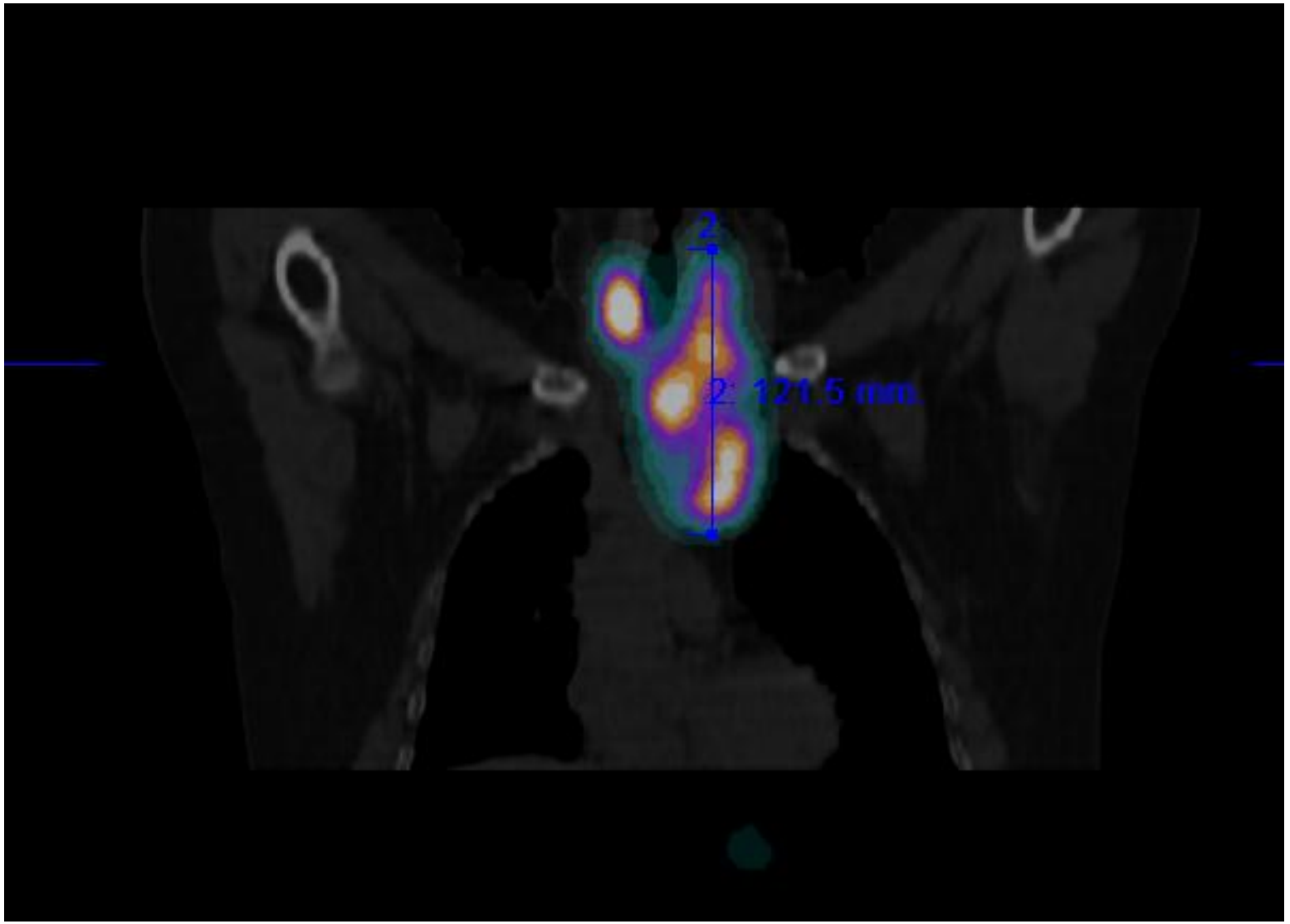
- Significantly more effective and easier to endure in regard to suppression therapy with thyroxine
- No significant side-effects (hypothyroidism).
- No increase in cancer risk in patients treated with ^{131}I.

Thyroxine suppression therapy

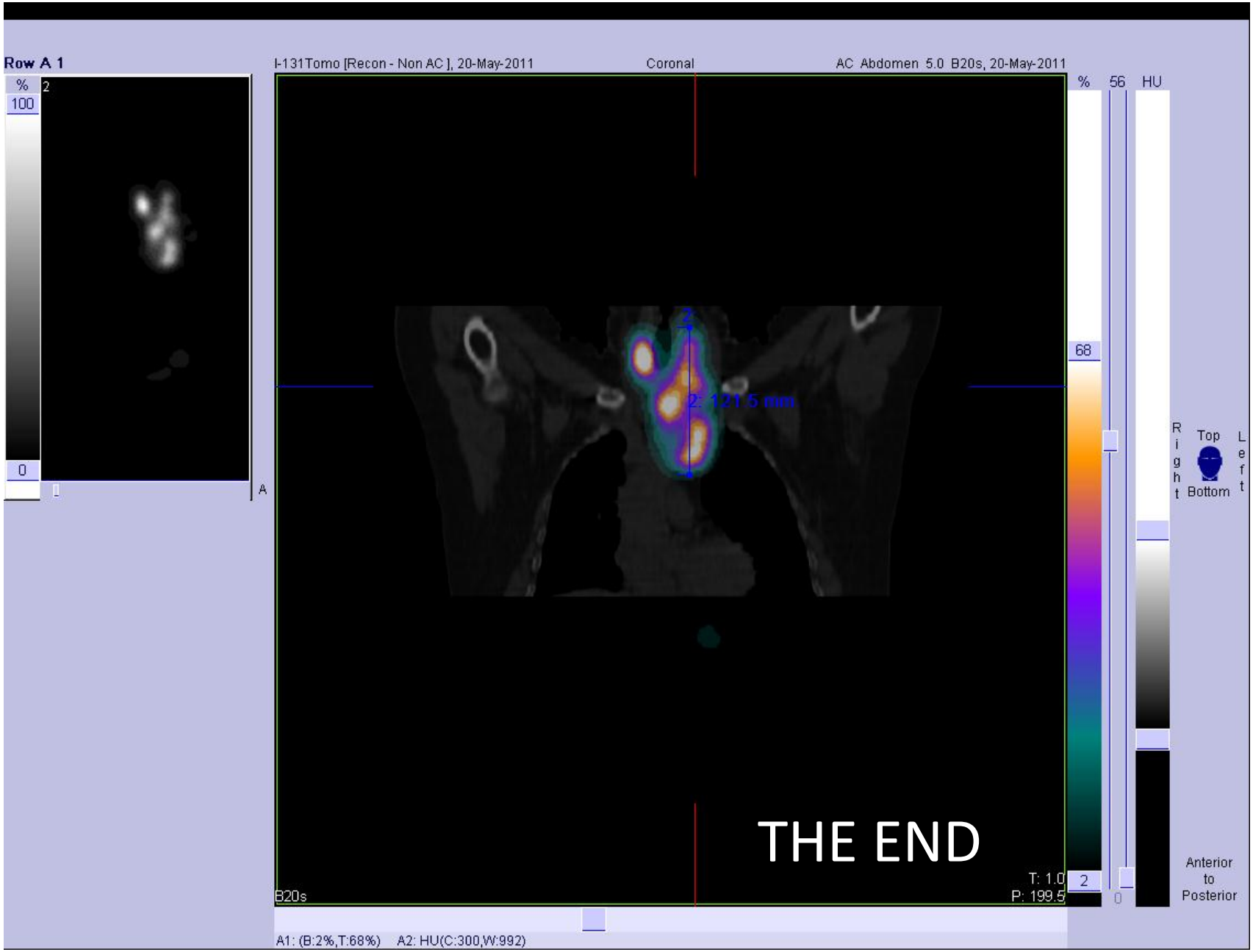
- Possible reduction of small non-toxic multinodular goiter
- Not indicated with suppressed TSH.
- Individual access (not recomended in cardiopaths and older patients).
- Relapse after discontinuation of therapy.

Follow up witout therapy

- Goiter stable for many years.
- Cytology: benigne.
- Ultrasound follow up of goiter and nodule's size every 6 -12 months with TSH level follow up.
- In case of growth of eather goiter or nodes and/or appearance of suspected nodes repeat FNAC.
- In case of appearance of TSH suppression: determine FT3, FT4 and do the thyroid scintigraphy.


2
2 121.5 mm


Row A 1
Transverse
Sagittal
Coronal
I-131Tomo [Recon - Non AC], 20-May-2011
AC Abdomen 5.0 B20s, 20-May-2011
%
102
32
0
KATIC NATASA A
2005201122061949
22-Jun-1949
20-May-2011
Thick MPR
R
L
B20s
kV: 130.0
mAs: 25
P
T: 2.4
S: 2.4
P: 184.6
77
KATIC NATASA H
2005201122061949
22-Jun-1949
20-May-2011
Thick MPR
P
A
R
L
T: 1.0
S: 1.0
P: 275.7
283
F
KATIC NATASA H
2005201122061949
22-Jun-1949
20-May-2011
Thick MPR
T: 1.0
S: 1.0
P: 205.2
211
%
105
2
75
HU
0


Row A 1
I-131Tomo [Recon - Non AC], 20-May-2011
Coronal
AC Abdomen 5.0 B20s, 20-May-2011
%
100
0
2
A
2
2: 121.5 mm
%
68
2
56
HU
0
Right
Top
Bottom
Left
THE END
T: 1.0
P: 199.5
B20s
Anterior
to
Posterior
A1: (B:2%,T:68%)
A2: HU(C:300,W:992)