CHAPTER V

Results

V:1. MULTIPLE ENDOCRINE NEOPLASIA SYNDROMES

V:1:1. Introduction

The presence of tumors in various endocrine organs is known under the term multiple endocrine neoplasia (MEN) syndrome. The first type, MEN 1, is characterized by the combined occurrence of tumors of the pituitary gland and pancreatic islets and by hyperparathyroidism. The frequent association of medullary thyroid carcinoma (MTC) with adrenal phaeochromocytoma was first described by Sipple in 1961 (1) and later called MEN 2. This is an autosomal dominant inherited disorder with a high degree of penetrance but varying in expression (2,3). MEN 2 is subdivided by Sizemore (4) into two phenotypes: MEN 2A and 2B. Type 2A or Sipple's syndrome is characterized by the occurrence of multifocal C-cell hyperplasia or medullary thyroid carcinoma, bilateral intra- and extra-adrenal phaeochromocytomas and hyperplasia, adenoma or even carcinoma of one or more of the parathyroid glands (5,6). Type 2B, the mucosoneural phenotype, is characterized by the combination of Sipple's syndrome with the development of multiple neuromas, a marfanoid habitus and without or only a slight hyperplasia of the parathyroid glands (4,7). In the Netherlands at least 10 large, nonrelated kindreds with the MEN 2A syndrome are known (6). We investigated the occurrence of thyroid lesions in 12 patients with the MEN 2A syndrome and in one patient with the MEN 2B syndrome with the aid of computed tomography.

V:1:2. Clinical aspects and biochemical screening tests

Patients with the MEN Type 2A syndrome have a clinical picture characterized by local tumor growth in the thyroid gland, with or without metastases in the neck region, or distant metastases, and sometimes by the effects of the release of peptide hormones into the circulation produced by the MTC and its metastases. This sometimes leads to secretory diarrhea or in extraordinary cases to a Cushing syndrome (8). On the other hand, complaints can be induced by the production of cathecholamines by a phaeochromocytoma, resulting in paroxysmal attacks of headache, changes in blood pressure, excessive palpitations or even stroke and myocardial infarction (5). Biochemical screening tests to detect autonomous secretion of calcitonin in early MTC are the pentagastrin stimulation test (PG test) and the short calcium infusion test (5,6,9). The reasons for CT investigations of the thyroid in patients belonging to a MEN 2-kindred are the following: first, this method is useful to confirm carcinoma in the presence of positive provocation tests; second, when a tumour is detected surgical treatment in an early stage of carcinoma is curative; the third reason is that the type of operation is determined by the diameter of the largest tumour focus. When the diameter is smaller than 0.5 cm, a total thyroidectomy is indicated. In cases of tumours
larger than 0.5 cm an additional cervical lymph node dissection is performed. In cases of cervical lymph node metastasis, a modified neck dissection is done.

**V:1:3. Conventional radiological signs**

Conventional radiography to detect early MTC is not useful (10). In patients with a more developed stage of the MEN 2 syndrome, secondary radiological signs can be obtained, including dense thyroid and cervical lymph node calcifications (11), nodular metastases in the lung and lytic bone metastases. Other organ systems involved in metastasis are liver, kidneys and adrenals. Incidental radiologic manifestations are chondrocalcinosis and signs of hyperparathyroidism. Selective arteriography of the thyroid in MEN 2 patients can reveal avascular foci of MTC surrounded by normal staining thyroid tissue. This in contradiction to the irregular vascular patterns in solitary MTC (12).

Isotope scanning with the aid of $^{99m}$Tc and $^{123}$I in cases of MTC is usually normal, except for areas of decreased uptake in large tumours (12,13).

**V:1:4. Computed tomography**

**V:1:4:1. Patients and methods**

In this group, thirteen patients, seven males and six females, ranging in age from 10 to 65 years, mainly in the second and third decade, were investigated by CT. Patients 1-12 are members of MEN 2 families; patient nr. 13 is classified as MEN 2B. Patients 1-8 received Lugol’s solution according to our protocol (see also chapter III:7) resulting in the administration of 300 mg iodine each day. Patients 9-13 were prepared with 5 potassium iodate capsules, resulting in the total administration of 500 mg iodine. A CT scan of the thyroid gland and neck region was performed according to our scanning protocol (see chapter III:8). In one patient (nr.2), contrast was administered intravenously during thyroid imaging.

Prior to the CT-examination and iodine administration, a $^{99m}$Tc scintigram was performed in five patients after administering a dose of 175 MBq of $^{99m}$Tc-pertechnetate intravenously. Twenty minutes after administration, images were obtained by a gamma camera in anterior, right anterior oblique and left anterior oblique projections. A total number of 150,000 counts was collected for each image.

In another two patients a rectilinear scintigram was made after 24 hrs of administration of 5,55 MBq of $^{123}$I. In advance of the radiological investigation, clinical screening tests were done, including the assessment of the plasma-level of CEA as a marker of medullary thyroid carcinoma. A short calcium infusion test to detect elevated serum calcitonin levels generated by the medullary thyroid tumour was performed.

Palpation of the thyroid gland revealed an enlarged gland in cases nr. 2, 3 and 5. Cervical and supravacular lymph nodes were palpable in case nr. 2.

**V:1:4:2. Results**

In ten of the thirteen patients investigated bilateral and sometimes multifocal hypodense areas, ranging in diameter from two to twenty-six millimeter, were detected with the aid of CT. In some cases small calcifications were scattered through the thyroid gland. One patient (case nr. 8) who was initially suspected clinically, had normal CT-findings, as were the biochemical parameters. He was not operated on. In the remaining two patients (case nrns. 10 and 12) no discrete hypodense areas were detected; the histopathological examination
**Figure V-1a.** A $^{123}$Iodine rectilinear scan made prior to the CT scan. There is a homogeneous distribution of activity.

**Figure V-1b.** CT-scan: cross-sections are serially obtained through the thyroid gland after pretreatment with inorganic iodine. Both thyroid lobes are well visualized. Areas of low density are not detected.

**Figure V-1c.** (see separate sheet on inside of backcover.) Microscopic specimen of the thyroid gland. No discrete nodules are present; only small foci of C-cell hyperplasia (white arrowheads) are surrounded by normal, colloid containing thyroid follicles (F). The follicular epithelium is flattened after the ingestion of iodine (Hema-toxylin-Eosin. × 320).
of these glands only revealed C-cell hyperplasia in both cases. In all cases with foci of MTC, CT was able to predict the localization of these foci in the pathological specimen, corresponding with the low density areas in the thyroid gland on CT examination. In cases of very small nodules of MTC, i.e. tumor diameters ranging from 2 to 6 mm, $^{99m}$Tc scintiscanning was negative in case nrs. 1, 6 and 7. In cases nr.4 and 5, who both had bilateral foci of MTC ranging in diameter from 5-12 mm, $^{99m}$Tc scanning revealed only one area with diminished uptake in the left lobe in nr. 4, and diminished uptake in the right lobe in patient nr. 5. In case nr. 11, with a focus of MTC in the left lobe of 5 mm and in the right lobe of 2 mm, a rectilinear scintigram with $^{123}$I was normal. In case nr. 2, cervical and supraclavicular lymph node metastases were detected. In case nr. 3, cervical lymph node metastases were predicted and histologically proven.

The density on CT of MTC, measured in 5 patients (nrs. 2-6) ranged from 18.3 to 54.0 H.U., with a mean density of 44.4 ± 14.8 H.U.

Small calcifications, ranging in diameter from 1 to 4 mm, were detected in 4 cases (nrs. 1,2,4 and 5).

Patient data are listed with the biochemical data, CT-findings, isotope scanning results and PA descriptions in table V:1.

Representative cases are shown in figures V: 1-6.

**V:1:4:3. Discussion**

In this particular group of patients with a MEN 2 syndrome the high spatial resolution of CT combined with selective contrast enhancement enables the detection of lesions of 1-2 mm easily under all circumstances. The importance of early detection and localization of foci of MTC has been stressed in this chapter (see Clinical Aspects and Biochemical Screening Tests). The main reason for CT investigations in this group is that, when a tumour is detected, the procedure of surgery can be choosen in advance, depending on the size of the tumour and the presence of metastases. In patients with a tumour diameter smaller than 5 mm, a total thyroidectomy is indicated. In cases with tumour diameters larger than 5 mm, a cervical lymph node dissection is done, too. In cases of cervical lymph node metastases, a modified neck dissection is performed. CT offers besides the possibility to detect small lesions and to measure their diameter, also the possibility to search for cervical metastases. The resolution of the gamma camera, using a pinhole collimator, permits the detection of cold nodules of 5-10 mm in size, dependent on the localization, and under optimal circumstances. In cases of familiar MTC, the early lesions are all located centrally in the thyroid gland. This is the explanation of the failure of $^{99m}$Tc- and of $^{123}$I-scanning to detect small lesions. Even large lesions up to 12 mm, which are surrounded and thus overshadowed by the normal functioning tissue, are missed or show only diminished uptake. In cases of MTC, very small calcifications are detected easily with CT scanning. In none of the investigated patients, except case nr. 5, CT revealed parathyroid hyperplasia.

In the non-familiar, i.e. sporadic form of MTC, the carcinoma is multicentric in 20% of the cases (16). Assessment of size and localization of the tumour might have clinical consequences. When only one lobe is affected, hemithyroidectomy would be sufficient, provided that the tumour is detected in an early stage.

**V:1:4:4. Conclusions**

Thyroid CT-scanning has the advantage of high spatial resolution in combination with a good contrast resolution; the latter can be influenced by using iodine to be taken up in
normal functioning thyroid tissue. As MTC does not show trapping or organification itself, small tumour foci can be detected as 'cold' spots surrounded by active thyroid tissue.

Notwithstanding the fact that calcitonin is a specific and sensitive tumour marker for MTC, false positive results are not uncommon, depending on the quality of the essay in use (17). Calcitonin can also be produced by breast carcinomas, lung tumors, phaeochromocytomas, etc. In addition, diffuse C-cell hyperplasia occurs in a normal population in 10–20% (63). Assessment of tumor localization by means of CT is a helpful method, not only in the confirmation of the presence of MTC, but also to obtain additional information concerning the extension of the lesions, which, in turn, determines the surgical strategy.

CT scanning of the thyroid gland after pretreatment with non-radioactive iodine in these cases is a procedure without risk. It offers specific and valuable information about the presence of small carcinomas, multi-centric carcinoma, metastases and infiltration in surrounding tissues. In studying patients with a MEN 2 syndrome by means of CT, we had the opportunity to test the value of this method in a unique clinical model with a histopathological verification of the CT-findings in nearly all patients.

The method used is an example of highly selective organ visualization with CT scanning by means of an organotrope contrast agent.

It has proved to be a reliable tool in the detection of small thyroid lesions, especially in such a distinct group as Sipple’s syndrome patients.

(case V-1, nr. 1).

Figure V-2a. (A-D) CT-scan. Serial cross sections through the thyroid gland (A-D). Small hypodense foci are recognized in the right lobe (small arrows). In the left lobe a larger hypodense area is seen (small arrows) with a calcification (large arrow).

Figure V-2b. (see separate sheet on inside of backcover.) Gross pathological specimen. Yellow-white nodules (arrows) are shown in both thyroid lobes (arrows). Histologically, these foci proved to be medullary thyroid carcinoma.
<table>
<thead>
<tr>
<th>Case Nr.</th>
<th>Sex</th>
<th>Age</th>
<th>Short CA Test</th>
<th>CEA ng/ml</th>
<th>99mTc Scan</th>
<th>CT Findings: Hypodense Areas and/or Calcifications Diameter in mm</th>
<th>PA Diagnosis</th>
<th>Diameter mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.M.t.Br</td>
<td>F</td>
<td>15</td>
<td>0.27 0.84 1.74</td>
<td>3.3</td>
<td>Normal</td>
<td>2.2 and 3 mm small calcification 3 mm.</td>
<td>Bilateral multifocal MTC</td>
<td>3-5</td>
</tr>
<tr>
<td>2.J.v.S.</td>
<td>M</td>
<td>49</td>
<td>35.0 60.0 90.0</td>
<td>182.0</td>
<td>Not done</td>
<td>26 mm calcifications 2-3 mm. Lymph node involvement</td>
<td>Patient not treated for religious reasons</td>
<td></td>
</tr>
<tr>
<td>3.d.R.v.L.</td>
<td>F</td>
<td>32</td>
<td>10.4 170.0 315.0</td>
<td>37.2</td>
<td>Normal</td>
<td>Max. 15 mm.</td>
<td>Bilateral multifocal MTC, with cervical lymph node metastases</td>
<td>12-15</td>
</tr>
<tr>
<td>4.W.v.L.</td>
<td>M</td>
<td>34</td>
<td>1.0 1.12 7.3</td>
<td>19.0</td>
<td>'Cold' nodule left lobe</td>
<td>Max. 12 mm. small calcifications</td>
<td>Bilateral multifocal MTC no lymph node metastases found</td>
<td>5-12</td>
</tr>
<tr>
<td>5.v.L.-Z.</td>
<td>F</td>
<td>65</td>
<td>5.0 80 105</td>
<td>38.0</td>
<td>Diminished uptake right lobe</td>
<td>Max. 14 mm. calcification 4 mm.</td>
<td>Bilateral multifocal MTC no lymph node involvement parathyroid hyperplasia</td>
<td>Max 12</td>
</tr>
<tr>
<td>6.E.C.</td>
<td>F</td>
<td>16</td>
<td>0.71</td>
<td>31.0</td>
<td>35.0</td>
<td>10.1</td>
<td>Normal</td>
<td>3-6 mm.</td>
</tr>
<tr>
<td>7.N.C.</td>
<td>M</td>
<td>24</td>
<td>0.12</td>
<td>0.32</td>
<td>9.9</td>
<td>4.6</td>
<td>normal</td>
<td>max. 5 mm.</td>
</tr>
<tr>
<td>8.J.R.</td>
<td>M</td>
<td>10</td>
<td>0.04</td>
<td>0.04</td>
<td>0.44</td>
<td>1.8</td>
<td>not done</td>
<td>normal</td>
</tr>
<tr>
<td>9.T.C.</td>
<td>M</td>
<td>23</td>
<td>0.45</td>
<td>5.7</td>
<td>6.1</td>
<td>2.8</td>
<td>not done</td>
<td>max 3 mm.</td>
</tr>
<tr>
<td>10.C.C.</td>
<td>M</td>
<td>26</td>
<td>0.04</td>
<td>0.34</td>
<td>0.28</td>
<td>1.4</td>
<td>¹³¹I scan: normal</td>
<td>normal</td>
</tr>
<tr>
<td>11.A.v.S.</td>
<td>F</td>
<td>16</td>
<td>0.8</td>
<td>1.2</td>
<td>4.7</td>
<td>3.7</td>
<td>¹²³I scan: normal</td>
<td>2 and 5 mm.</td>
</tr>
<tr>
<td>12.L.V.</td>
<td>F</td>
<td>15</td>
<td>0.14</td>
<td>0.44</td>
<td>0.67</td>
<td>0.8</td>
<td>not done</td>
<td>normal</td>
</tr>
<tr>
<td>13.v.D.</td>
<td>M</td>
<td>16</td>
<td>3.9</td>
<td>12</td>
<td>14</td>
<td>28.5</td>
<td>not done</td>
<td>2 and 3 mm</td>
</tr>
</tbody>
</table>

* Patient nos. 2 and 8 were not operated on.
** Short calcium test: after an overnight fast, baseline was sampled (0 min) for calcitonin estimation before the administration of calcium (Sandoz) (2.5 mg/kg) by rapid intravenous infusion (30 sec). Samples were taken again 2 and 5 minutes after infusion.
Figure V-3a. $^{123}$Iodine rectilinear scan. The distribution of activity is homogeneous. The left lobe is somewhat smaller as compared to the right lobe.

Figure V-3b. CT-scan. Serial cross sections (A-D) obtained after pretreatment with inorganic iodine. In the right lobe (A), a small hypodense nodule is seen (arrows). In the left lobe (A, B and C), a larger hypodense area is demonstrated (arrows), measuring 5 mm in diameter.

Figure V-3c. (see separate sheet on inside of backcover.) Longitudinal section through both lobes of the gross pathological specimen. A yellow-white tumour focus is seen in the left lobe (arrows). The smaller focus in the right lobe seen at CT was detected too at histological examination. Both foci proved to be medullary thyroid carcinoma histologically.
Figure V-4a (1, 2 and 3). $^{99m}$Tc-scintigraphy of the thyroid gland with a right anterior oblique (RAO) and a left anterior oblique view (LAO). In the RAO-view, a slightly decreased uptake in the middle of the right lobe can be observed.

Figure V-4b. CT-scan. Consecutive cross sections obtained through the thyroid gland reveal bilateral hypodense areas (arrows) surrounded by normally functioning thyroid tissue. Note the isthmus of the thyroid gland.

Figure V-4c. (see separate sheet on inside of backcover.) Gross pathological specimen. Both thyroid lobes are sliced in the frontal plane and turned like the pages of a book. There are bilateral yellow-white nodules centrally located in the normal thyroid tissue. At histological examination these nodules proved to be medullary thyroid carcinoma.
Figure V-5. Large, hypodense areas are seen bilaterally in the thyroid gland. Only a small rim of white, functioning tissue is remained in the ventral part of both lobes. At histological examination these hypodense lesions consisted of medullary thyroid carcinoma.
V:2. THE SINGLE THYROID NODULE

V:2:1: Introduction

The discovery of a single nodule in the thyroid is a common event that makes further examination necessary because of the risk of malignancy. The incidence of a palpable nodule in studies in populations with an adequate dietary iodine level is reported to be between 3 and 4 per cent (18-20). Thyroid nodules are some seven times more common in females than in males.

In most series of excised cold, solid, single nodules between 10 and 20 per cent proved to be carcinomas on histological examination (21,22). It is generally agreed that carcinoma comprise a far greater proportion of single nodules found in people younger than 20 years and older than 60 years than in other age groups and in males regardless of age (23).

V:2:2: Imaging modalities and clinical aspects

The different imaging modalities are reviewed in chapter II. Isotope scanning and ultrasound application will be briefly discussed, being the common procedures in the daily routine examination. The earliest developed and most durable method is the evaluation of thyroid structure using the isotopes of radioiodine (24). The radioactive iodine is taken up and organified by the thyroid gland. $^{99m}$Technetium-pertechnetate has also become widely used for thyroid imaging. It is a decay product of $^{99}$molybdenum and is only trapped and not organified in the thyroid tissue (25). A drawback is that some lesions which are 'hot' with technetium do not organify radioiodine, implicating that some thyroid tumours may be missed (26,27). However, the incidence of such occurrences has been very low and mainly of benign nature (28). A good approach is to reinvestigate all lesions, proven to be hot at a $^{99m}$Tc-scan, with $^{123}$I. The usefulness of classifying thyroid nodules according to their capacity of concentrating radioiodine is well established (29). A radioactive iodine scan will indicate whether a nodule concentrates isotope normally, or whether there is increased or diminished uptake with respect to the normal, surrounding tissue. A hot or hyperfunctioning nodule represents an autonomous functioning adenoma or normal concentrating tissue surrounded by areas of degeneration or thyroiditis. A hyperplastic lobe or absence of the contralateral lobe can give the same picture (30). Such non-toxic nodules make up 25 per cent of solitary or dominant thyroid nodules and have rarely proven to be malignant. Patients with autonomous nodules are clinically or subclinically thyrotoxic, as can be shown by a blunted response of TSH to TRH.

(case V-1, nr. 2)

Figure V-6. Scans A and C obtained after pretreatment with inorganic iodine. Large hypodense areas are seen in the thyroid gland (white arrowheads). Small calcifications are present in both lobes (small arrows). Scans B and C. Additional information is obtained at the same level after administration of contrast medium intravenously. There is no enhancement of the hypodense areas. The remainder of the thyroid tissue is enhanced and the blood vessels become clearly visible (1-3). Enlarged lymph nodes are easily recognized in the post-contrast scans (large arrows).  
1 = common carotid artery.  
2 = internal jugular vein.  
3 = external jugular vein.
Absence of iodine organification indicates that the nodule is cold. Non-functioning thyroid nodules, however, constitute a heterogeneous group that includes adenomas, cysts, subacute and chronic thyroiditis, multinodular goiter, various fibrotic, hemorrhagic and necrotic processes and thyroid cancer. Cancer accounts for 20% of the hypofunctioning or solid, single, non-functioning nodules; 20% of the cases are cysts proven to be infrequently malignant and 40-60% of the cases are benign adenomas. Other possibilities are local thyroiditis, colloid nodules and multinodular goiter (21,22,31).

Application of radio-nuclides other than the iodine isotopes, such as \textsuperscript{75}selenium-methionine, \textsuperscript{67}gallium, \textsuperscript{99m}technetium-bleomycin and \textsuperscript{131}cesium can indicate cellular activity in protein synthesis. Complementary use with radiiodine scanning could further differentiate the nature of cold nodules. However, these isotopes have given conflicting results and are not in current use (32-34). \textsuperscript{201}Thallium has proven to be of value in the postoperative detection of thyroid cancer (35).

Application of ultrasound to investigate cold nodules has become a routine procedure, as ultrasound is able to discriminate between solid nodules and cysts (36).

\textit{V:2.3. Computed tomography}

\textit{V:2.3.1. Introduction}

Computed tomography in patients with a palpable and scintigraphically cold nodule is not frequently performed (see also chapter II, section II). Yoshikawa (37), applying CT, found that the nature of the wall of a thyroid lesion might be clinically useful in differentiating a benign tumor from a malignant one. Pirschel (39) emphasized the usefulness of densitometric measurements in different thyroid lesions, especially in multinodular goiter, cysts and thyroiditis.

Sekiya (38) differentiated thyroid lesions with respect to the border (well-defined or ill-defined) the inner wall (smooth or irregular), the density and the contrast-enhancement.

In our study, 19 patients with a palpable and mostly cold single thyroid nodule have been studied.

\textit{V:2.3.2. Patients and methods}

Nineteen patients with a palpable single nodule, four males and fifteen females, were investigated by CT. Patients ranged in age from 12 to 73 years, mainly in the fourth and fifth decade. Eleven patients had a \textsuperscript{99m}Tc-scintigram and two patients had a \textsuperscript{131}I-scintigram before CT-scanning. Nine patients were prepared with iodine according to our protocol.

All patients who received iodine were euthyroid and stayed euthyroid, when not operated on, for at least one year afterwards.

Patient data, clinical findings, scintigraphic and ultrasound results and CT findings are listed in table V:2, including the diagnosis after the histopathological examination.

\textit{V:2.4. Results}

Two of the nineteen patients investigated appeared to have a malignancy on histopathological examination (cases nr. 4 and 19). The malignant nature of these lesions was shown and predicted on CT. The inhomogeneous staining after contrast enhancement, the irregular border and inner wall of the scintigraphic cold lesions were according to the descriptions for malignancy given by Sekiya (38).
Ten patients received inorganic iodine; none of them had a malignancy. Aberrant thyroid tissue was seen twice (cases nr. 1 and 14). A real cyst was diagnosed in case 2 and 17. Multinodular goiter, presenting as a cervical cold nodule, was seen in cases nrs. 5, 7, 10 and 15. Functioning nodules were seen in case nrs. 12 and 14. Well-defined hypodense nodules were seen in case 6. The $^{99m}$Tc-isotope scan showed only one cold area in the right lobe. A sister of this patient had a follicular/papillary carcinoma at age 12. After medullary carcinoma had been excluded biochemically, the suspicion of malignancy strongly decreased by finding two nodules. But of precaution, the patient was operated on. The lesion in the right lobe proved to be a follicular adenoma.

In one case, nr. 3, presenting with a palpable nodule, dual energy measurements pointed in the direction of a hemorrhage. The patient was operated on; the histopathological diagnosis confirmed the CT-findings. In one case (nr. 13) the cold area appeared to be a calcified nodule. In one case a cyst was detected with hyperdense tissue inside. This proved to be a thyroglossal duct cyst containing functioning thyroid tissue; one case (nr. 9) had a thyroiditis. In a total number of 8 patients, surgery was performed followed by histopathological examination.

The patients who received iodine and who were not operated on were reported to be euthyroid one year afterwards.

V:2:5. Discussion

Computed tomography of cold nodules indeed results in additional information that was not obtained by the isotope scintigraphy. As has been shown, malignancy has characteristic features. These cases were tumours of the anaplastic type. Nevertheless, we are convinced that computed tomography is not always able to differentiate between benign and malignant, not even in the case when these lesions turn out to have benign CT characteristics. Density measurements are helpful in ranging thyroid disorders. However, there is an overlap between cysts and adenomas; when a nodule shows iodine uptake, it can be characterized as benign. In addition, a multinodular aspect suggests a benign lesion. Calcification in typical forms appeared to be associated with benign lesions.

V:2:6. Conclusions

Application of computed tomography certainly has proven to be of additional value in suggesting the correct pre-operative diagnosis. This can lead to a change in surgical approach. CT investigation of cold nodules shows substantially more anatomic detail than can be obtained with any other imaging procedure. However, in any case of doubt, a cold nodule deserves histopathological examination under all circumstances, whether by needle biopsy or by surgical intervention.
<table>
<thead>
<tr>
<th>Case nr.</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical Findings</th>
<th>Scintigram</th>
<th>Ultrasound</th>
<th>CT findings</th>
<th>PA diagnosis</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.M.H.M.M.</td>
<td>20</td>
<td>F</td>
<td>enlarged right thyroid lobe</td>
<td>not done</td>
<td>solid</td>
<td>aberrant thyroid tissue</td>
<td>not operated on</td>
<td>prepared with iodine</td>
</tr>
<tr>
<td>2.F.G.-G.</td>
<td>60</td>
<td>F</td>
<td>palpable nodule right</td>
<td>$^{99m}$Tc: cold nodule right</td>
<td>cystic</td>
<td>cyst; no enhancement</td>
<td>not operated on</td>
<td>prepared with iodine</td>
</tr>
<tr>
<td>3.B.c.R.</td>
<td>19</td>
<td>F</td>
<td>palpable nodule right</td>
<td>$^{131}$I: cold nodule right</td>
<td>cystic with internal reflections</td>
<td>cyst isodense with blood</td>
<td></td>
<td>scanned with Dual Energy received no iodine</td>
</tr>
<tr>
<td>4.J.D.</td>
<td>58</td>
<td>M</td>
<td>palpable nodule right</td>
<td>$^{131}$I: cold nodule right</td>
<td>not done</td>
<td>ill defined nodule with irregular enhancement</td>
<td>anaplastic carcinoma (bilateral)</td>
<td>received no iodine</td>
</tr>
<tr>
<td>5.J.G.L.</td>
<td>52</td>
<td>M</td>
<td>palpable nodule left</td>
<td>$^{99m}$Tc: cold nodule left</td>
<td>not done</td>
<td>nodular aspect</td>
<td>multinodular dysplastic goiter</td>
<td>prepared with iodine</td>
</tr>
<tr>
<td>6.M.H.</td>
<td>13</td>
<td>F</td>
<td>palpable nodule right</td>
<td>$^{99m}$Tc: cold nodule right</td>
<td>not done</td>
<td>well defined, hypodense nodule right lobe; small, well defined nodule left lobe</td>
<td>follicular adenoma</td>
<td>sister had follicular/papillary carcinoma at age 12 received no iodine</td>
</tr>
<tr>
<td>7.H.v.d.S.</td>
<td>53</td>
<td>M</td>
<td>palpable nodule left</td>
<td>$^{99m}$Tc: cold nodule</td>
<td>not done</td>
<td>multinodular goiter cervico-thoracal</td>
<td></td>
<td>received no iodine</td>
</tr>
<tr>
<td>8.J.D.-v.H.</td>
<td>49</td>
<td>F</td>
<td>palpable nodule right</td>
<td>$^{99m}$Tc: cold nodule</td>
<td>not done</td>
<td>well-defined nodular goiter</td>
<td></td>
<td>received no iodine</td>
</tr>
<tr>
<td>Patient ID</td>
<td>Age</td>
<td>Gender</td>
<td>Clinical Findings</td>
<td>Imaging Findings</td>
<td>Histological Findings</td>
<td>Treatment</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>9.C.A.Y.</td>
<td>46</td>
<td>M</td>
<td>Palpable nodule right</td>
<td>$^{99m}$Tc: cold nodule</td>
<td>Not done</td>
<td>Hypodense, with diffuse, irregular uptake</td>
<td>Thyroiditis</td>
<td>Prepared with iodine</td>
</tr>
<tr>
<td>10.W.K.-V.</td>
<td>56</td>
<td>F</td>
<td>Palpable nodule left</td>
<td>$^{99m}$Tc: cold nodule left</td>
<td>Not done</td>
<td>Multinodular goiter</td>
<td>Not operated on</td>
<td>Received no iodine</td>
</tr>
<tr>
<td>11.J.B.</td>
<td>12</td>
<td>F</td>
<td>Palpable nodule</td>
<td>Not done</td>
<td>Not done</td>
<td>Cyst containing tissue isodense with thyroid tissue</td>
<td>Cyst of ductus thyreoglossus</td>
<td>Prepared with iodine</td>
</tr>
<tr>
<td>12.F.K.-G.</td>
<td>48</td>
<td>F</td>
<td>Palpable nodule</td>
<td>$^{99m}$Tc: increased uptake</td>
<td>Not done</td>
<td>Well defined, hyperdense nodule with enhancement</td>
<td>Not operated on</td>
<td>Prepared with iodine</td>
</tr>
<tr>
<td>13.W.B.</td>
<td>54</td>
<td>F</td>
<td>Palpable nodule</td>
<td>$^{99m}$Tc: cold nodule</td>
<td>Not done</td>
<td>Calcified nodule</td>
<td>Not operated on</td>
<td>Prepared with iodine</td>
</tr>
<tr>
<td>14.B.-G.</td>
<td>29</td>
<td>F</td>
<td>Palpable nodule</td>
<td>Not done</td>
<td></td>
<td>Aberrant thyroid tissue</td>
<td>Not operated on</td>
<td>Prepared with iodine</td>
</tr>
<tr>
<td>15.C.M.H.</td>
<td>73</td>
<td>F</td>
<td>Palpable nodule</td>
<td>$^{99m}$Tc: cold nodule</td>
<td>Not done</td>
<td>Multinodular goiter</td>
<td>Not operated on</td>
<td>Received no iodine</td>
</tr>
<tr>
<td>16.G.H.</td>
<td>43</td>
<td>F</td>
<td>Palpable nodule left</td>
<td>$^{99m}$Tc: irregular uptake</td>
<td>Not done</td>
<td>Patchy hyperdense areas in regular, hypodense thyroid gland</td>
<td>Not operated on</td>
<td>Received no iodine</td>
</tr>
<tr>
<td>17.J.v.R.</td>
<td>68</td>
<td>F</td>
<td>Palpable nodule left</td>
<td>$^{99m}$Tc: cold nodule</td>
<td>Cystic</td>
<td>Cyst, well defined</td>
<td>Not operated on</td>
<td>Received no iodine</td>
</tr>
<tr>
<td>18.L.-H.</td>
<td>48</td>
<td>F</td>
<td>Palpable nodule right</td>
<td>Not available</td>
<td>Not done</td>
<td>Well-defined functioning nodule with enhancement</td>
<td>Follicular adenoma</td>
<td>Prepared with iodine</td>
</tr>
<tr>
<td>19.F.B.</td>
<td>61</td>
<td>F</td>
<td>Palpable nodule left</td>
<td>$^{131}$I: cold nodule left</td>
<td>Not done</td>
<td>Ill-defined mass with irregular hancement</td>
<td>Anaplastic carcinoma</td>
<td>Received no iodine</td>
</tr>
</tbody>
</table>
Figure V-7. A woman twenty years old presenting with an enlarged right thyroid lobe. Investigation with ultrasound revealed that the right lobe was solid. With the aid of CT hyperdense tissue is demonstrated isodense with the thyroid gland (black arrow and white arrowheads). The diagnosis 'aberrant thyroid tissue' was made by CT.

Figure 8A. A woman sixty years old presenting with a palpable nodule in the right thyroid lobe. The nodule proved to be cold with a $^{99m}$Tc-isotope scan. The CT-scan demonstrates a sharply delineated hypodense area with a smooth inner wall (c) and a density of 18 H.U.

Figure 8B. Slice obtained during intravenous bolus injection of contrast. There is no enhancement of the hypodense area. The hypodense area was diagnosed as a cyst. Note the anterior jugular veins (white arrowheads).

1 = common carotid artery.
2 = jugular vein.
Figure V-9. A girl nineteen years old presenting with a palpable nodule in the right thyroid lobe. With ultrasound, the lesion proved to be semi-solid. CT-scanning shows a hypodense area (arrows) isodense with blood (scanned with Dual Energy). The CT-diagnosis was: hemorrhage (H) in the right thyroid lobe. A radioiodine scan was performed and revealed a cold nodule. Patient was operated on. The lesion was histologically diagnosed as a hemorrhage in the right thyroid lobe.

1 = common carotid artery.
2 = internal jugular vein.
H = Hemorrhage.
S = Sternocleidomastoid muscle.

Figure V-10. A man, 58 years old presenting with a palpable nodule in the right thyroid lobe. The nodule was cold at $^{131}$I-iodine isotope scanning. On CT, the nodule is irregular enhanced and has an irregular inner wall. The border is not well defined (arrows). The lesion was presumed to be malignant by its CT appearance. The histopathological investigation revealed a bilateral anaplastic thyroid carcinoma.
A girl thirteen years old presenting with a palpable nodule in the right lobe; her sister had a follicular-papillary carcinoma at age 12. With ultrasound, the lesion proved to be semi-solid. With serial CT-scanning, a hypodense lesion is seen in the right thyroid lobe, partially surrounded by a small rim of normal thyroid tissue. Moreover, in the left thyroid lobe a smaller hypodense area is seen (11-B, arrows). Medullary thyroid carcinoma was excluded biochemically. Because the diagnosis malignancy is unlikely in thyroid glands with multifocal hypodense areas, the patient underwent hemithyroidectomy. The lesion in the right lobe proved to be a follicular adenoma histologically.

A girl twelve years old, presenting with a palpable nodule medio-lateral in the right thyroid lobe. The CT-scan demonstrates a cystic lesion less than 10 mm in diameter (arrows). Within the cyst, a small rim of tissue, isodense with the thyroid gland is recognized.
Figure 13A. A woman forty eight years old presenting with a palpable nodule. Within the hypodense thyroid gland (T) a hyperdense nodule is seen (arrows). A $^{99m}$Tc-isotope scan showed increased uptake.

Figure 13B. CT scan obtained at the same level after administration of contrast agent intravenously, resulting in the enhancement of the whole thyroid gland. The diagnosis hyperfunctioning nodule in a euthyroid patient was suggested. The vascular structures (1-5) are well demonstrated.

1 = common carotid artery.
2 = internal jugular vein.
3 = anterior jugular vein.
4 = vertebral artery.
5 = vertebral vein.

Figure 12B. (see separate sheet on inside of backcover.) General view of the histological specimen. The lesion could be identified as a thyroglossal duct cyst containing thyroid tissue inside.
Figure V-14a (A-D). Patient presenting with a palpable nodule in the right thyroid lobe. A series of non-enhanced CT-scans shows a regular hypodense nodule (arrows) with compression of the remaining thyroid tissue (A-D).

Figure V-14b (A'-D'). Serial dynamic scans (A'-D') obtained during injection of contrast agent intravenously. The hypodense nodule is enhanced. The border is well defined and the inner wall is smooth (arrows). After histopathological examination the lesion proved to be a follicular adenoma.
V:3. NON-TOXIC GOITER

V:3:1. Introduction

Non-toxic goiter, which can be diffuse, multinodular or uninodular is exceedingly common in the world. It is estimated that 200 million people suffer from widely spread endemic goiter (40). Even in areas where iodine deficiency has been excluded, palpable goiters occurs in 10 per cent of the female population (41).

In the aetiology of goiter formation, some main categories can be detected. These include iodine deficiency, goitrogen, enzymatic defects, hereditary, and immunologic mechanisms. Evidence has been obtained in mice that the pathogenesis of hot, cold and autonomous follicles, which evolve during the slow process of goiter growth, is genetically determined. During goitrogenesis, daughter follicles differing in iodine turnover may be newly generated by continuous replication of some selected clones of normal, genetically differently endowed epithelial cells of mother follicles (43).

This, and changes in the need for thyroid hormones during life is thought to be associated with cyclic hyperplasia and involution of the thyroid gland, resulting in goiter formation.

V:3:2. Clinical aspects

A goiter when large in diameter often leads to mechanical complaints in swallowing and breathing, particularly in cases with intrathoracic extension. Intrathoracic goiter is one of the first diagnostic considerations to be made in the evaluation of a superior mediastinal mass.

V:3:3. Conventional diagnostic signs

The value of conventional radiology in the assessment of a goiter is described in chapter II, section 2. Ultrasound is useful only when the goiter is located in the neck region, because the mediastinum is not accessible for ultrasound waves.

Radioisotope scanning in the detection of mediastinal extent of the thyroid gland is only successful when $^{123}$I or $^{131}$I is used, and routine scanning with $^{131}$I has been advocated in the evaluation of any mediastinal mass (44). The main drawbacks of $^{131}$I are reviewed in chapter II section 8.

V:3:4. Computed tomography

V:3:4:1. Introduction

Clinical application of CT to evaluate diffuse and nodular goiters was not performed until 1979. Yoshikawa found that four of the five single nodular goiters with smooth walls proved to be benign adenomas; five of the seven single nodular goiters with irregular walls were adenocarcinoma (36). In 1979, Pirschel was able to demonstrate multinodular goiters with certitude, considering configuration, absorption values of the nodules and outlines of the mass (38).

The first reports on mediastinal goiter diagnosed by CT were made by Binder (45) in 1980 and by Morris (46) in 1982. In 1982 Glazer (47) described five characteristic features which made accurate diagnosis of a mediastinal goiter as the cause of a mediastinal mass possible.
These signs include: anatomic continuity with the cervical thyroid; focal calcifications; relatively high CT-numbers; rise in CT number after bolus administration of iomlinated contrast media and prolonged enhancement after i.v. contrast administration.

In 1983, Bashist (48) stressed the characteristic patterns of extension of a goiter into the mediastinum.

V:3:4:2. Patients and Methods
Fifteen patients with a known, euthyroid goiter, four males and eleven females, ranging in age from 21 to 74 years, mainly in the fifth and sixth decade, were investigated by CT.

In all patients, except nr. 9, the goiter was palpable and multinodular. Additional information was obtained from chest X-rays, ultrasound and isotope scans. The reason for investigating these patients by CT was mapping of their thyroidal mass pre-operatively or to evaluate possible changes of the extent and/or character of the goiter in time.

Patients nrs. 1-8 were prepared with Lugol's solution according to our protocol resulting in a total amount of administered iodine of 600 mg over two days.

Patient nr. 2 received an additional dose of 600 mg pre-operatively and was scanned twice.

Patient nr. 7 was investigated three times, receiving iodine before every scanning procedure. She was on levothyroxin medication after the first scanning procedure.

In cases nr. 3, 7, 13 and 15, contrast enhanced slices were obtained during intravenous bolus-injection of contrast with the aid of rapid-sequence scanning.

One patient, nr. 11, had a history of previous thyroid surgery; patient nr. 10 received \(^{131}I\)-therapy to reduce goiter size.

Case 7 received levothyroxin therapy before iodine intake and CT-scanning.

Patient data, CT findings and PA diagnoses are listed in table V:3.

V:3:5. Results

Administration of iodine (600 mg according to our protocol) in patients with an euthyroid goiter resulted in density values ranging from 44.0 to 91.2 H.U., with a mean density of 72.7 ± 16.7 H.U., as measured in the homogeneous areas. In goitrous patients without preparation with iodine, density ranged from 46.3 to 86.2 H.U., with a mean density of 63.0 ± 12.6 H.U. In one patient (case nr. 2) iodine administration was continued over 6 days, prior to surgery. With this amount of iodine, low density nodules could be forced to take up iodine, resulting in a local increase in density from 28 ± 3 H.U. to 70 ± 5 H.U. in cold nodules, as is shown. Patients receiving levothyroxin medication (cases nr. 3 and 7) have densities in the range of the mean density in the non-pretreated group. In case nr. 7, the general density in the thyroid tissue decreased during levothyroxin medication; however zones surrounding hypodense nodules became hyperdense, indicating the autonomous character of the nodules.

One patient, case nr. 4, received 20 ml Lugol's solution at one dose by accident. Despite this amount of iodine, the CT-numbers are very low, possibly reflecting an enzymatic defect in the transport or organification of iodine, one of the mechanisms leading to goiter formation.

One patient, case nr. 14, who received 50 ml contrast agent intravenously, showed a transient increase in thyroid hormone levels in the range of moderate hyperthyroidism.

In 11 cases, the goiters were inhomogeneous with well defined low-density areas. Intravenous administration of iodinated contrast always resulted in enhancement of normal.
thoracic and cervical structures, with the lesion being the most prominent feature. The thyroid tissue of approximately 25-30 H.U. The nodular character of a goiter becomes more clear during contrast infusion, and the delineation of the mass from surrounding tissues becomes sharper. In six cases of this series the trachea is displaced to the right. The left border is formed by the aortic arch and great vessels. Displacement of the trachea to the left was seen in three cases. The extent of the goiter along both sides of the trachea was seen in one case.

A connection between the cervical and thoracic part of the goiters or with the normal cervical thyroid gland with the intrathoracic goiter was present in all cases. Using a direct coronal scanning technique, slices can be obtained which clearly show this connection.

Calcifications were seen in 9 cases. Calcifications were punctate in 1 and coarse in 8 cases. In one case (9) an additional dense calcification was seen representing a calcified adenoma. Histopathological analysis of the CT findings could be obtained in 6 patients, of which four were pretreated with iodine.

V:3:6 Discussion

In our experience the non-homogenic aspect of a goiter mass, the non-enhancing low-density areas and their sharp delineation after contrast injection and the sharp borders are additional features of a goiter mass. The raise in attenuation values after the intake of (free) iodine is an absolute criterium in the recognition of thyroid tissue. However, the administration of free iodine does not lead to an increase in attenuation values in all cases of multinodular goiter. Enhancement can be obtained only in susceptible patients. Therefore, there is no significant difference between the attenuation values in the group receiving iodine and the non-pretreated group (see also table IV:1).

Computed tomography shows substantially more detail than other studies, especially in the 'hidden area' of conventional radiology, the mediastinum. Distinct anatomical information about extent of a mass, displacement of surrounding structures and growth pattern of a lesion can be obtained. Using one of the intrinsic properties of CT, i.e. density measurements, the type of lesion can be characterized, because normal thyroid tissue has higher attenuation values than soft tissues according to its iodine content. However, low density areas, even with lower densities than soft tissues, are common and characteristically in contrast with their environment. Additional information can be obtained using iodinated contrast agents intravenously. During rapid sequence scanning, the vessels are clearly visualized, serving as a landmark for the mediastinal mass. The thyroid tissue itself shows also enhancement in the normal tissue, with less or no enhancement in the low-density areas. These areas are clearly outlined, as are the borders of a goitrous mediastinal mass, which becomes properly delineated from surrounding structures, accentuated by non-enhancing surrounding tissue.

Another criterium in the diagnosis of mediastinal goiter is the detection of calcifications, which, in different forms, are easily shown by CT. However, psammomabodies are beyond the level of detection by CT.

The increase in attenuation values after the intake of free iodine is an absolute criterium in the recognition of thyroid tissue. So far, free-iodine is the only organ-specific, selective contrast agent in CT. However, administration of iodine in goitrous patients is not without risk.
Table V: Clinical Data, Imaging Findings and P.A. Diagnosis in 15 patients with a known goiter.

<table>
<thead>
<tr>
<th>case</th>
<th>sex</th>
<th>age</th>
<th>clinical diagnosis made by:</th>
<th>CT-findings</th>
<th></th>
<th>PA diagnosis</th>
<th>remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.J.v.L.</td>
<td>M</td>
<td>65</td>
<td>-palpation -stridor -chest X-ray</td>
<td>cervico-thoracic trachea displaced to R</td>
<td>71 ± 10, inhomogeneous, no calcifications, level of descent</td>
<td>at manubrium sterni</td>
<td>not operated on</td>
</tr>
<tr>
<td>2.G.B.-z.</td>
<td>F</td>
<td>61</td>
<td>-palpation -stridor -99mTc-scan</td>
<td>cervico-thoracic trachea in midline</td>
<td>after 900 mg KI: 66 ± 7 after 1800 mg KI 91 ± 7, inhomogeneous, no calcifications</td>
<td>at level aortic arch</td>
<td>multinodular goiter</td>
</tr>
<tr>
<td>3.L.P.</td>
<td>M</td>
<td>71</td>
<td>palpation -chest X-ray -131I-scan</td>
<td>cervical trachea displaced to R</td>
<td>52 ± 7, inhomogeneous, coarse calcifications</td>
<td>multinodular goiter with follicular adenoma left</td>
<td>levothyroxin medication cold nodule left</td>
</tr>
<tr>
<td>4.M.A.G.</td>
<td>F</td>
<td>63</td>
<td>-palpation -chest X-ray -ultrasound -99mTc-scan</td>
<td>cervico-thoracic trachea displaced to R with narrowing</td>
<td>44 ± 5, homogeneous punctate calcifications</td>
<td>at aortic arch</td>
<td>diffuse goiter with follicular adenoma received 20 ml Lugol by accident</td>
</tr>
<tr>
<td>5.H.E.G.-H.</td>
<td>F</td>
<td>74</td>
<td>-palpation -chest X-ray</td>
<td>cervico-thoracic trachea slightly displaced to R</td>
<td>57 ± 8, inhomogeneous, coarse calcifications</td>
<td>at aortic arch</td>
<td>not operated on</td>
</tr>
<tr>
<td>Patient</td>
<td>Age</td>
<td>Method(s)</td>
<td>Side</td>
<td>Density</td>
<td>Calcifications</td>
<td>In Situ</td>
<td>Site</td>
</tr>
<tr>
<td>---------</td>
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<tr>
<td>6.I.D.-D.</td>
<td>F 21</td>
<td>palpation - ultrasound cervical</td>
<td></td>
<td>86 ± 3</td>
<td>inhomogeneous</td>
<td>no</td>
<td>at thoracic inlet</td>
</tr>
<tr>
<td>7.J.V.-dH.</td>
<td>F 30</td>
<td>palpation - ultrasound - ¹³¹I-scan cervical</td>
<td></td>
<td>1.66 ± 5 11.60 ± 4 111.55 ± 5 94 ± H.U. in hyperdense zone in nodule</td>
<td>inhomogeneous</td>
<td>no</td>
<td>at thoracic inlet</td>
</tr>
<tr>
<td>8.M.S.-v.d.H.</td>
<td>F 66</td>
<td>palpation - chest X-ray cervico-thoracic trachea displaced to R</td>
<td></td>
<td>80 ± 6</td>
<td>inhomogeneous</td>
<td>no</td>
<td>at tracheal bifurcation</td>
</tr>
<tr>
<td>9.R.M.</td>
<td>F 68</td>
<td>palpation cervical</td>
<td></td>
<td>86 ± 5 in dense areas</td>
<td>inhomogeneous with dense zone around nodules calcified nodule and scattered coarse calcifications</td>
<td>at thoracic inlet</td>
<td>not operated on</td>
</tr>
<tr>
<td>10.A.F.</td>
<td>M 66</td>
<td>chest X-ray thoracic trachea to R displaced</td>
<td></td>
<td>60 ± 6</td>
<td>homogenous</td>
<td>no</td>
<td>at level of left subclavian vein</td>
</tr>
<tr>
<td>11.E.B.</td>
<td>F 59</td>
<td>palpation - stridor - chest X-ray cervico-thoracic slight tracheal compression ¹³¹I-scan</td>
<td></td>
<td>46 ± 6</td>
<td>inhomogeneous</td>
<td>scattered coarse calcifications</td>
<td>at subclavian vein right</td>
</tr>
<tr>
<td>12.G.v.B.</td>
<td>F 64</td>
<td>chest X-ray ultrasound cervico-thoracic trachea to left ¹³¹I-scan</td>
<td></td>
<td>67 ± 5</td>
<td>homogenous</td>
<td>no</td>
<td>at thoracic inlet</td>
</tr>
<tr>
<td>case</td>
<td>sex</td>
<td>age</td>
<td>clinical diagnosis made by:</td>
<td>CT-findings</td>
<td>PA diagnosis</td>
<td>remarks</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>extent</td>
<td>density in H.U.</td>
<td>aspect</td>
<td>calcifications</td>
</tr>
<tr>
<td>13. J. K.-V.</td>
<td>F</td>
<td>69</td>
<td>- palpation ^131^I-scan</td>
<td>cervico-thoracic trachea displaced to L</td>
<td>59 ± 11</td>
<td>homogenous</td>
<td>coarse calcifications</td>
</tr>
<tr>
<td>14. J. A.</td>
<td>M</td>
<td>66</td>
<td>- palpation</td>
<td>cervico-thoracic trachea displaced to R</td>
<td>55 ± 7 H.U.</td>
<td>inhomogeneous</td>
<td>coarse calcifications</td>
</tr>
<tr>
<td>15. W. K.-V.</td>
<td>F</td>
<td>60</td>
<td>- palpation</td>
<td>cervical</td>
<td>57 ± 6</td>
<td>inhomogeneous</td>
<td>scattered calcifications</td>
</tr>
</tbody>
</table>
Conclusions

Computed tomography is able to diagnose a mediastinal mass being of thyroidal origin with a high degree of certainty. Our findings are in accordance with those reported in the literature (7-12).

Criteria for the diagnosis mediastinal goiter are:
1. anatomic continuity with the cervical part of the thyroid gland (except in occasional cases of ectopic mediastinal thyroid tissue only);
2. focal calcifications;
3. relatively high CT-numbers;
4. rise in CT numbers and prolonged enhancement after intravenous injection of contrast media;
5. minimal or non-enhancing low-density areas;
6. characteristic patterns of extent;
7. selective uptake of iodine.

The future application of Dual Energy will offer more detailed information, especially about the iodine content. So far, we do not advocate the use of potassium iodide because of the risk of the induction of hyperthyroidism by autonomous functioning nodules (see also chapter IV).

(case V-3, nr. 4)

Figure V-15A. A woman 63 years old known with a large goiter. CT scan at the sternal notch. A large hypodense mediastinal mass is present, displacing the trachea (white arrowhead) and the esophagus (small white arrowhead) to the right. The vessels are displaced laterally. A small calcification is seen.

Figure V-15B. Direct coronal scan of the same patient. The mass is expanding from the cervical region to the aortic arch (Ao). The displacement of the trachea to the right (arrows) and the extension of the mass are very well demonstrated.

Note: This patient received an overdosage of inorganic iodine. However, the mass was not enhanced and the patient stayed euthyroid (For explanation, see chapter IV).
Figure V-16 (A-D'). A man 66 years old known with a goiter. A series of plain scans of the mediastinum at the level of the manubrium to the aortic arch (A-D) was obtained. In addition, a series of scans was made at the corresponding levels during contrast administration intravenously (A'-D'). A large mediastinal mass displaces the trachea to the right (arrows) and the esophagus to the right and posteriorly (white arrowhead). On the left the border of the mass is formed by the great vessels, which are displaced to the left and anteriorly. In the mass, coarse calcifications are present (● in A' and B'). During contrast injection the vessels (1-8) and the mass are strongly enhanced (A'-D'). The nodular character of the mass becomes clear and the borders are well defined. At the level of the aortic arch there is a sharp interface between the mass and the aorta.

1 = aortic arch.
2 = left subclavian artery.
3 = left common carotid artery.
4 = brachiocephalic trunk.

5 = right brachiocephalic vein.
6 = left brachiocephalic vein.
7 = confluence of brachiocephalic veins.
8 = superior caval vein.
Figure V-17 (A-D). A woman 64 years old known with a goiter. A $^{131}$I-isotope scan (A) was performed prior to the CT examination. Uptake is present in an enlarged thyroid gland. The uptake is slightly inhomogeneous (see also figure V-18). Some retrosternal activity can be seen. B-D: serial CT scans through the mediastinum show a mass on both sides of the trachea without tracheal displacement. The mass has a nodular character and sharp borders. The vessels (arrowheads) are displaced laterally.
Figure V-18A. CT scan of the neck after pretreatment with 900 mg inorganic iodine prior to the CT examination. A hyperdense cervical mass with a nodular character is present on both sides of the trachea.

Figure V-18B. CT scan at approximately the same level performed after pretreatment with 1800 mg inorganic iodine. Hypodense nodules as seen in scan A (arrows) are forced to take up iodine and become hyperdense (B).

Note: patient was operated on shortly after this procedure.
V:4. THE MEDIASTINAL MASS

V:4:1. Introduction

The additional diagnostic yield of computed tomography, with its unique capacity for displaying bone, soft tissue and airway, beyond conventional radiographic studies of the chest is greatest in the ‘hidden’ area i.e. the mediastinum (49,50). In order to evaluate the nature of a mediastinal mass, whether it might be of thyroidal origin or not, patients were investigated by CT according to our scanning protocol.

(case V-4, nr. 1)
Figure V-19 (A-G). A woman 73 years old presenting with a mediastinal mass. Serial CT scans through the mediastinum from the level of the manubrium to the tracheal bifurcation are obtained during contrast infusion (A-G). At the level of the manubrium (A) the mass is located on both sides of the trachea. At the more caudad levels, the mass is located on the right side and posteriorly compressing the trachea slightly (arrows). The trachea and esophagus (white arrowhead) are not displaced. Some small and punctate calcifications are present in a mass which is nodular in character, accentuated by the enhancement after contrast infusion. The mass is sharply delineated from the surrounding structures. The mass was diagnosed as a mediastinal goiter. Note the clearly enhanced vascular structures (1A, 1D, 2-9).

Small arrow: confluence of the azygos vein (9) and the superior caval vein (8).

1A = Ascending aorta.
1D = Descending aorta.
2 = Left subclavian artery.
3 = Left carotid artery.
4 = Brachiocephalic trunk.
5 = Right brachiocephalic vein.
6 = Left brachiocephalic vein.
7 = Confluence of brachiocephalic veins.
8 = Superior caval vein.
9 = Azygos vein.
<table>
<thead>
<tr>
<th>Case nr.</th>
<th>Age</th>
<th>Sex</th>
<th>CT-diagnosis</th>
<th>PA diagnosis</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.J.v.S-G.</td>
<td>73</td>
<td>F</td>
<td>multinodular goiter</td>
<td>multinodular goiter</td>
<td></td>
</tr>
<tr>
<td>2.A.K.v.d.S.</td>
<td>70</td>
<td>F</td>
<td>multinodular goiter</td>
<td>not operated on</td>
<td></td>
</tr>
<tr>
<td>3.L.v.d.G.</td>
<td>82</td>
<td>F</td>
<td>multinodular goiter</td>
<td>multinodular goiter</td>
<td></td>
</tr>
<tr>
<td>4.K.M.</td>
<td>86</td>
<td>M</td>
<td>multinodular goiter</td>
<td>not operated on</td>
<td></td>
</tr>
<tr>
<td>5.J.v.d.V.</td>
<td>45</td>
<td>M</td>
<td>irregular mass enlarged lymphnodes</td>
<td>Non-Hodgkin lymphoma</td>
<td>CT-guided biopsy</td>
</tr>
<tr>
<td>6.J.V.</td>
<td>64</td>
<td>M</td>
<td>multinodular goiter</td>
<td>not operated on</td>
<td></td>
</tr>
<tr>
<td>7.G.T.</td>
<td>80</td>
<td>M</td>
<td>multinodular goiter</td>
<td>not operated on</td>
<td></td>
</tr>
<tr>
<td>8.J.v.D.</td>
<td>50</td>
<td>M</td>
<td>irregular tumor mass;</td>
<td>bronchus carcinoma</td>
<td>CT-guided biopsy</td>
</tr>
</tbody>
</table>
V:4:2. Patients and methods

Nine patients, three men and six women, ranging in age from 48 to 86 years, mainly in the 5th and 6th decade, were investigated. None of these patients received iodine before CT-scanning. Iodinated contrast was applied intravenously in all cases after the plain scanning procedure. In a few cases, a needle biopsy was done to obtain cytological material.

V:4:3. Results

Six out of nine patients, the mediastinal mass proved to be a thoracic goiter according to the radiological criteria as described in section 2 of this chapter. Two patients with enlarged lymph nodes had a CT-guided biopsy. Malignant Non-Hodgkin lymphoma was diagnosed after histopathological examination. In one case the diagnosis bronchogenic carcinoma was made histopathologically after CT-guided biopsy. Patient data are listed in table V:4.

V:4:4. Discussion

Computed tomography has become the imaging method of choice in the evaluation of suspected mediastinal abnormalities (49-52). CT has the ability to distinguish density differences as well as to provide a two-dimensional cross-sectional view of anatomic relations unobscured by overlapping shadows.

Many recent articles in the radiological literature have discussed the value of CT in examining the mediastinum and the CT-characteristics of the mediastinal masses. The normal thymus (51), thymoma (53,54) thymic cysts and other diseases involving the thymus (i.e. cystic teratoma, Hodgkin's disease, malignant germ-cell tumors) have been described (55,56). Thymomas, which can be encapsulated or infiltrative, can have cystic changes and can be calcified. When located high in the mediastinum, they may be difficult to distinguish from goiter, but will generally have no continuity with the cervical thyroid (53,54). However, CT is not able to suggest the histologic nature of a thymic lesion with certitude (55).

Evaluation of mediastinal lymph nodes by CT has, of all radiologic techniques, emerged as the most valuable procedure (57).

In bronchogenic cysts, attenuation values can range from 0-20 H.U., thus apparently similar to other mediastinal cysts (50,51). However, bronchogenic cysts with much higher CT numbers, ranging from 30-70 H.U., have been described recently (58).

Vascular masses, whether anomalous vessels or aneurysms, generally enhance more than soft tissue structures and can be traced on serial levels (57). Nevertheless, enhancement on CT does not exclude para-vascular neoplasms (59).

V:4:5: Conclusions

Computed tomography of the mediastinum is, after performing standard radiography and conventional tomography, the technique of choice to evaluate the mediastinal mass. The density, its extension, relation to other structures and its growth pattern can be evaluated.

However, the histologic nature of a mediastinal mass can not be suggested, except in cases of intrathoracic goiter (see section three of this chapter).

CT-guided biopsy in non-goitrous lesions has generally proven to be a reliable tool to confirm the diagnosis cytologically.
Figure V-20 (A). A man 86 years old presenting with a mediastinal mass and complaints in swallowing. Serial CT-scans (A-D) through the mediastinum are obtained. The trachea (arrow) and the esophagus (white arrowhead) are displaced to the right and posteriorly. There is stasis of food in the esophagus.

The mass was considered to be a mediastinal goiter by its characteristic CT appearance.
Figure V-21 (A-B'). A woman 70 years old presenting with a mediastinal mass. Serial CT-scans through the mediastinum before (A and B) and after contrast infusion (A' and B') at the corresponding levels. Compression of the trachea and displacement to the right (arrows). Displacement of the esophagus posteriorly (white arrowhead). Coarse calcifications are present in the mass. After contrast infusion, the mass and the vascular structures (1-8) are clearly enhanced. The mass has the characteristic CT-appearance of a multinodular goiter.

1 = aorta.
2 = left subclavian artery.
3 = left common carotid artery.
4 = brachiocephalic trunk.
5 = right brachiocephalic vein.
6 = left brachiocephalic vein.
7 = confluence of brachiocephalic veins.
8 = superior caval vein.
V:5. MISCELLANEOUS

V:5:1. Introduction

In this chapter some single case studies are presented, including patients with parathyroid adenomas, patients presenting with thyroiditis and patients with a carcinoma of unknown origin.

V:5:2. Parathyroid adenoma localization in patients with hyperparathyroidism

The application of CT in the localization of parathyroid adenoma is well known (60,61,62). A true positive percentage of 70 is reported (62). We investigated two patients for localization of an expected parathyroid adenoma. In one case, a left-sided enlarged parathyroid gland was detected; histopathological examination revealed a parathyroid adenoma.

In our opinion, preparation of patients with iodine prior to localization of suspected parathyroid glands is helpful because the parathyroid glands are known to be located incidentally in the thyroid gland (see figure V:22).

V:5:3. Patients presenting with thyroiditis

Two patients with thyroiditis were investigated by CT. The density measured in the thyroid gland was low and in the range of muscular tissue. Some patchy dense areas were seen. (see also chapter II, section 11 and figure V:23).

V:5:4. Patients presenting with metastases of a carcinoma of unknown primary

Five patients with metastases of a carcinoma of unknown primary (CUP) were investigated. The thyroid gland appeared to be normal in all cases.

(case V-5, nr. 2)

Figure V-22. A women sixty years old presenting with hyperparathyroidism. An enlarged nodular structure (white arrowheads) was detected, which proved to be a parathyroid adenoma by histopathological investigation.

1 = common carotid artery.
2 = internal jugular vein.
3 = sternocleidomastoid muscle.
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Figure V.23. A women 46 years old presenting with a thyroiditis. Note the hypodense appearance of the thyroid gland (A). There are a few patchy hyperdense areas. After contrast infusion (B) the thyroid gland is clearly enhanced.
1 = common carotid artery.
2 = internal jugular vein.


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