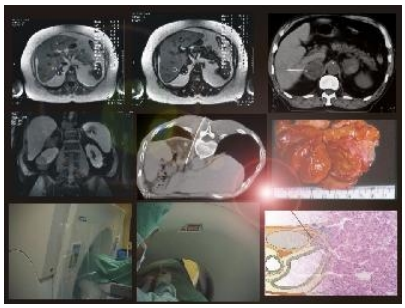

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Web design, HTML and JAVA program : S. GUTH MD

A special note of gratitude goes to Stephen Ferron, Petra Gangi and Nathalie Chalus for checking the presentation.

1) Adrenal diseases with increased function

Pheochromocytoma

Pheochromocytoma is a rare catecholamine secreting tumor. This catecholamine secretion leads to the clinical manifestations of the tumor which are : headache, palpitation, excessive sweating, hypertension. Some patients may have minor or atypical clinical symptoms. A few number of patients are even asymptotic.

- 10 % of pheochromocytomas arise in extra adrenal locations and then often referred as paragangliomas
- 10 % of cases are malignant
- 10 % of cases are bilateral
- 10 % of cases are associated with several syndromes :
  - multiple endocrine adenoma or neoplasia MEA IIA (Sipple‘s syndrome) IIB, III
  - There is an increased incidence of pheochromocytomas in patients with neurocutaneous syndromes (neurofibromatosis, Von Hippel-Lindau, tuberous sclerosis, Sturge-Weber, Carney’s syndrome)
  - some cases are familial (inherited)

Pheochromocytomas are usually large tumors (over 2-5 cm). On CT they have usually a non homogenous tissular density with areas of necrosis, hemorrhage, or even fluid levels.

Intravenous contrast medium injection is not essential and may be dangerous ; there is usually an enhancement of the tissular parts of the tumor after contrast medium administration. On MRI they are usually isointense or hypointense on T1-weighted spin echo and hyperintense on T2-weighted spin echo. Although classical patterns have been described on CT and moreover MRI, approximately 1/3 of the cases have a nonspecific appearance that may overlap the appearance of other tumors, especially adrenal cortical carcinoma. Definitive diagnosis is usually made on elevated catecholamine levels in serum and urine. CT and MR imaging are essentially used to localize the tumor or evaluate its extension before surgery. The optimal treatment is prompt surgical removal.

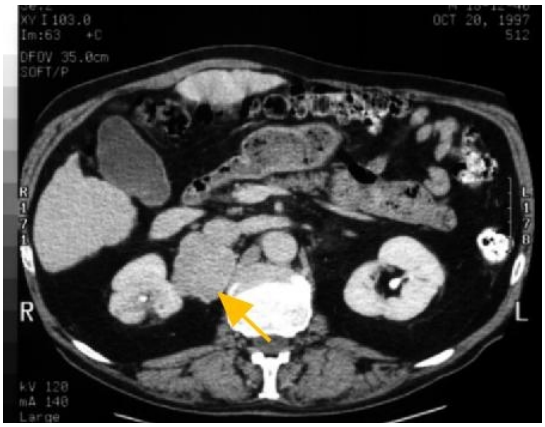


Fig 1: Right adrenal pheochromocytoma CT (yellow arrow)

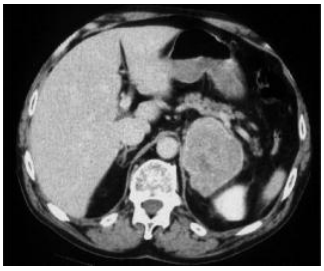


Fig 2: Left adrenal pheochromocytoma CT

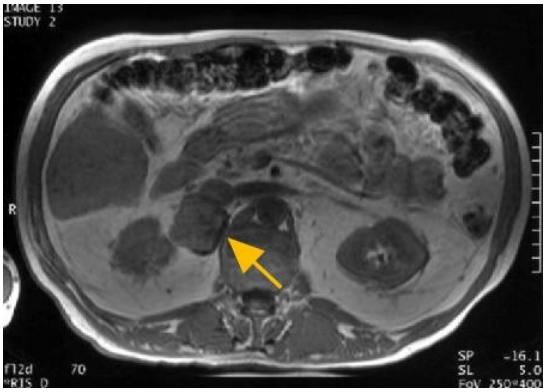


Fig 3: Right adrenal pheochromocytoma T1 weighted sequence (yellow arrow)

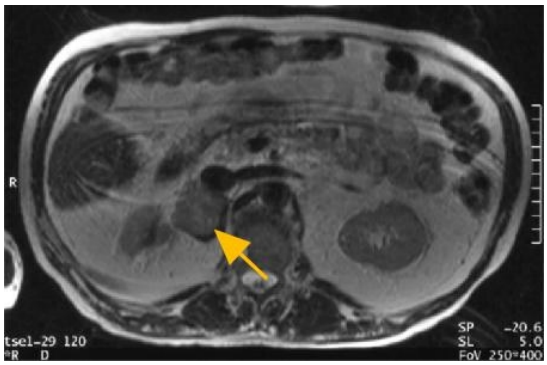


Fig 4: Right adrenal pheochromocytoma T2 weighted sequence (yellow arrow)

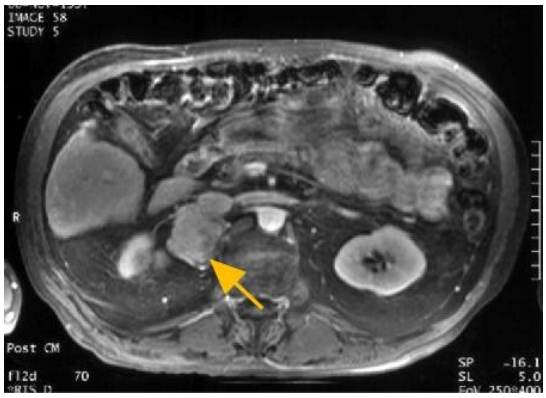


Fig 5: Right adrenal pheochromocytoma T1 weighted sequence with fat suppression and after contrast medium injection (yellow arrow)

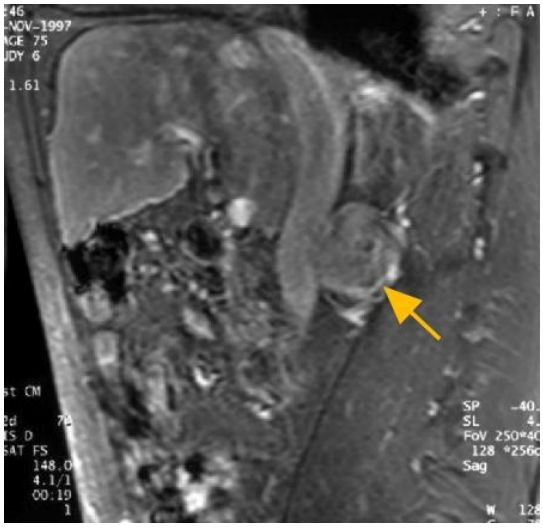


Fig 6: Right adrenal pheochromocytoma sagittal T1 weighted sequence with fat suppression and after contrast medium injection (yellow arrow)

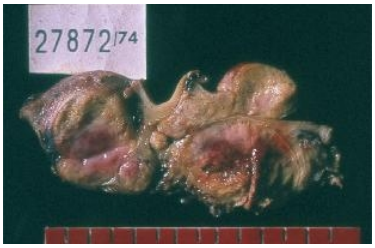


Fig 7: Pheochromocytoma, photograph of the gross specimen

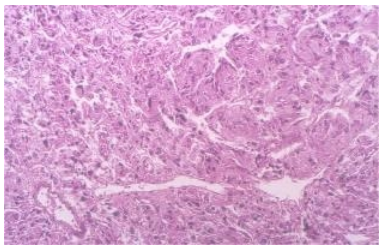


Fig 8: Pheochromocytoma, photomicrograph (hematoxylin-eosin stain)

2) Adrenal diseases with inconstant increased function

Adenoma

Adrenal adenoma are very common tumors. The prevalence of incidentalomas on CT scan is 0.3% of studies. The prevalence of all adrenal adenomas is 6.8 % to 8.7% of adults in autopsy series. In 10 to 20% of the cases found incidentally, adenomas are reported after biochemical evaluation as hormonally active. In the other 80% to 90% of the cases they are not secreting and reported as incidentalomas. 15% of all Cushing's syndromes cases are caused by adenomas (50% of the cases) or carcinomas (50% of the cases). 80% of all Conn syndromes cases are caused by adenomas (the remaining 20% are caused essentially by adrenal hyperplasia rarely by carcinomas).

On unenhanced CT typical adenomas appear classically as small --less than 3cm in size, well defined , homogenous masses with a density inferior to 0-20 UH. Density on

unenhanced CT is an important diagnosis criteria, as shown in Fig 9, it is correlated to the high lipid concentration usually found in adenomas. A low density on unenhanced CT, especially below 10 or 0 UH results high diagnosis specificity. On CT adenomas show a much earlier washout after contrast enhancement than do other tumors ; 15 to 30 mn delayed enhenced CT scan has also been proposed to differenciate adenomas (threshold value of 37 UH at 15 mn for Korobin et al)

Fig 9: Diagnosis of adenoma on unenhanced CT

Critreria	Sensitivity	Specificity	Number of cases	Slice thickness (mm)	Date revue and author of the series
Density < 0 UH	47%	100%	66	10	Lee et al 1992 Radiology
Density < 11 UH	61%	100%	78	5	Szolar et al 1997 Radiology
Density < 12 UH	94%	100%	37	5	Mc Nicholas et al 1995 AJR
Density < 13 UH	100%	100%	66	5	Boland et al 1997 Radiology
Density < 10 UH	95%	100%	41	5,10	Van Erkel et al 1994 JCAT
Density < 18 UH	85%	100%	135	5,10	Korobin et al 1996 AJR
Density < 18 UH	70%	100%	44	1,5,10	Outwater et al 1996 Radiology

On MRI, typical adenomas appear hypointense to the liver on T1-weighted sequences and iso- to hypointense to the liver on T2-weighted sequences. Hypointensity compared to the liver on T2-weighted sequences, although suggestive of adenoma versus metastasis, has insufficient specificity (there is 20 to 30% overlap). Chemical shift imaging appears actually to be the most reliable tool for diagnosis of adenomas, especially versus metastasis. The principle of chemical shift imaging uses as CT high lipid concentration usually found in

adenomas. A signal intensity index defined as D = (Signal in phase - Signal out of phase)/Signal in phase superior to 25% is used as positive diagnosis criteria for adenoma. Mc Nicholas et al found that MR imaging could be used to characterize additional adenomas undetermined on CT, reducing thereby the number of biopsies.

Fig 10: Diagnosis of adenoma on MRI chemical shift imaging				
Critreria	Sensitivity	Specificity	Number of cases	Date revue and author of the series
D > 25%	81%	100%	25	Reining et al Radiology 1992
D > 25%	82%	100%	-	Mayo et al AJR 1995
D > 25%	100%	100%	41	Bilbey et al AJR 1995

Adrenal adenomas in Conn’s syndromes tend to be small, usually with 1 cm or less diameter. Adrenal adenomas in adrenal Cushing’s syndromes tend to be bigger, usually with 2 to 3 cm diameter. A subgroup of adrenal adenomas seem to be larger and atypical and could be referred as "giant" adenomas with sizes superior to 3 - 5 cm. In this subgroup adenomas tend to be more heterogeneous, more frequently calcified, even central necrosis or hemorrhage have been described. There is an overlap especially in this group with the appearance of other tumors, especially adrenal carcinomas. In this case resection is required for definitive diagnosis.

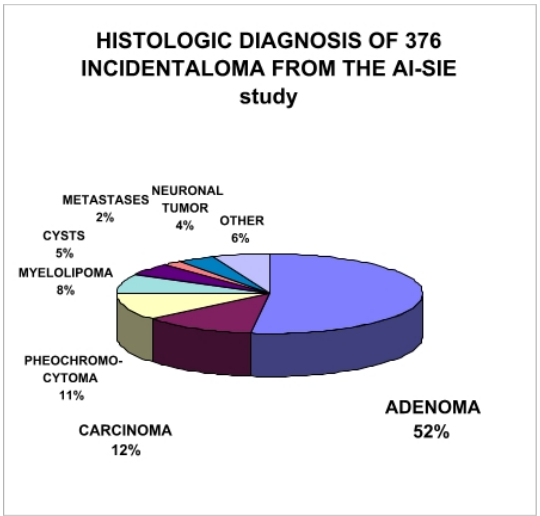


Fig 23: Histologic diagnosis of 376 incidenalomas from the AI-SIE study

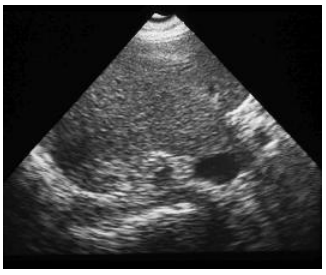


Fig 11: Adenoma, ultrasonography

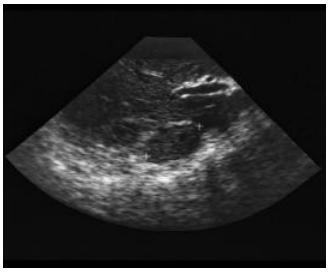


Fig 12: Adenoma, ultrasonography

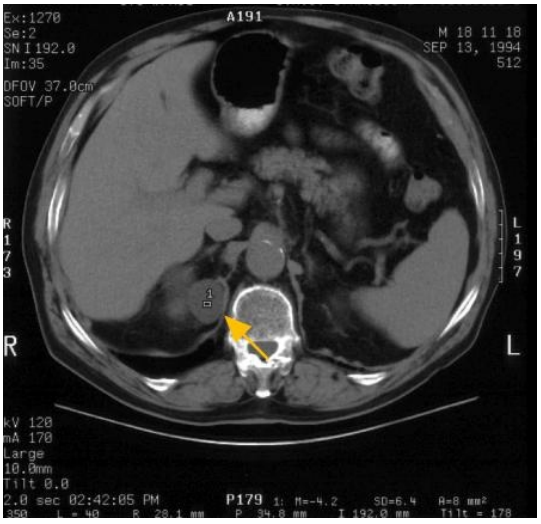


Fig 13: Adenoma (density = - 4 UH) unenhanced CT (yellow arrow)

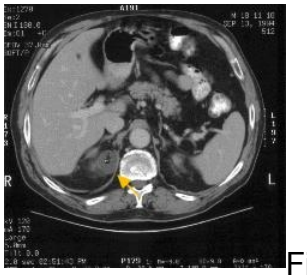


Fig 14: Adenoma enhanced CT (yellow arrow)

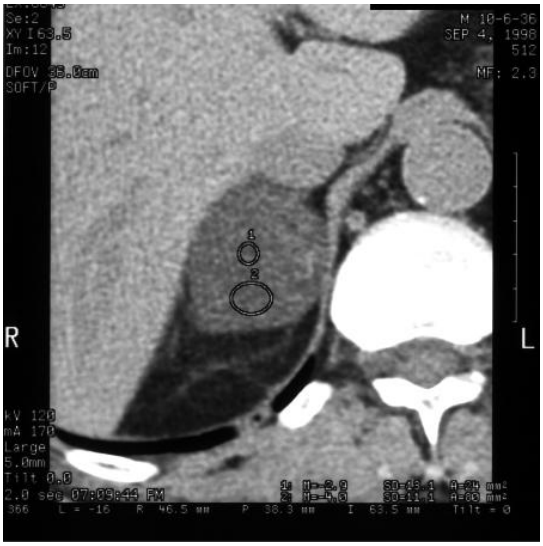


Fig 15: Atypical "giant" adenoma unenhanced CT (density = - 2 UH)

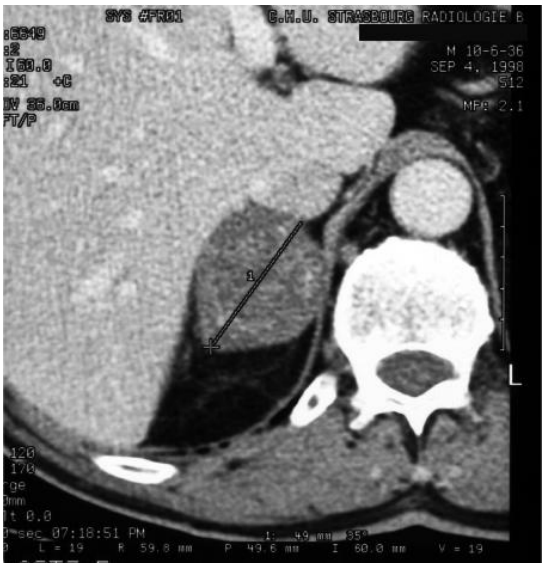


Fig 16: Atypical "giant" Adenoma enhanced CT (size = 49mm)

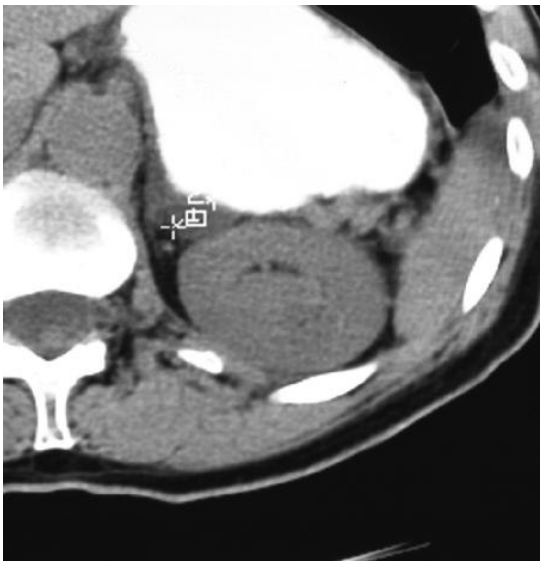


Fig 17: Small functional adenoma causing Conn syndrome, unenhanced CT

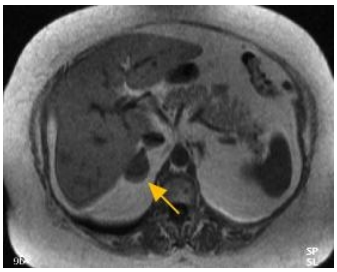


Fig 18: Right adrenal adenoma MR T1-weighted sequence (yellow arrow)

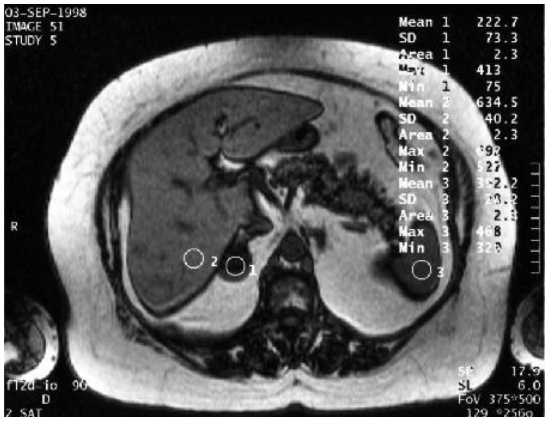


Fig 20: Adenoma, chemical shift MR imaging demonstrating a significant lost of signal on out-of-phase image compared to the in-phase image (433 versus 222 = 49% signal loss)

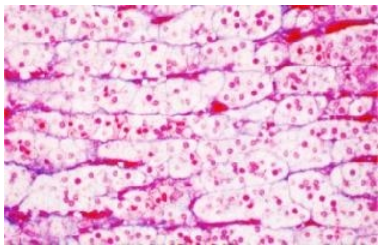


Fig 21: Adenoma, photomicrograph

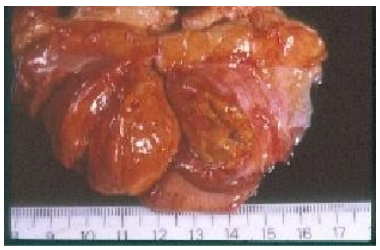


Fig 22: Adenoma photograph of the gross specimen

Adrenal carcinoma

Adrenal carcinoma is a rare tumor accounting for 0.05% to 0.02% of all cancers. A bimodal age distribution has been reported with a first peak occurring before the age of 5 years and the second in the fourth to fifth decade. There is a strong female predominance (65% to 90% of the reported cases). In 2% to 10% of patients adrenal cancer is found bilaterally. 46% of the patients had hormonal abnormality in a study encompassing 129 cases (Cushing, Conn or adrenogenital syndromes). On CT adrenal carcinomatous masses are usually large over 5 cm in size, heterogeneous with areas of low liquid or intermediate density representing tumor necrosis or hemorrhage. After contrast medium injection there is usually an enhancement of the peripheral part of the tumor while central necrosis remains hypodense. Calcifications are frequent occurring in 30% of the cases. Findings like direct invasion of adjacent structures (inferior vena cava, kidney liver, adenopathy) or metastasis are if present suggesting malignancy. At MR imaging the tumor appears usually hyperintense and heterogeneous on both T1 and T2-weighted sequences. In a small number of cases islands of high lipid concentration with consistent finding of low density on CT and typical signal loss on chemical shift MR imaging have been described in

adrenal carcinomas. Therefore in atypical adrenal masses over 5 cm in size containing areas demonstrating low density on CT or signal loss on chemical shift MRI, histologic confirmation may be mandatory. There is an overlap especially in this group, with the appearance of other tumors, especially adrenal atypical giant adenomas.

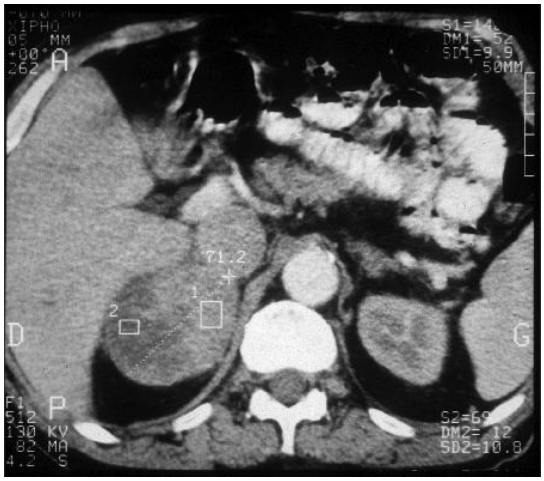


Fig 24: CT Right adrenal carcinoma

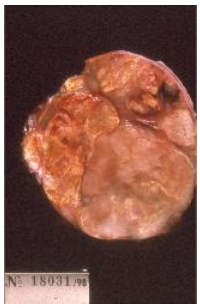


Fig 25: Adrenal carcinoma photograph of the gross specimen

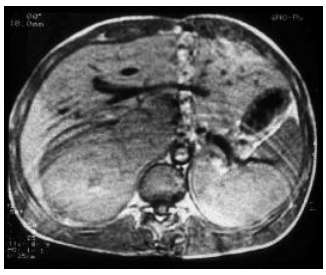


Fig 26: Right adrenal carcinoma, T1-weighted MR sequence

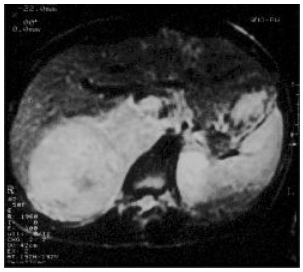


Fig 27: Right adrenal carcinoma, T2-weighted MR sequence

Adrenal hyperplasia

Adrenal hyperplasia can be involved in cushing's ACTH dependent (Cushing's disease) or independent syndromes, Conn's syndromes or virilizing syndromes. On CT and MRI the adrenal appears usually as bilateral diffuse enlargement with elongation and thickening of the limbs (superior to 7-10 mm), without a distinct tumor or with bilateral nodularity. The CT density of these lesions is identical to normal adrenal glands. In the macronodular form of adrenal hyperplasia (adrenocorticotropin-independant) there is a massive bilateral multinodular tumor-like enlargement with nodules up to 3-5 cm in size. MRI signal of these lesions is hypointense compared with the liver on T1-weighted sequences and usually hyperintense compared with the liver on T2-weighted sequences.

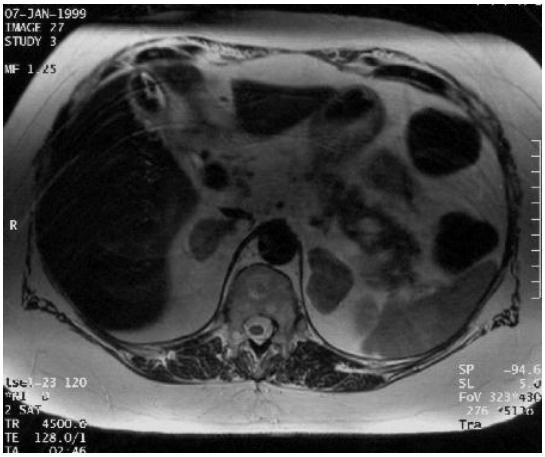


Fig 28: Adrenal hyperplasia, MRI T2-weighted sequence

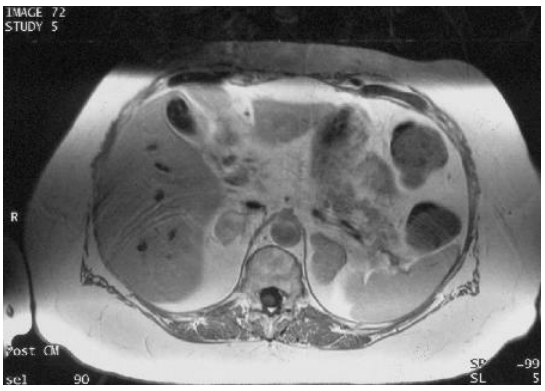


Fig 29: Adrenal hyperplasia, MRI T1-weighted sequence

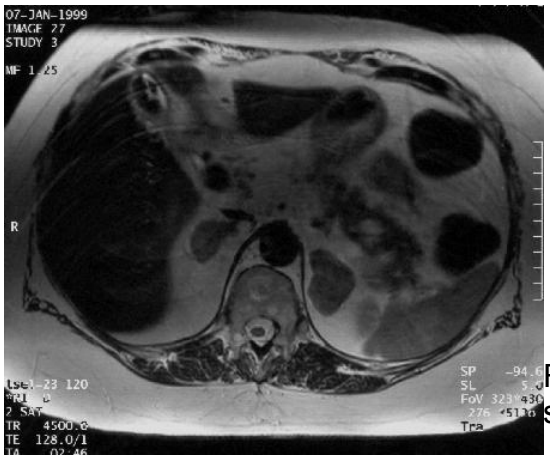


Fig 30: Adrenal hyperplasia, MRI T2-weighted sequence

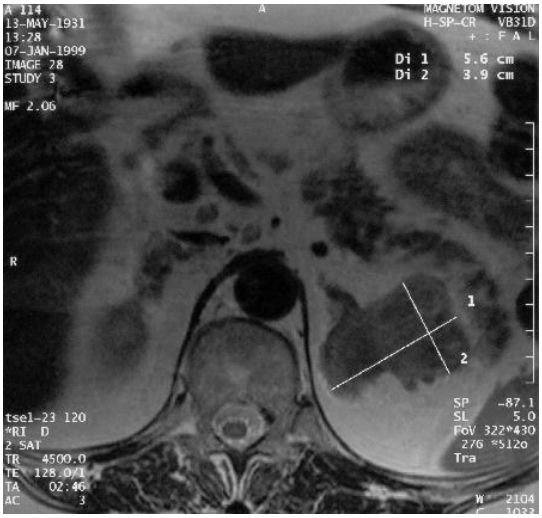


Fig 31: Adrenal hyperplasia, MRI T2-weighted sequence

3) Adrenal tumors with normal function

Metastasis

Adrenal metastasis should be suspected in any patient with underlying cancer. It is the fourth most frequent metastasis localization and the first one for lung cancer. On CT adrenal metastasis tend to be larger, less homogenous and have more irregular borders as adenomas. But alone these criteria have a poor specificity and only additional evaluation by nonenhanced CT or MR chemical shift imaging should exclude typical adenomas on the presence of intracytoplasmic fat. Undetermined cases are the counterpart of the high specificity of these criteria and are indications of percutaneous biopsy. In some cases of large metastasis especially after chemotherapy, massive tumoral necrosis is able to produce an atypical cyst-like feature with central liquid densities of 15 - 25 UH that may be equivocal (see Fig 32b). The large tumor size is helpful in these cases.

The five following images belong to one case with adrenal metastasis of lung cancer

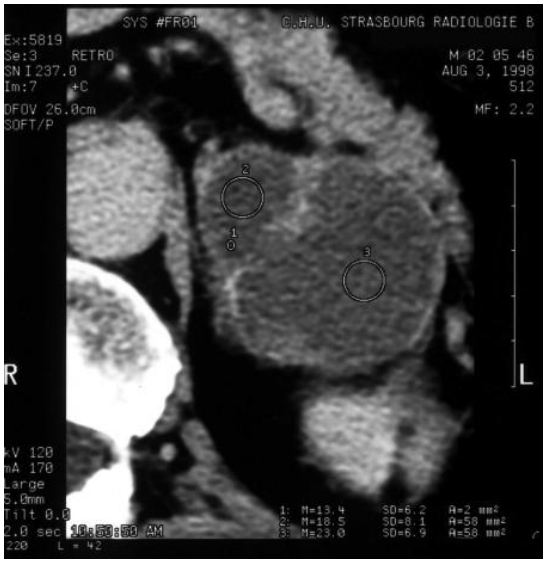


Fig 32a: Metastasis, enhenced CT

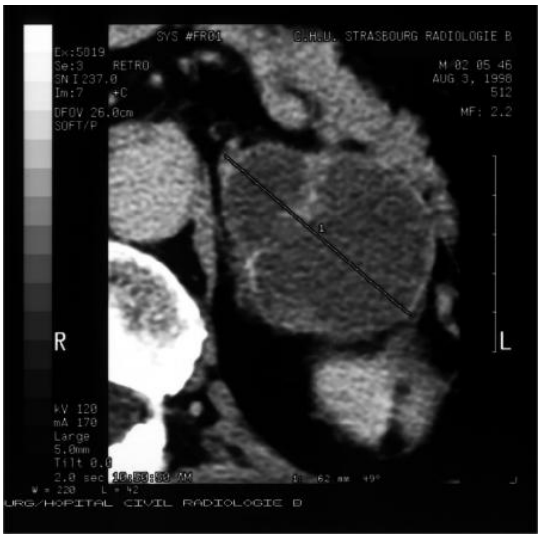


Fig 32b: Metastasis, enhenced CT, low density (13-18 UH) in areas of necrosis, size = 6,2 cm

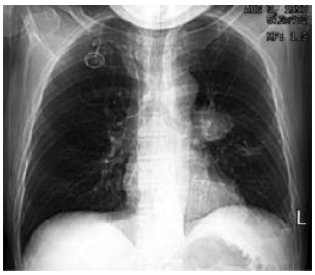


Fig 32b: Plain radiograph, lung cancer

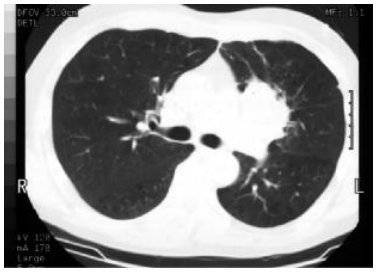


Fig 32c: CT, lung cancer

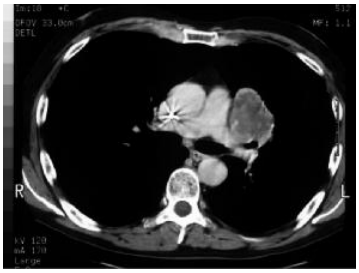


Fig 32d: CT, lung cancer

Other cases

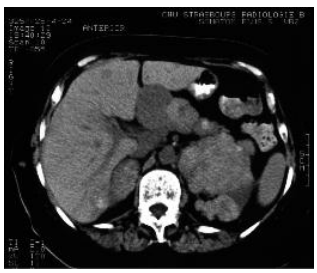


Fig 33: Unenhanced CT, adrenal bilateral metastasis of melanoma

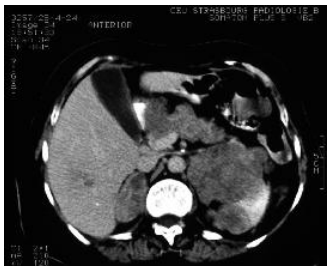


Fig 34: Enhanced CT, adrenal bilateral metastasis of melanoma

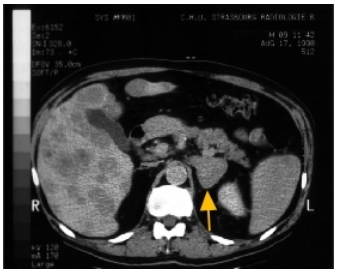


Fig 35: Enhanced CT, adrenal left metastasis of lung cancer (yellow arrow)

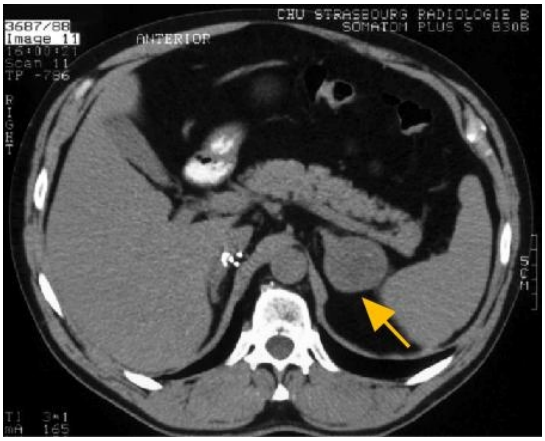


Fig 36a: Unenhanced CT, adrenal left metastasis of clear cell renal carcinoma (yellow arrow)

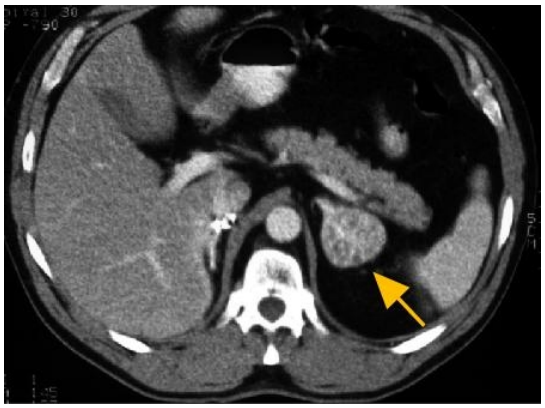


Fig 36b: Enhanced CT, adrenal left metastasis of clear cell renal carcinoma (yellow arrow)

Myelolipoma

Myelolopoma is a rare benign tumor composed of mature fat cells and hematopoietic tissue. Myelolipomas are usually asymptomatic and when diagnosed no further treatment is required. Occasionally large tumor may cause pain or bleeding spontaneously. On CT, myelolipomas are usually large tumors with a mean size of 4 cm but tumor size have been reported from 1 to 15 cm. Usually myelolipomas have heterogeneous density with areas of nonspecific tissular or intermediate density but nearly all contain definitive fat density areas below -20 UH. The amount of fat areas is highly variable ranging from 90% of the tumor to tiny foci (10% of the tumor) but these foci of definitive fat density are highly specific to the tumor. Calcification is seen in 30% of the cases. On MR these areas appear as hyperintense on both T1- T2-weighted sequences. Decrease of signal on fat suppressed images or out-of-phase images is confirmatory but decrease of signal on out-of-phase images is inconstant and is usually not present in mature fat areas which are very specific to the tumor (see Fig 41i). After contrast medium injection there is a significant nonspecific enhancement of the tumor.

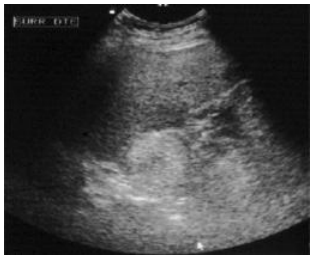


Fig 37: Ultrasonography, myelolipoma

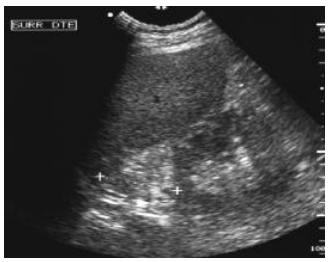


Fig 38: Ultrasonography, myelolipoma

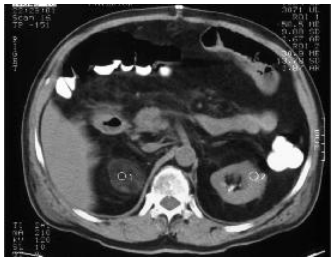


Fig 39: CT, myelolipoma, fat density areas below -20 UH

Fig 40: Myelolipoma, photograph of the gross specimen

All following images belong to one case with adrenal myelolipoma fortuitously associated to a renal carcinoma (papillary type) and simple cysts

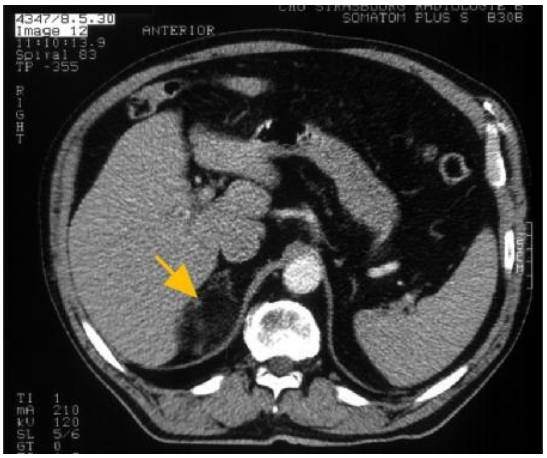


Fig 41a : Myelolipoma, CT (yellow arrow) fat density areas below -20 UH

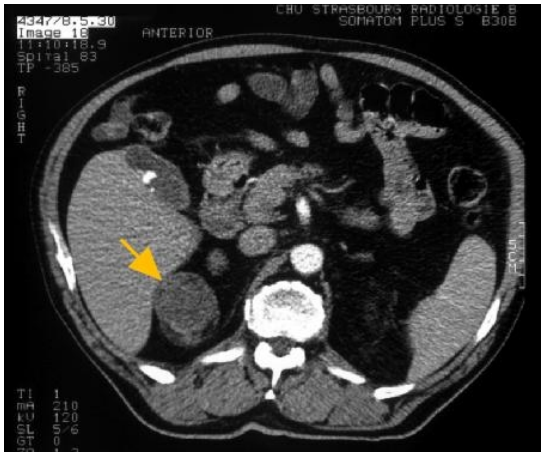


Fig 41b : Same myelolipoma, CT (yellow arrow) tissular density part

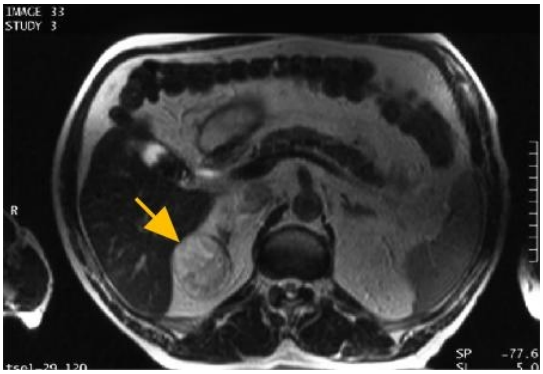


Fig 41c : Myelolipoma, MRI T2-weighted sequence (yellow arrow)

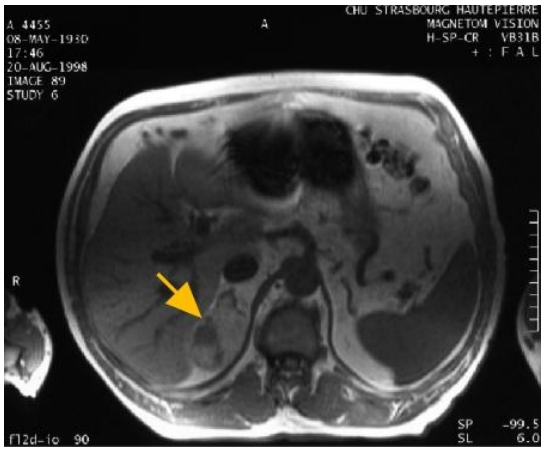


Fig 41d : Myelolipoma, MRI T1-weighted sequence (yellow arrow)

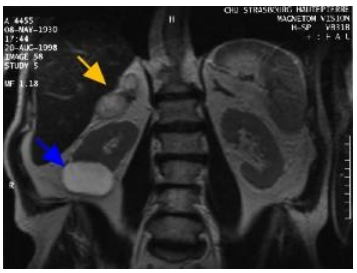


Fig 41e : Myelolipoma, MRI T2-weighted sequence (yellow arrow), typical cyst of the right kidney (blue arrow)

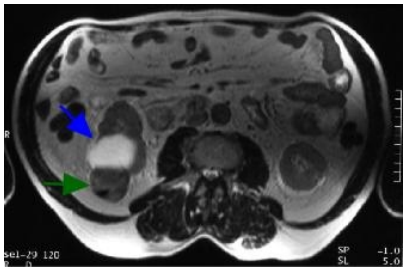


Fig 41f : Renal (green arrow) carcinoma (papillary type), typical cyst of the right kidney (blue arrow)

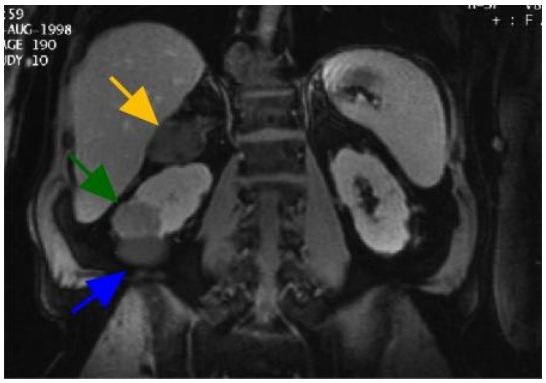


Fig 41g : MRI T1-weighted sequence with fat suppression and contrast medium injection. Myelolipoma(yellow arrow), renal (green arrow) carcinoma (papillary type), typical cyst of the right kidney (blue arrow)

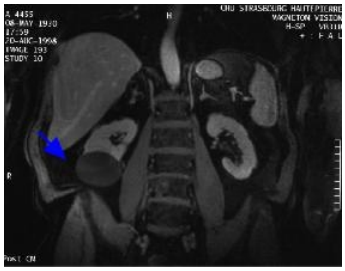


Fig 41h : MRI T1-weighted sequence with fat suppression and contrast medium injection, typical cyst of the right kidney (blue arrow)

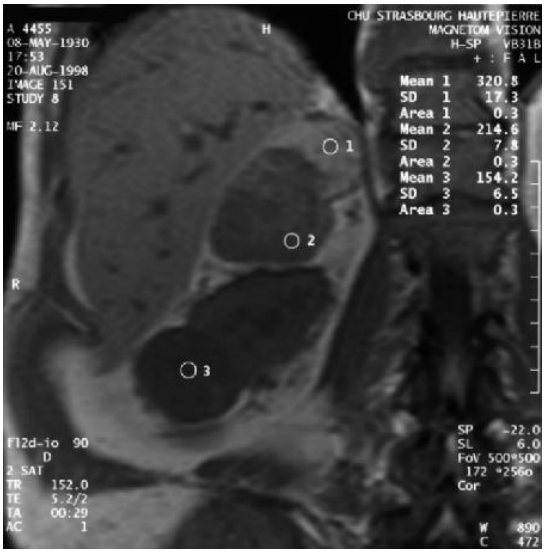


Fig 41i : Chemical shift MR imaging demonstrating a significant lost of signal on out-of-phase image compared to the in-phase image (214 versus 74 = 60% signal loss) in the area n°2 of the tumor. Area n°1 representing mature fat shows no significant signal loss.

Rare and nonspecific tumors

Adrenal cysts : They are a rare tumor, usually asymptomatic. The most frequent type is endothelial cysts which are commonly lymphangiomatous cysts. Another type is represented by pseudocysts which are most often a sequela of hemorrhage. The remaining are parasitic cysts (Echinococcus) and epithelial cysts. Concern about malignancy is justified only in complicated cysts, which may show atypical densities, thick enhancing walls or septations. In these cases percutaneous aspiration or surgical resection may be required.

Hemangioma : Haemangioma is a rare, usually benign adrenal tumor. It is frequently a very large tumor, over 10 cm in size. CT findings are nonspecific : peripherical contrast enhancement with hypodense nonenhancing center. Calcifications are frequent (28-87%). MRI findings can be more characteristic : hypointensity on T1-weighted images, hyperintensity on T2-weighted images, peripherical contrast enhancement after contrast medium injection that persists on delayed imaging. Surgical removal is usually required especially in large masses for diagnosis.

Adrenal hemorrhage : Adrenal hemorrhage occurs by adults in severe trauma ; spontaneously (in cases of severe illness : shock, burns); or as iatrogenic complications of anticoagulation, surgery or percutaneous biopsy. CT findings are unilateral or bilateral adrenal masses with tissular or higher density and poor enhancement. MRI shows a more specific pattern : High signal intensity on both T1 and T2-weighted sequences in the acute phase and a peripherical low intensity rim on both T1 and T2-weighted sequences in chronic cases.

Other rare adrenal tumors or tumor-like lesions: Lymphoma, Castelman's disease, inflammatory granulomatous disease (tuberculosis and histoplasmosis), ganglioneuromas, neuroblastoma occurs usually in childhood.

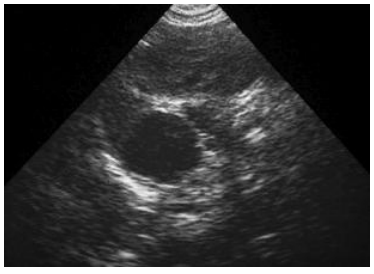


Fig 42: Ultrasonography, pseudocyst

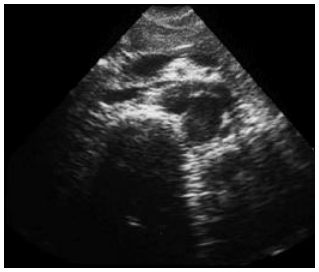


Fig 43a: Ultrasonography, lymphangiomatous cyst

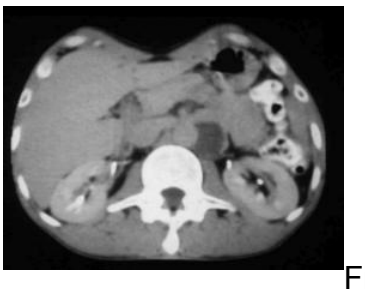


Fig 43b: Enhanced CT, lymphangiomatous cyst

4) Adrenal biopsy

Indications and contraindications

Indications

- Adrenal masses not typical of adenoma in patients with malignancy
- Atypical adrenal incidentalomas
- Other primary adrenal tumors, not typical of adenomas. However percutaneous biopsy is not recommended to differentiate between an adenoma and adrenocortical carcinoma, futhermore if these lesions are planned for surgical resection.

Contraindications

- Adrenal pheochromocytoma. Biopsy of an unsuspected pheochromocytoma can lead to hypertensive crisis and even to death. If the patient provides a history of hypertension, flushing, headaches or any clinical or radiological suspicion of pheochromocytoma, it should systematically be evaluated with serum catecholamine measurements
- Hemorragic diathesis

Material

- 18 to 20-gauge coaxial biopsy gun (Temno or Achieve Allegiance®)
- Sterile drapes, tampons
- 22-gauge needle for anesthesia, scalpel
- Iodine, 1% lidocaine

Fig 44: 20 gauge coaxial biopsy gun (Allegiance®)

Fig 45: 18 gauge coaxial biopsy gun (Allegiance®)

Fig 46: CT control

Technique

Adrenal biopsies are usually performed on an outpatient basis. For uncomplicated biopsy, the patient is discharged after 3 to 4 hours observation. At the end of this period patients are discharged. Adrenal biopsy is performed under local anesthesia and CT guidance. Ultrasonography control is not recommended routinely for adrenal biopsy, MRI can be used but is time consuming.

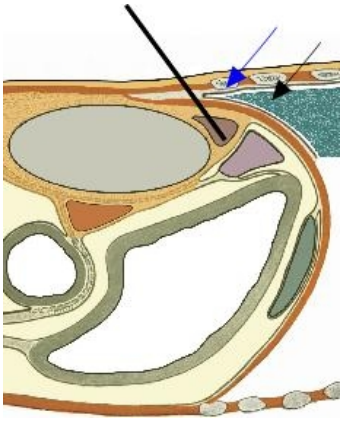


Fig 47: Biopsy of the adrenal gland.Sagittal view. Posterior route 15-20 degree gantry tilt. Patient placed in a prone position on the CT table. Lung (black arrow), pleural recess (blue arrow)

Three pathways can be used for right adrenal biopsy :

- transhepatic approach with patient placed in a supine position (Fig 48)

- posterior approach with patient placed in a prone position on the CT table, CT-gantry 15-20° tilted
- posterior approach with patient placed on the right side (Fig 50)

Two pathways can be used for left adrenal biopsy :

- posterior approach with patient placed in a prone position on the CT table, CT-gantry 15-20° tilted (Fig 47-49)
- posterior approach with patient placed on the left side (Fig 51)

In order to avoid pleural injury which could lead to pneumothorax, the posterior approach (prone position) is used with a 15 to 20 degree oblique pathway by inclination of the CT-gantry. To avoid intensive respiratory motion oxygen can be used. The biopsy pathway should avoid : kidney, nerve root, furthermore pancreas, spleen or pleural recesses. In very difficult cases the biopsy can be performed after injection of 10-20 cc physiologic saline solution into the paravertebral space, creating a wider route for needle insertion.

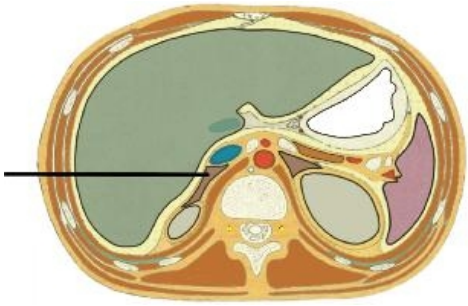


Fig 48: Biopsy of the right adrenal gland. Axial view, transhepatic approach

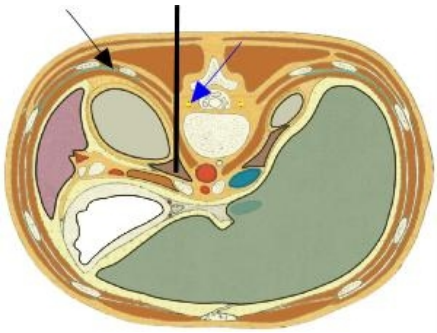


Fig 49: Biopsy of the left adrenal gland, axial view posterior route with patient placed in prone position . Pleural recesses (black arrow), nerve root (blue arrow)

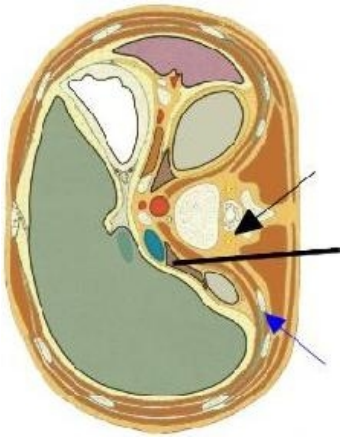


Fig 50: Biopsy of the right adrenal gland, axial view posterior right approach with patient placed on the right side. Pleural recesses (black arrow), nerve root (blue arrow)

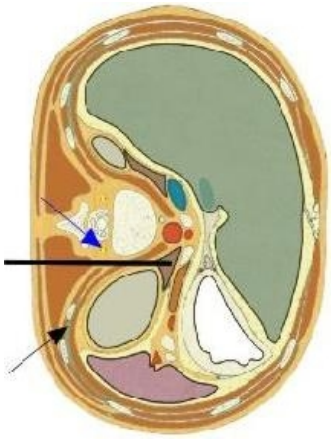


Fig 51: Biopsy of the left adrenal gland, axial view posterior left approach with patient placed on the left side. Pleural recesses (black arrow), nerve root (blue arrow)

5) Complications

- The most frequent complication is pneumothorax. One case of spontaneously resolving asymptomatic pneumothorax was observed in our series
- Hematoma
- Hypertensive crisis or even death caused by biopsy of an unsuspected pheochromocytoma. If the patient provides a history of hypertension, flushing,

headaches or any clinical or radiological suspicion of pheochromocytoma, serum catecholamine measurements are mandatory
- Other complications are very uncommon under precise CT guidance: pancreatitis, kidney or splenic bleeding

6) Adrenal tumor biopsy results

Results in 64 patients

Fig 52: Cytologic specific diagnosis (Fine Needle Aspiration)	Results
Sensitivity	Specificity
58%	100%

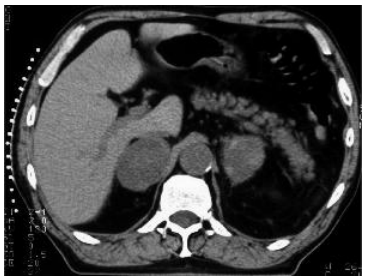
Fig 53: Histologic specific diagnosis (biopsy with 18 to 20-gauge gun)	Results
Sensitivity	Specificity
88%	100%

Discussion

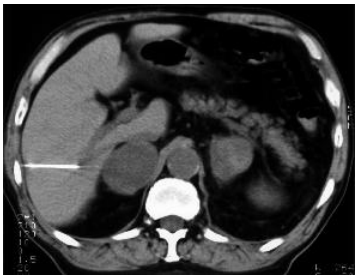
- Optimal biopsy results are obtained with a coaxial 18 to 20-gauge biopsy gun.
- In terms of malignant diagnosis, cytologic samples are sufficient. However, in 7% to 17% the sample is insufficient for accurate diagnosis.
- Metastases : Necrosis represents the cytologic key feature of diagnosis. Even when carcinomatous cells are lacking, necrosis strongly supports this diagnosis.
- Cortical adenoma FNA and/or biopsy of both normal cortical tissue and adenoma show similar cytologic and histologic patterns. Pathologic study can only confirm a diagnosis which depends on CT data.

7) Cases

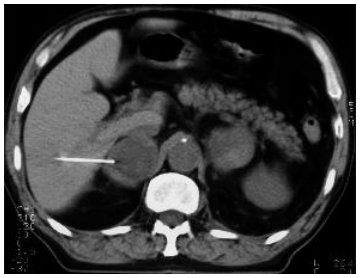
Case 1 Adrenal biopsy result : metastasis of lung cancer



CT

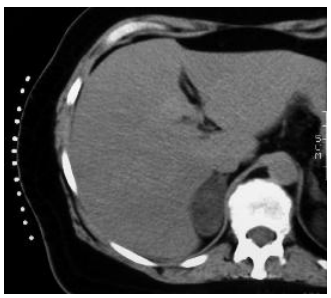


Transhepatic approach with patient placed in a supine position

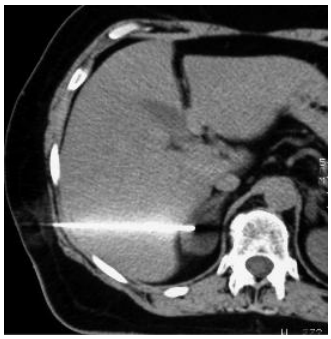


Adrenal biopsy

Case 2 Adrenal biopsy result : Adenoma

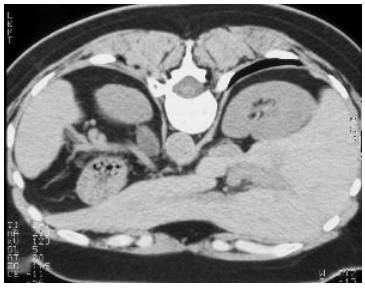


CT

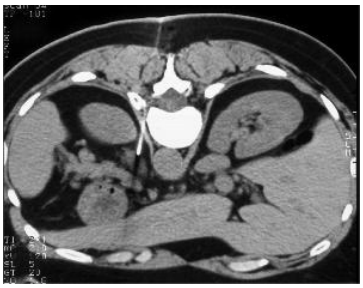


Adrenal biopsy, CT control, transhepatic approach with patient placed in a supine position

Case 3 Adrenal biopsy result : Adenoma

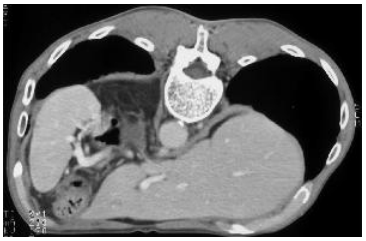


Adrenal biopsy :



Adrenal biopsy, CT control, posterior approach with patient placed in a prone position on the CT table

Case 4 Adrenal biopsy : Metastasis of melanoma



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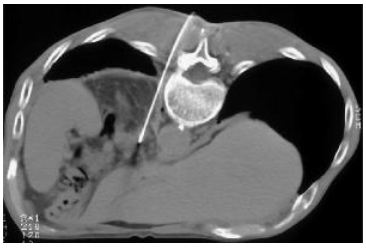
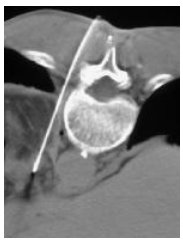
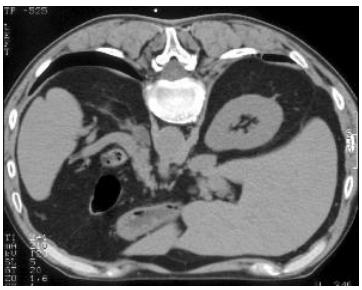


Adrenal biopsy, CT control, posterior approach with patient placed in a prone position on the CT table



Adrenal biopsy, no injury of the pleural recess

Case 5 Adrenal biopsy result : Adenoma



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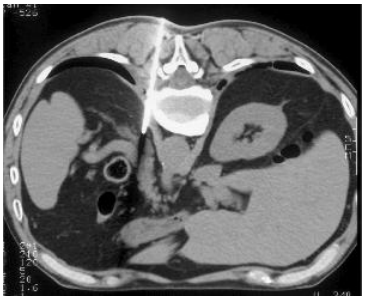
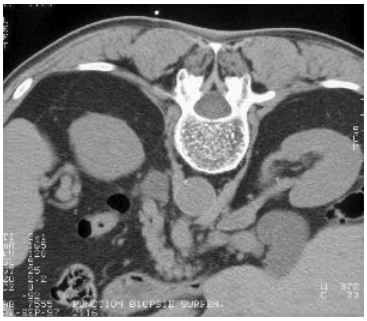


Adrenal biopsy, CT control, posterior approach with patient placed in a prone position on the CT table

Case 6 Adrenal biopsy result : Adenoma



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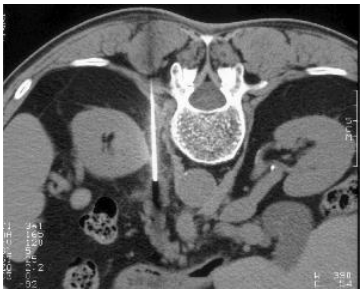
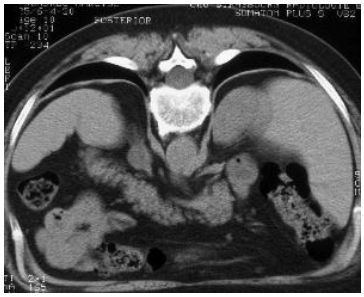
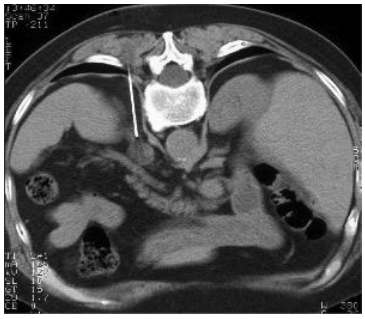


Adrenal biopsy, CT control, posterior approach with patient placed in a prone position on the CT table

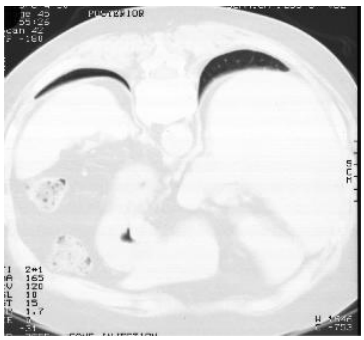
Case 7 Adrenal biopsy result : metastasis



CT

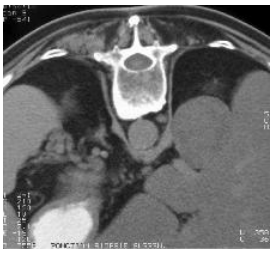


Adrenal biopsy, CT control, posterior approach with patient placed in a prone position on the CT table

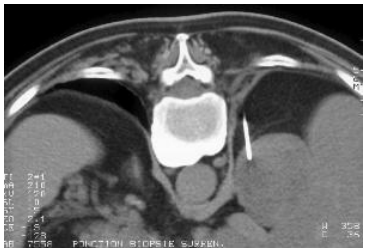


Adrenal biopsy : CT control, no pneumothorax

Case 8 Adrenal biopsy result : metastasis

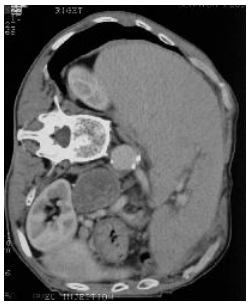


CT

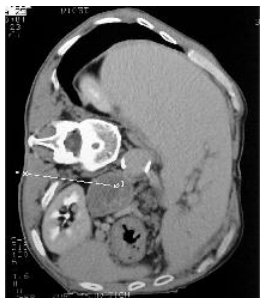


Adrenal biopsy, CT control, posterior approach with patient placed in a prone position on the CT table

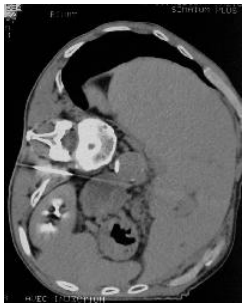
Case 9 Adrenal biopsy result : metastasis of lung cancer



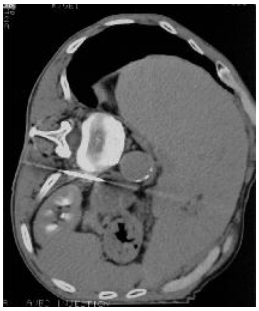
CT



CT pathway, posterior approach with patient placed on the left side



Adrenal biopsy CT control



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