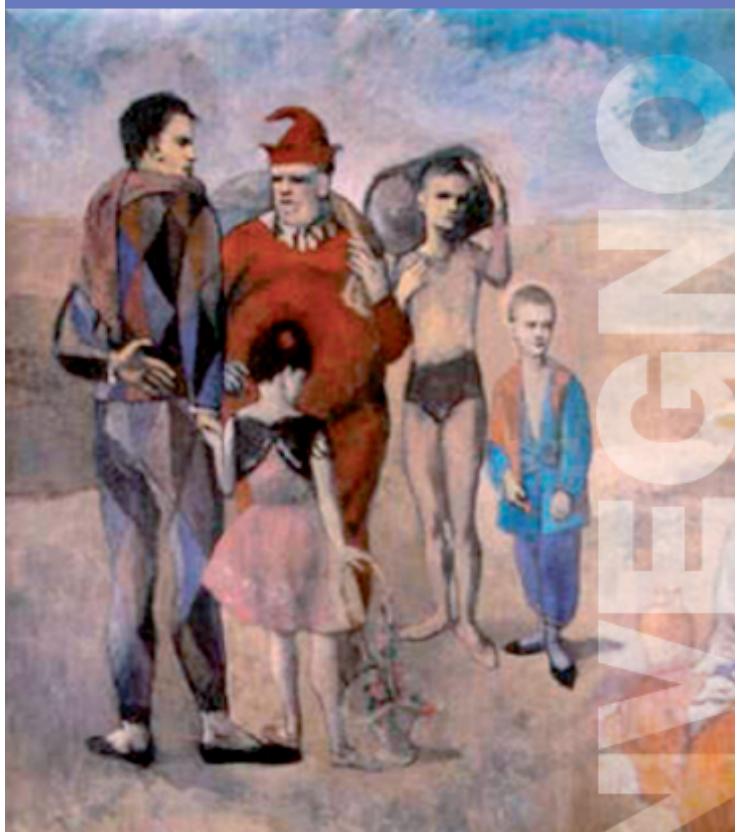




ASSOCIAZIONE MEDICI
ENDOCRINologi
PER LA QUALITÀ CLINICA



1° CONVEGNO AME EMILIA-ROMAGNA

1° CONVEGNO AME EMILIA-ROMAGNA

III Sessione

Incidentaloma surrenalico: problemi aperti

Moderatori: M. Nizzoli, M. Zini

*Incidentaloma surrenalico
in paziente in nota operatoria
per altra patologia :
quale gestione?*

Marco Grandi

Direttore Dipartimento di Medicina
Nuovo Ospedale Civile di Sassuolo
AUSL di Modena

Socio AME dell'Anno - 2009



*Le PROBLEMATICHE di QUESTO
PAZIENTE NON DIFFERISCONO
SOSTANZIALMENTE da QUELLE di
QUALSIASI ALTRO PAZIENTE per il
QUALE E' STATA POSTA DIAGNOSI di
INCIDENTALOMA SURRENALICO*

In 1974 Lewinsky and colleagues described as a "very rare" condition the presence of *clinically silent adrenocortical tumors* in 178 patients.

During the last 25-30 years, the widespread application of noninvasive imaging techniques has led to *an increased detection* of these incidental adrenal masses.



Prevalenza

Serie Autoptiche (dimensioni > 1 cm)	1.0 - 9.0 %	Abecassis M, McLoughlin MJ, Langer B, et al.. Serendipitous adrenal masses: prevalence, significance, and management. <i>Am J Surg</i> 1985;149:783-8 Kloos RT, Gross MD, Francis IR, et al.. Incidentally discovered adrenal masses. <i>Endocr Rev</i> 1995;16:460– 84 Barzon L, Sonito N. Prevalence & natural history of adrenal incidentalomas. <i>Eur J Endocrinol</i> 2003;149:273–85.
TC	4.0 %	Prinz RA, Brooks MH, Churchill R, et al.. Incidental asymptomatic adrenal masses detected by computed tomographic scanning. Is operation required? <i>JAMA</i> 1982;248 :701–4 Herrera MF, Grant CS, van Heerden JA, et al.. Incidentally discovered adrenal tumours: an institutional perspective. <i>Surgery</i> 1991;110:1014–21. Bovio S, Cataldi A, Reimondo G, et al.. Prevalence of adrenal incidentaloma in a contemporary computerized tomography series. <i>J Endocrinol Invest</i> 2006
Ecografia	0.1 - 0.4%	Masumori N, Adachi H, Noda Y, Tsukamoto T. Detection of adrenal and retroperitoneal masses in a general health examination system. <i>Urology</i> 1998;52:572-576. Kluglich M, Duelli R, Zoller WG, Middeke M. Ultrasound of incidental tumors of the adrenal gland and endocrine hypertension. <i>Bildgebung</i> 1993;60:144-46
Eta'	1.0% fino a 30 a 7.0% oltre i 70 a	Kloos RT, Gross MD, Francis IR, Korobkin M, Shapiro B. Incidentally discovered adrenal masses. <i>Endocr Rev.</i> 1995;16:460-484. Nawar R, Aron D. Adrenal incidentalomas—a continuing management dilemma. <i>Endocr Relat Cancer.</i> 2005;12: 585-598.

The spectrum of adrenal incidentaloma

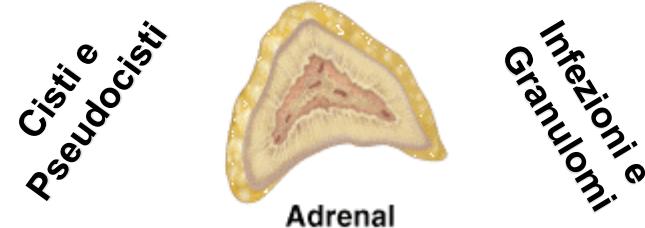
Midollare

Feocromocitoma
Ganglioneuroma
Ganglio-Neuroblastoma
Neuroblastoma
Carcinoma

Mielolipoma ,Xantoma
Lipoma ,Teratoma
Linfoma , Amartoma
Emangioma
Angiomolipoma

Corticale

Adenoma
• Non Funzionante
• Steroido Produttore
• Aldosterono Prod.
Iperplasia Nodulare
Carcinoma



Metastasi

Polmone
Mammella
Ovaio
Fegato
Melanoma
Linfoma

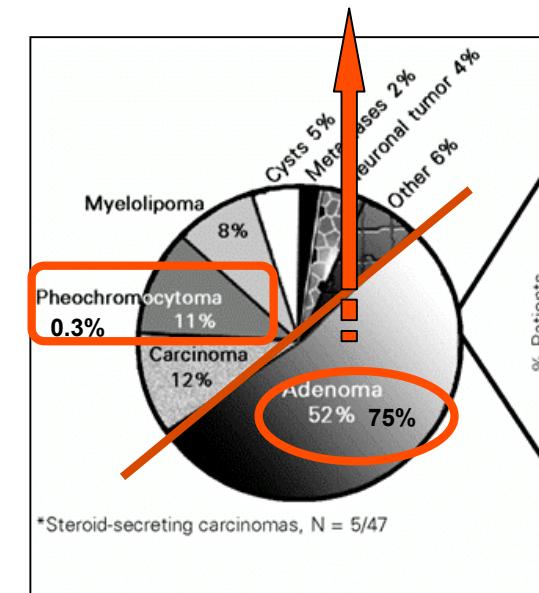
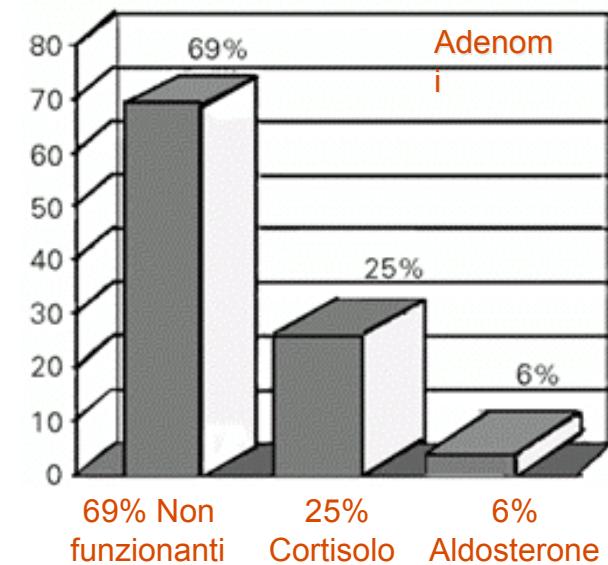
Ematomi ed Emorragie

Pseudo Masse Surrenaliche

Stomaco
Pancreas
Rene
Fegato
Linfonodi
Lesioni Vascolari
Artefatti

Diagnosis	No. (%) of Lesions
Adenoma	788 75 %
Myelolipoma	68 6%
Hematoma	47 4%
Cyst	13 1%
Pheochromocytoma	3 0.3%
Macronodular hyperplasia	1 0.1%
Adrenal cortical neoplasm, unknown malignant potential	1 0.1%
Presumed benign by imaging or clinical stability	128 12%
Total	1.049

Am J Roentgenol. 2008;190(5):1163-1168



From the results of the Study Group of the Italian Society of Endocrinology on Adrenal Incidentaloma JCEM -2000

INCIDENTALOMA SURRENALICO

*Stabilirne
la “Funzionalita’ ”
o meno*

*La Diagnostica
Ormonale*

*Stabilirne
la “ Natura”*

*La Diagnostica
per Immagini*

*Attuare un
opportuno
Follow Up*

*“Radiologico”
“Laboratoristico”*

**INCIDENTALOMA
SURRENALICO**

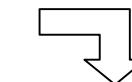
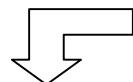


Anamnesi / Esame Clinico



Prima Valutazione Ormono - Funzionale :

- Overnigh DMX 1mg Test
- Catecolamine Urinarie
- Aldosterone/Renina Ratio



Funzionante



Completamento Diagnostico



Non Funzionante



> 6 cm



< 6 cm

Considerare l'Intervento

Sospetta

Non Sospetta



**Tipologia della
Diagnostica per Immagini**



**Rivalutazione “Radiologica”
a 3 - 6 - 12 Mesi**

**Rivalutazione Laboratoristica
a 12 Mesi**



Modificazioni Morfo-Strutturali > a 1 cm

o

Modificazioni Funzionali



**INCIDENTALOMA
SURRENALICO**



Anamnesi / Esame Clinico



Prima Valutazione Ormono - Funzionale :

- Overnigh DMX 1mg Test
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- Aldosterone / Renina Ratio



Hormonal work-up

Glucocorticoid excess (minimum 3 of 4 tests)

Dexamethasone suppression test (1 mg, 2300 h)

Excretion of free urinary cortisol (24 h urine)

Basal cortisol (serum)

Basal ACTH (plasma)

DHEA-S (serum)

17-OH-progesterone (serum)

Androstendione (serum)

Testosterone (serum)

17 β -estradiol (serum, only in men and postmenopausal women)

Potassium (serum)

Aldosterone to renin ratio (only in patients with arterial hypertension and/or hypokalemia)

Catecholamine excretion (24 h urine)

Meta- and normetanephrines (plasma)

Sexual steroids and steroid precursors

Mineralocorticoid excess

Exclusion of a pheochromocytoma (1 of 2 tests)

Rivalutazione "Radiologica"

a 3 - 6 - 12 Mesi

Rivalutazione Laboratoristica

a 12 Mesi

Modificazioni Morfo-Strutturali > a 1 cm

o

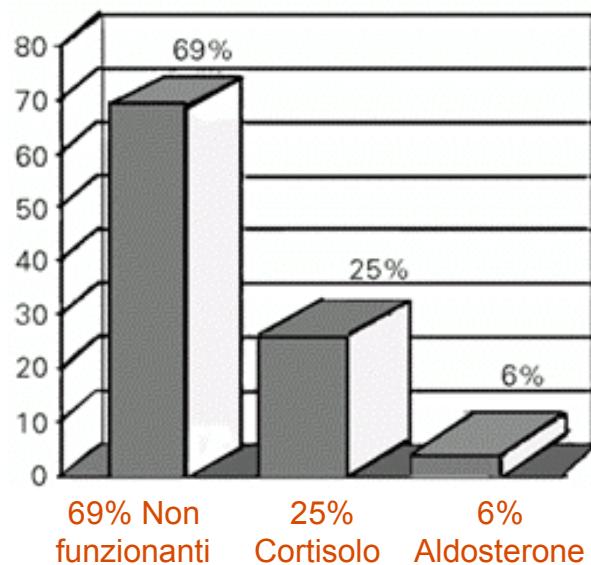
Modificazioni Funzionali



VALUTAZIONE FUNZIONALE

11% FEOCROMOCITOMI

52 % ADENOMI di cui :



Diagnosi	Tests Biochimici
Feocromocitoma	Catecolamine urinarie Metanefrine plasmatiche
Iperaldosteronismo Primario	Potassiemia Ratio Renina / Aldosterone
S. di Cushing o S. di Cushing "silente"	Cortisoolemia e ACTH basali Cortisolo libero urinario Overnight 1-mg DMX test
	DHEAs ,17OH P , Testosterone ,17 BE2

Step II:

1. confirmatory test (only if the corresponding test results are abnormal)
2. high-dose dexamethasone (8 mg) suppression test.
If pathologic:
CRH test, analysis of diurnal cortisol secretion, 24 h cortisol excretion
3. Fludrocortisone suppression test or saline infusion test, orthostasis test with measurement of aldosterone and PRA, 24-h excretion of aldosterone metabolites (i.e. 18-glucuronide aldosterone).
In selected cases bilateral adrenal vein catheterization with determination of aldosterone and cortisol

Step III: reevaluation

1. repeat screening tests after 1 years in patients with a tumor size of > 3 cm

Characteristics and baseline measures of NFA subjects adjusted to the development of sCS during follow up (2-6 years).

	Non Funzionanti “Stabili” 112/120	Non Funzionanti → Cushing Sub. 8/120	p
Age	55.5±11.6	57.3±9.3	0.685
Gender (M/F)	32/80	2/6	0.982
Tm size (mm)	20 (8-60)	25 (20-40)	0.017
Initial 8.00 cortisol (μg/dl)	14.2±5.8	12.4±3.7	0.546
Initial post DST cortisol (μg/dl)	1.33±0.37	1.36±0.25	0.615
Initial ACTH (pg/ml)	18.01±8.9	27.3±18.7	0.320
Initial DHEAS (μg/dl)	96.1±95.6	94.3±45.9	0.470
Follow up duration (months)	24 (6-132)	62 (16-80)	0.009

**INCIDENTALOMA
SURRENALICO**



Anamnesi / Esame Clinico



Prima Valutazione Ormono - Funzionale :

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- Aldosterone / Renina Ratio



Funzionante



Completamento Diagnostico



Non Funzionante

> 6 cm

DIMENSIONI

< 6 cm



Tipologia della
Diagnostica per Immagini



Non Sospetta



Rivalutazione "Radiologica"
a 3 - 6 - 12 Mesi

Rivalutazione Laboratoristica
a 12 Mesi



Sospetta

Considerare l'Intervento



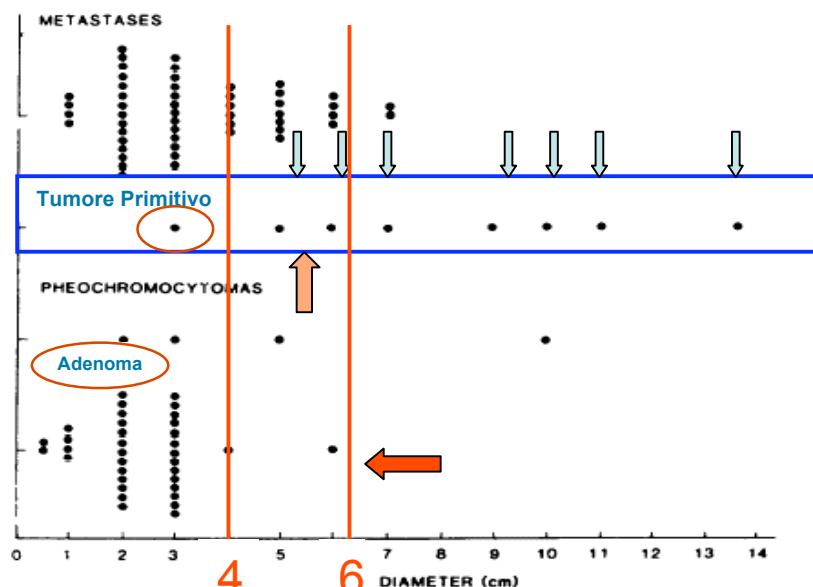
Modificazioni Morfo-Strutturali > a 1 cm

o

Modificazioni Funzionali



Size and shape of the incidentaloma



Adrenal Adenoma
Last Updated: January 14, 2002

A review of 1300 **A /** reported in non-surgical series over the last decade showed that

- 2% of masses ≤ 4 cm,
- 6% between 4 and 6 cm
- 25% > 6 cm in size

were adrenal carcinomas

Herrera MF, Grant CS, van Heerden JA, et al..
Incidentally discovered adrenal tumours: an institutional perspective. *Surgery* 1991;110:1014–21

...a cutoff of 4 cm comes from a retrospective, multicenter survey of 1096 patients with an adrenal incidentaloma, in which this cutoff value **had 93 percent sensitivity for distinguishing between benign and malignant tumors...**

Mantero, F, Terzolo, M, Arnaldi, G, et al. A survey on adrenal incidentaloma in Italy. Study Group on Adrenal Tumors of the Italian Society of Endocrinology. *J Clin Endocrinol Metab* 2000; 85:637.

However, there are several limitations in considering size of the A I as the sole criterion in making management decisions

A size cut-off of 4 cm has a low specificity for the diagnosis of an adrenal carcinoma, as, while

- 90% of the primary adrenal cancers are > 4 cm in size at the time of their detection,*
- only 25% of AI < 4 cm in size are malignant.*
- In addition, size underestimation on a CT scan has been reported to range from 20 to 47% of cases.*
- It is also an important consideration that if an adrenal carcinoma is detected early when it is smaller, the patient has a greater chance of being cured.*
- In view of these limitations, other imaging characteristics have to be considered in risk assessment of A I, although all lesions > 6 cm in size should be removed.*

*Nel Caso si decida per l'Attendismo “Armato”
occorre ricordare pero’...*

*Radiological characteristics of the follow up group
adjusted to the initial clinical diagnosis*

	Non Funzionanti Cushing Subclinico Feocromocitoma	Non Funzionanti	Cushing Subclinico	Feocromocitoma	Altri
Age	56.6±11.3	55.3±11.6	62.4±8.4	50.4±11.3	43.3±18.1
Gender (M/F)	39/104	32/80	7/20	0/4	2/5
Initial Tm size ^{§±} (mm)	20 (7-60)	20 (8-60)	28 (7-55)	11 (10-20)	35 (20-65)
Median follow up (months)	24 (6-159)	24 (6-159)	17 (6-187)	26 (6-45)	36 (8-62)
Increase in tm size (n) (%)	25 (17.4%)	22 (19.6%)	3 (11.1%)	-	1 (14.3%)
Increase ≥ 10 mm (n)	7	5	2	-	1
Decrease in tm size (n) (%)	7 (4.8%)	5 (4.4%)	2 (7.4%)	-	-
Decrease ≥ 10 mm (n)	1	1	-	-	-

**INCIDENTALOMA
SURRENALICO**



Anamnesi / Esame Clinico



Prima Valutazione Ormono - Funzionale :

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Funzionante



Completamento Diagnostico



Considerare l'Intervento



Non Funzionante



> 6 cm

< 6 cm

Tipologia della Diagnostica per Immagini

Sospetta



Non Sospetta



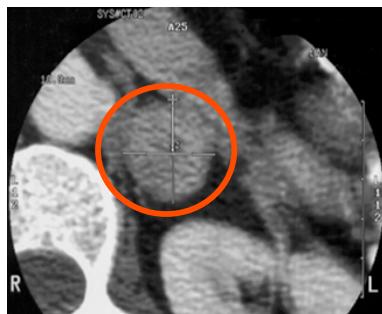
Rivalutazione "Radiologica"
a 3 - 6 - 12 Mesi
Rivalutazione Laboratoristica
a 12 Mesi



Modificazioni Morfo-Strutturali > a 1 cm
o
Modificazioni Funzionali



Size and shape of the incidentaloma



Adrenocortical adenoma
round or oval lesions
smaller than 3 cm and with
a density of less than
10 Hounsfield units



Adrenocortical carcinomas:
heterogeneous
higher intensity on unenhanced CT
may have calcifications



Pheochromocytoma
the characteristic hyperintense
signal on T2-weighted image

Adrenal adenomas are

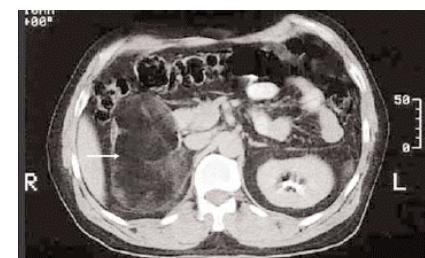
- *homogenous* and have
- *a more well-defined margin* in comparison with malignant lesions, which have an irregular outline.
- *Changes of calcification, necrosis and haemorrhage are rarely seen in benign adrenal tumours.*

*In view of large overlap,
none of these features is
sufficiently discriminatory to
be useful in excluding
malignancy*

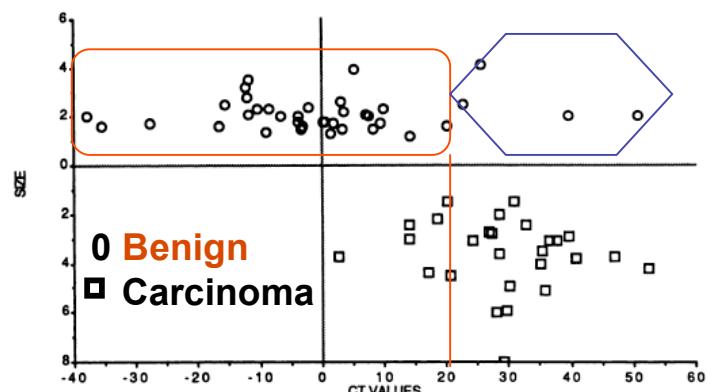
Large cyst



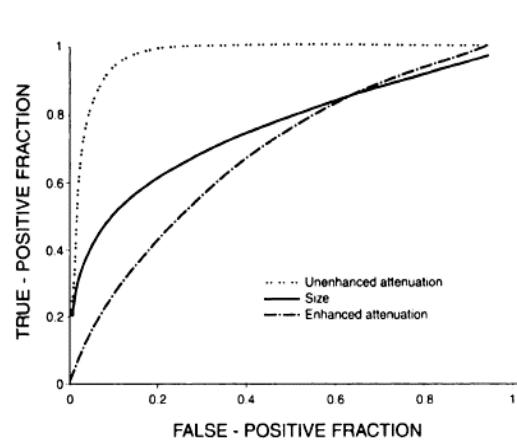
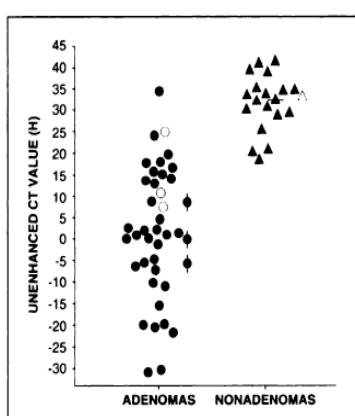
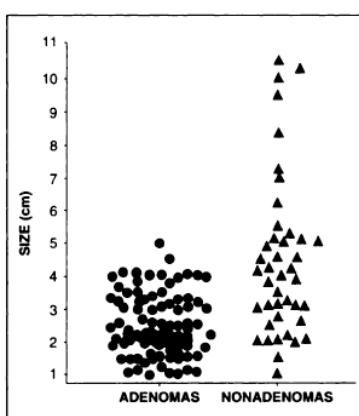
Myelolipoma



Attenuation value



Raw data scattergram plots size (in centimeters) versus CT attenuation coefficients, in Hounsfield units for benign (0) and malignant adrenal lesions. For clarity of illustration, malignant lesions appear below the abscissa.



All masses with H values of less than 18 were adenomas. Curve for unenhanced CT attenuation is higher and to left of other two, Indicating larger area under curve and greater ability to differentiate adenomas from non adenomas.

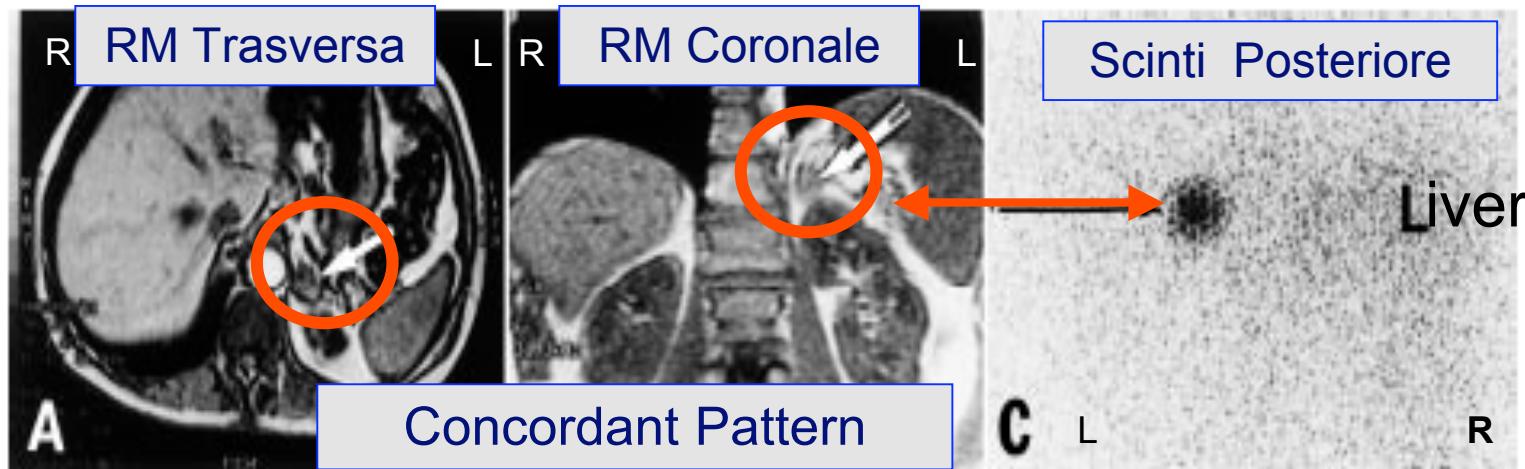
Attenuation value of an adrenal lesion on an unenhanced CT scan is measured as **Hounsfield units (HU)** and is a reflection of its intracytoplasmic fat content which has a low attenuation value.

Benign adenomas usually have a higher amount of fat and therefore a lower attenuation value as compared with adrenal carcinomas which are lipid-poor.

The **sensitivity and specificity** for **10 and 20 HU** cutoff values to differentiate adenomas/hyperplasias from non adenomas were **40.5 and 100%** and **58.2 and 96.9%, respectively**

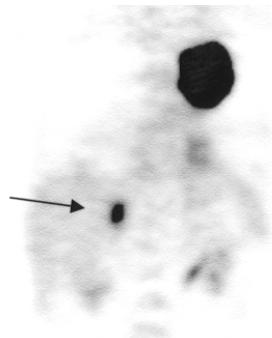
Lee MJ, Hahn PF, Papanicolaou N, et al.. Benign and malignant adrenal masses: CT distinction with attenuation coefficients, size, and observer analysis. *Radiology* 1991;179:415–18
Korobkin M, Brodeur FJ, Yutzy GG, et al.. Differentiation of adrenal adenomas from nonadenomas using CT attenuation values. *Am J Roentgenol* 1996;166:531–6

Scintigrafia Surrenalica

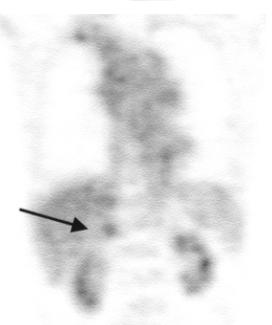


- A "discordant" scintigraphic pattern, i.e., demonstrating decreased or absent radiocholesterol uptake by the affected adrenal gland, is compatible with malignancy (primary and secondary) and other non-functioning space-occupying **or destructive** adrenal lesions.
- Conversely, **unilateral adrenal visualization** with virtual absence of the contralateral gland constitutes a "concordant" pattern almost typical of cortical benign adenoma.
- Nonetheless, well-differentiated carcinomas with radiotracer uptake have sometimes been described.

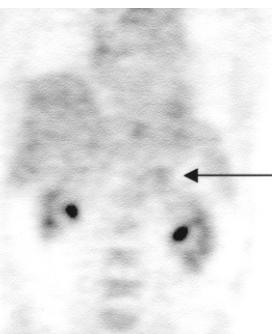
Positron-emission tomography with 18 F-fluorodeoxyglucose



Coronal view of FDG PET shows intense FDG uptake in **large primary cancer of left upper lung**. Lesion in right adrenal gland (arrow) shows significantly higher FDG uptake than that of liver and was confirmed as **metastasis from lung cancer by surgery**.



Coronal view of FDG PET shows small, round focus with FDG uptake equal to or slightly higher than liver in right adrenal gland (arrow). Patient has history of **neuroendocrine tumor in right upper lobe of lung**. Lesion in adrenal gland underwent surgery and was proven to be **metastatic cancer with neuroendocrine differentiation**.



Patient with history of **medullary thyroid cancer**. Coronal view of FDG PET shows focal area with FDG uptake less than that of liver in left adrenal gland (arrow). Lesion measured 3.5 cm on CT scan and did not change for 15 mo on follow-up.
MRI showed findings that are diagnostic of benign adenoma

This form of scanning is highly sensitive in detecting metastatic malignant lesions and is used for patients who have a known primary cancer.

However, it has a limited use in the context of an adrenal incidentaloma identified in a patient without a known malignancy.

It is also expensive .

Yun M, Kim W, Alnafisi N, Lacorte L, et al.. 18F-FDG PET in Characterizing Adrenal Lesions Detected on CT or MRI J Nucl Med 2001;42:1795–9

INCIDENTALOMA SURRENALICO

