PHEOCHROMOCYTOMA

1905 poll coined the term

3-4/million in U.S. yearly

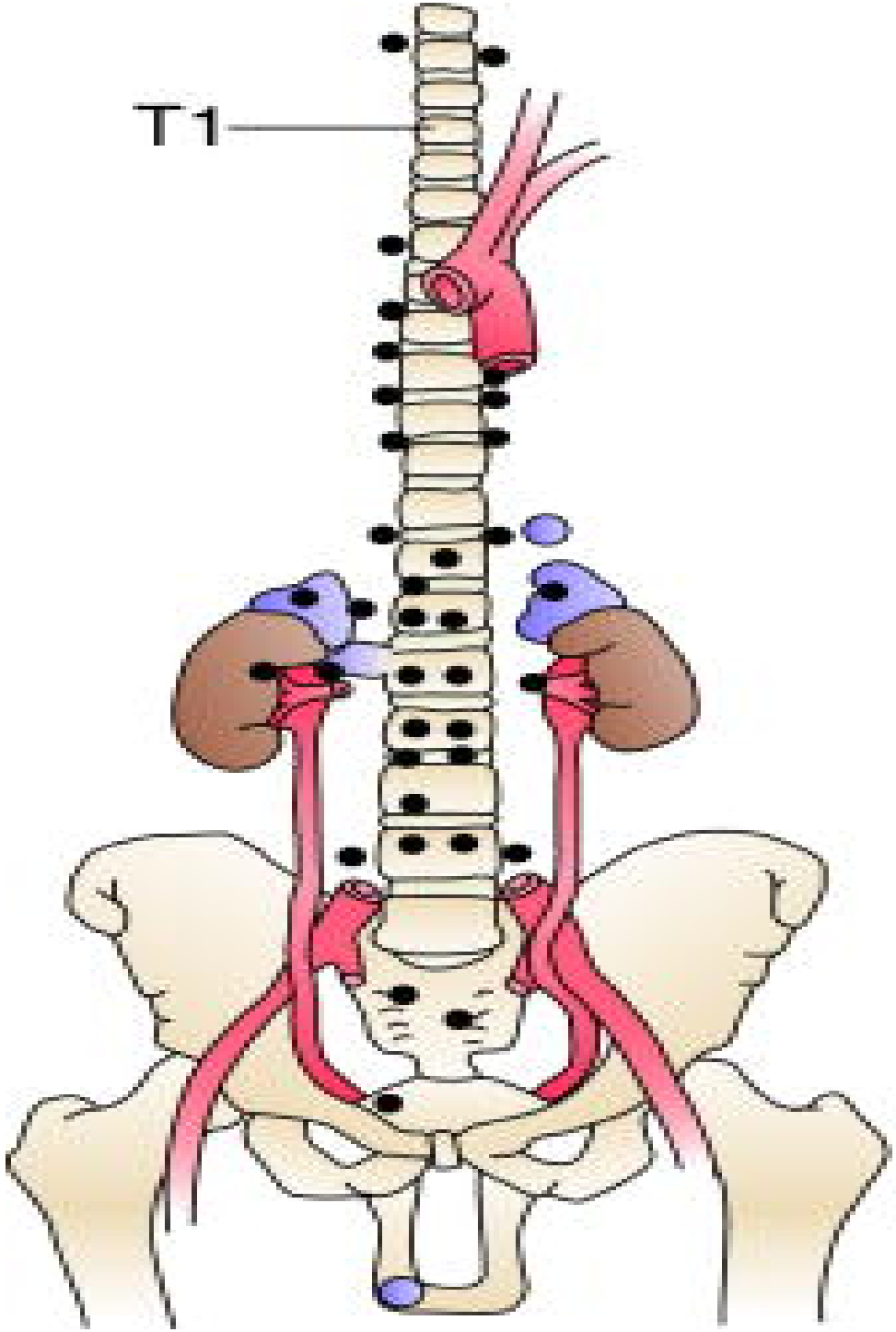
0.1% of hypertensive pt.

PHEOCHROMOCYTOMA

- Originates from

1. adrenal medulla
2. extraadrenal sympathetic paraganglia cells from skull base to bladder(9-23%)= para gangliomas

Neural crest cells migrate to para-aortic and paravertebral and along adrenal vein



Adrenal

- Medullary
- Cortical

PHEOCHROMOCYTOMA

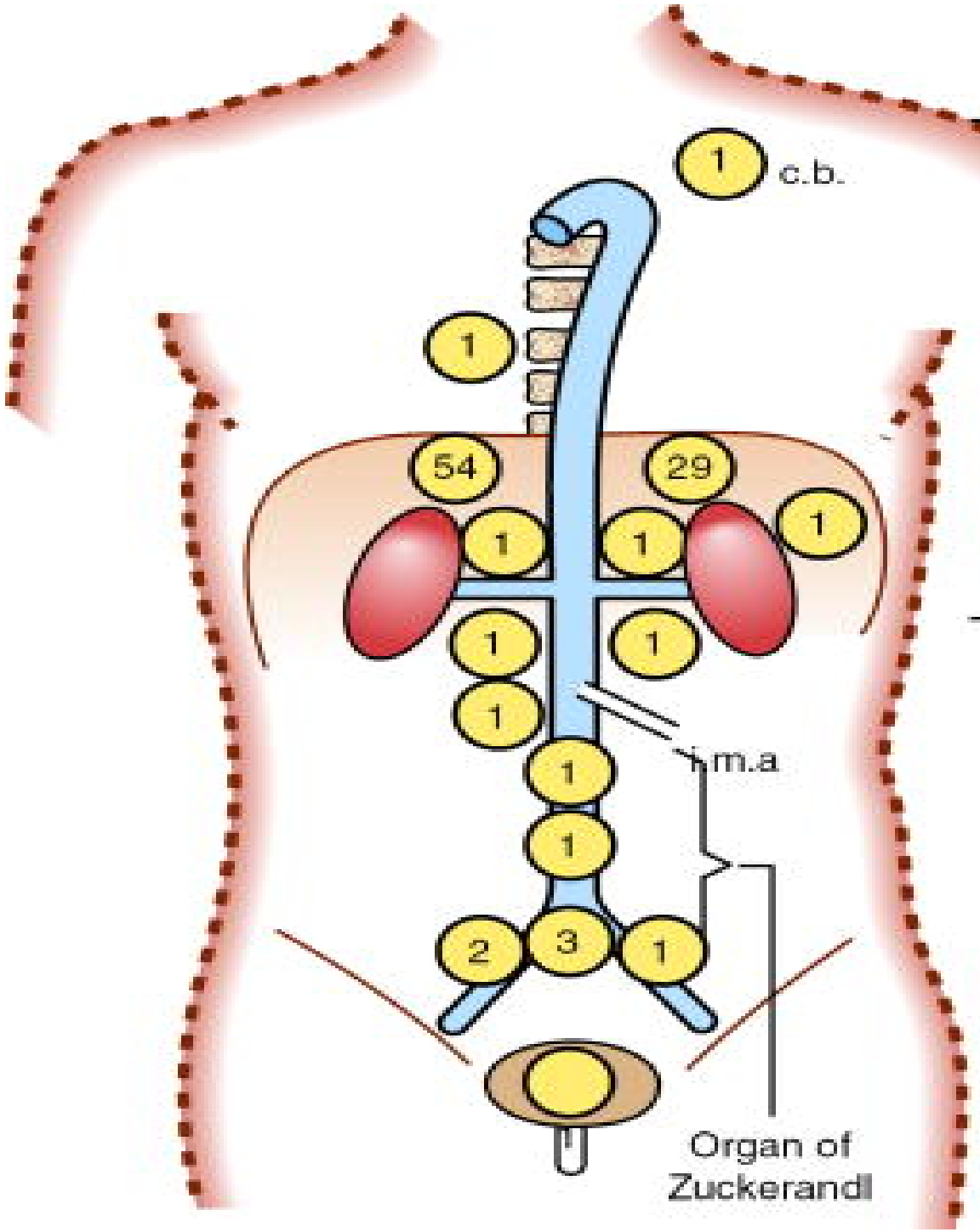
Most extra-adrenal chromaffin cells regress

OOZ 75%

Mediastinum 10%

Bladder 10%

Head,Neck,Pelvis 5%



Adults 89
40 , 49

Intraadrenal 77 patients
(2 bilateral)

Extraadrenal 12 patients
Abdominal paraganglia-5
Organ of Zuckerkandl-6
Bladder-1

Children 11
7 d (63%), 4

Intraadrenal 6 patients
(1 bilateral)

Extraadrenal 5 patients
Abdominal paraganglia-5
Organ of Zuckerkandl-3
Thorax-1

PHEOCHROMOCYTOMA

10% tumor

- **Bilateral**
- **Malignant(26-35%)**
- **Multifocal**
- **Extraadrenal**
- **Children(30-43% extra,X-focaL)**
- **Familial(50% bil.)**
- **Metasatatic disease @ initial work up**

PHEOCHROMOCYTOMA

15-20% in neuroectodermal tumor

VHL,VRH,TS

30- 50%MEN 2

Bilateral and multifocal

Child with pheo.

1/3 bil. And familial

¼ sporadic **have RET gene**

PHEOCHROMOCYTOMA

Malignant pheo.

NO histologic,lab,clinical or imaging criteria from benign and malignant

Locoregional invasion /mets

Present where paraganglia cells are not present

PHEOCHROMOCYTOMA
"the great disguise"

Only ½ classic symptoms and signs

10% incidentaloma

Hx. Of HTN

- refractory
- new onset
- paroxysmal
- Recently excacerbated

PHEOCHROMOCYTOMA
"the great disguise"

TETRAD:

1. **HTN**
2. **Headache**
3. **Sweating**
4. **Palpitations**

Sp 93.8%

Sn 90.9%

Extensive differential

PHEOCHROMOCYTOMA
"the great disguise"

10% "pheocrisis"

No role for FNA

Metaneph.,normeth.,VMA(metabolites)

Epi :adrenal &OOZ (PNMT)

PHEOCHROMOCYTOMA

- Biochemical diagnosis is often based on institutional experience
- Plasma metanephrines have high Sn &Sp
- (Mayo clinic,NIH,Vienna)
- Because secretion may be episodic but metabolism is continuous i.e leak

PHEOCHROMOCYTOMA/ plasma metanephrines

Indicated in high risk and not in sporadic cases

Hereditary cases: Sn 97%
Sp 96%

Sporadic cases : Sn 99%
Sp 82%

Plasma (nmol/liter)	Upper reference limit	Sensitivity (%)		Specificity (%)	
		Hereditary	Sporadic	Hereditary	Sporadic
Free metanephrines		97 (74/76)	99 (137/138)	98 (328/339)	82 (249/305)
Normetanephrine	0.8				
Metanephrine	0.3				
Catecholamines		69 (52/75)	92 (126/137)	89 (303/339)	72 (220/304)
Norepinephrine	2.9				
Epinephrine	0.5				

Sensitivity was calculated from patients with pheochromocytoma and false negative test results for both normetanephrine and metanephrine

Plasma (nmol/liter)	Upper reference limit	Sensitivity (%)		Specificity (%)	
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Norepinephrine	2.9				
Epinephrine	0.5				

Sensitivity was calculated from patients with pheochromocytoma and false-negative test results for both normetanephrine and metanephrine

Urine (µmol/d)	Upper reference limit	Sensitivity (%)		Specificity (%)		
		Hereditary	Sporadic	Hereditary	Sporadic	
Fractionated metanephrines		96 (26/27)	97 (76/78)	82 (327/288)	45 (73/164)	
Normetanephrine						
Women	1.7					
Men	3					
Metanephrine						
Women	0.7					
Men	2					
Catecholamines		79 (54/68)	97 (91/107)	96 (312/324)	75 (159/211)	
NE	0.5					
E	0.5					
Total metanephrines	6	60 (27/45)	88 (61/69)	97 (91/94)	89 (79/89)	
Vanillylmandelic acid	40	46 (30/65)	77 (66/58)	99 (310/312)	86 (132/153)	

Biochemical Test	Sensitivity (%)	Specificity (%)	Sensitivity at 100% Specificity (%)
Plasma metanephrine level	99	89	82
Plasma catecholamine	85	80	38
Urinary catecholamine	83	88	64
Urinary metanephrine	76	94	53
Urinary vanillylmandelic	63	94	43

Sensitivity was determined for tests in 151 patients with mainly sporadic pheochromocytoma, and specificity was determined for tests in 349 patients studied at the National Institutes of Health. *Reprinted with permission from Pacak K, Linehan WM, Eisenhofer G, et al: Recent advances in genetics, diagnosis, localization, and treatment of*

PHEOCHROMOCYTOMA

Combination of urinary total metanephrines and cathecholamines indicating a **specificity** of 98%in Mayo

PHEOCHROMOCYTOMA

97%intraabdominal

One of few curable causes of hypertension

3 patterns

- Sustained
- Sustained with paroxysm
- Paroxysmal with intermittent normotension

PHEOCHROMOCYTOMA/ LOCALIZATION STUDIES

Localization :combination of anatomic and functional studies

Adrenal masses 5-9% population

Most of which are benign,nonfunctional incidentalomas

6.5% are PHEO.

PHEOCHROMOCYTOMA/ LOCALIZATION STUDIES

Can be always localized preop. Allowing a focused surgical approach without general abdominal exploration

Noncontrast **CT rarely misses a lesion:97%intraabdominal and >2 cm**

<10 HU

PHEOCHROMOCYTOMA/ LOCALIZATION STUDIES

CT Sn adrenal 85-94%

extra 90%

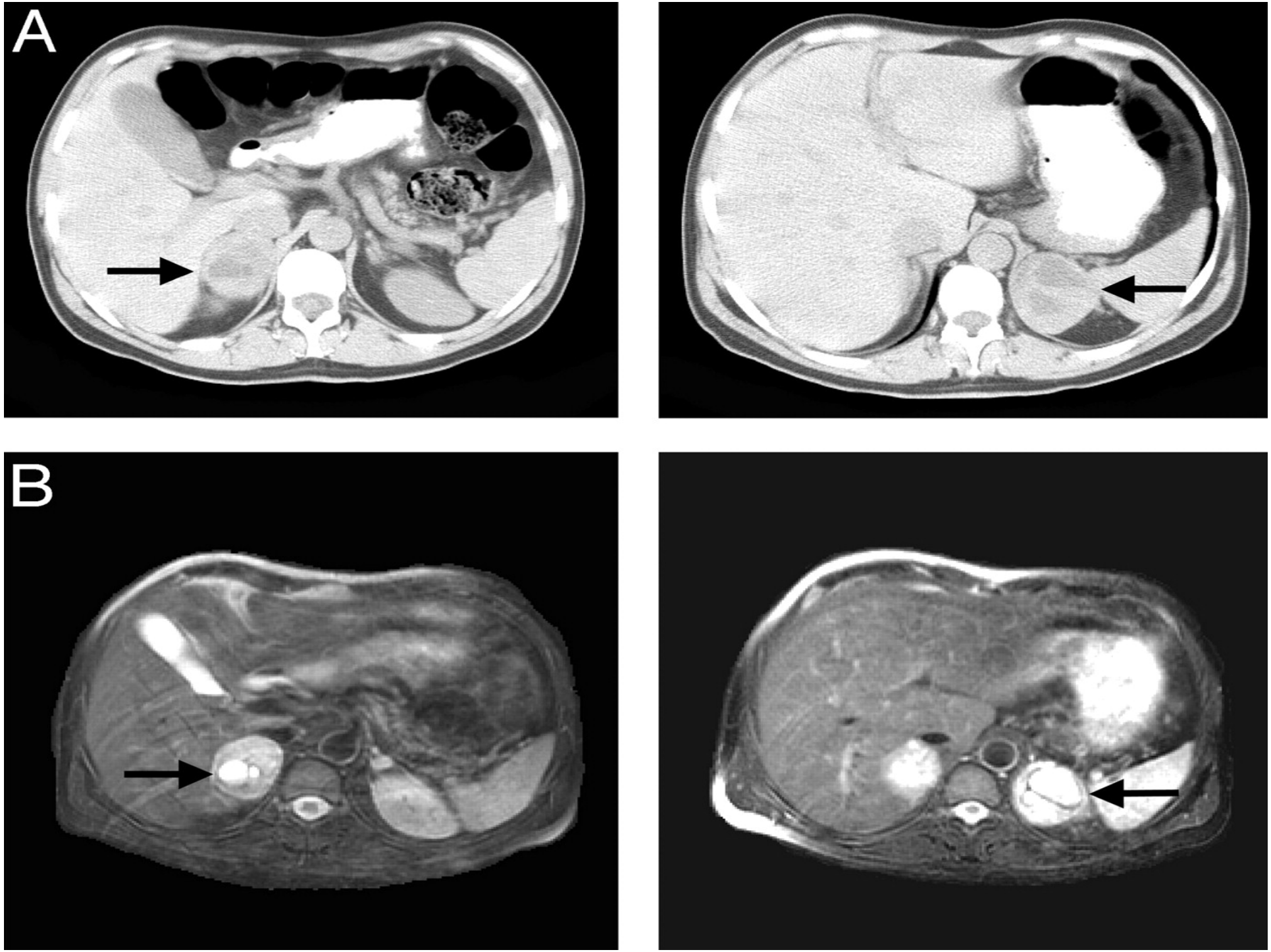
Sp 70%

PHEOCHROMOCYTOMA/ LOCALIZATION STUDIES

MRI 90%bright on T2 and have high water density (Test of choice in pregnant pt. And children)

It is also indicated in large tumors >6cm and large extraadrenal tumors to r/o any vascular invasion

Sn 93-100%,Sp 67%


A
B

PHEOCHROMOCYTOMA/ LOCALIZATION STUDIES

MIBG NE ANALOG

- **Sn 80-90%(78%);Sp 100%**
- **extraadrenal**
- **multifocal**
- **recurrent pheochromocytoma**
- **less sensitive**

Need to block thyroid

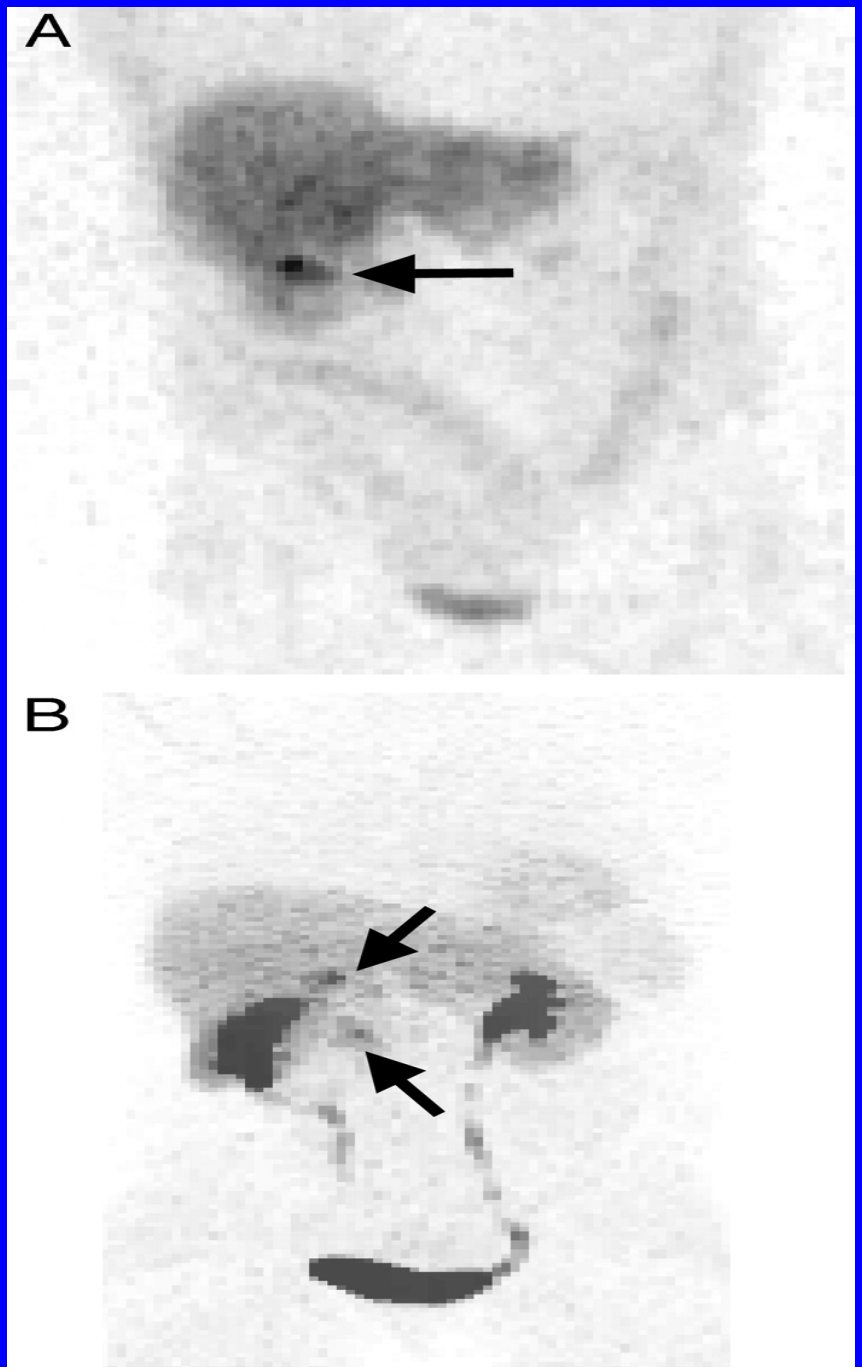
PHEOCHROMOCYTOMA/ LOCALIZATION STUDIES

Sn 77-90%(78%)

Sp 95-100%

[^{1}8] FDG PET

SSRS(Octreoscan)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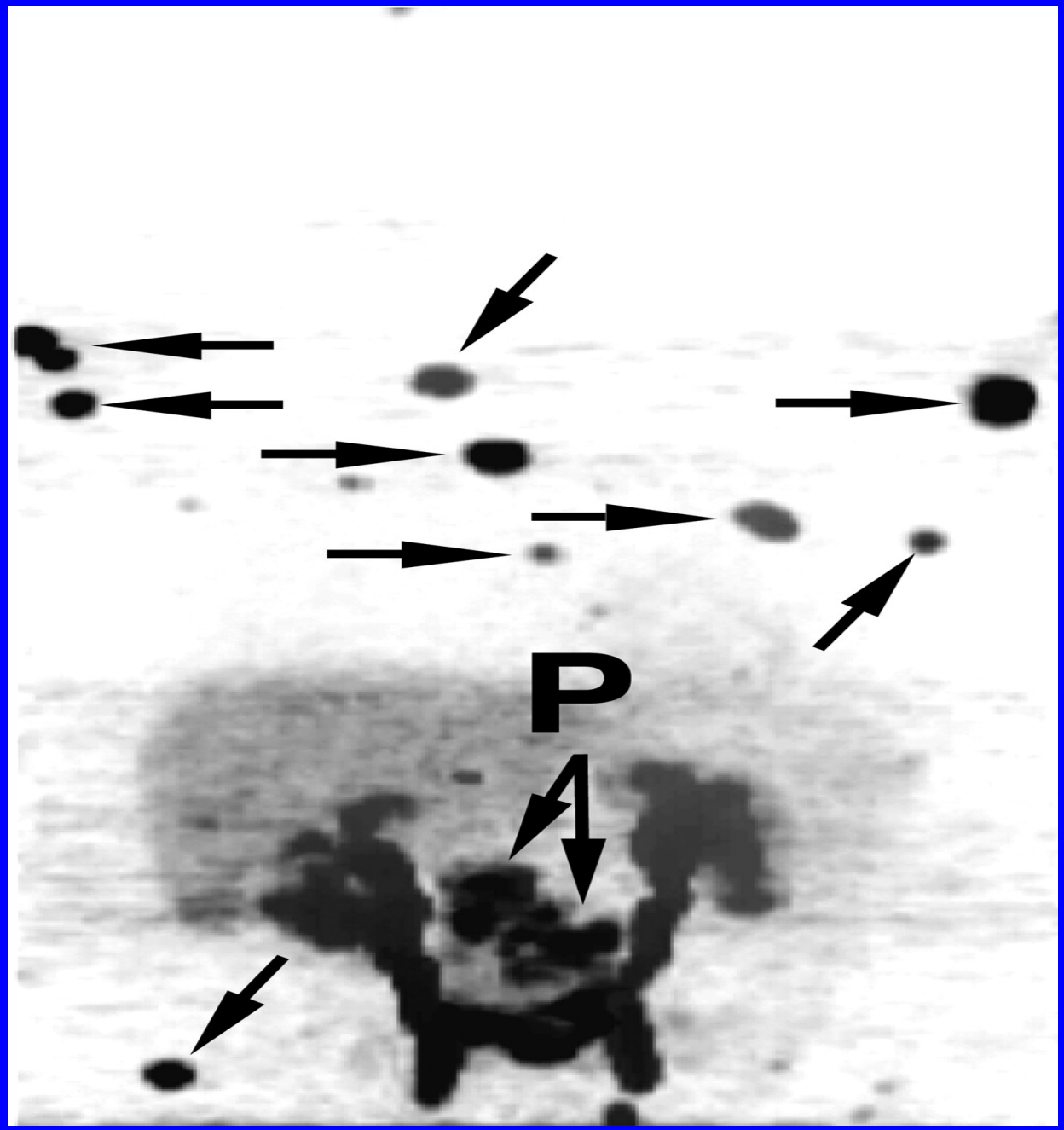
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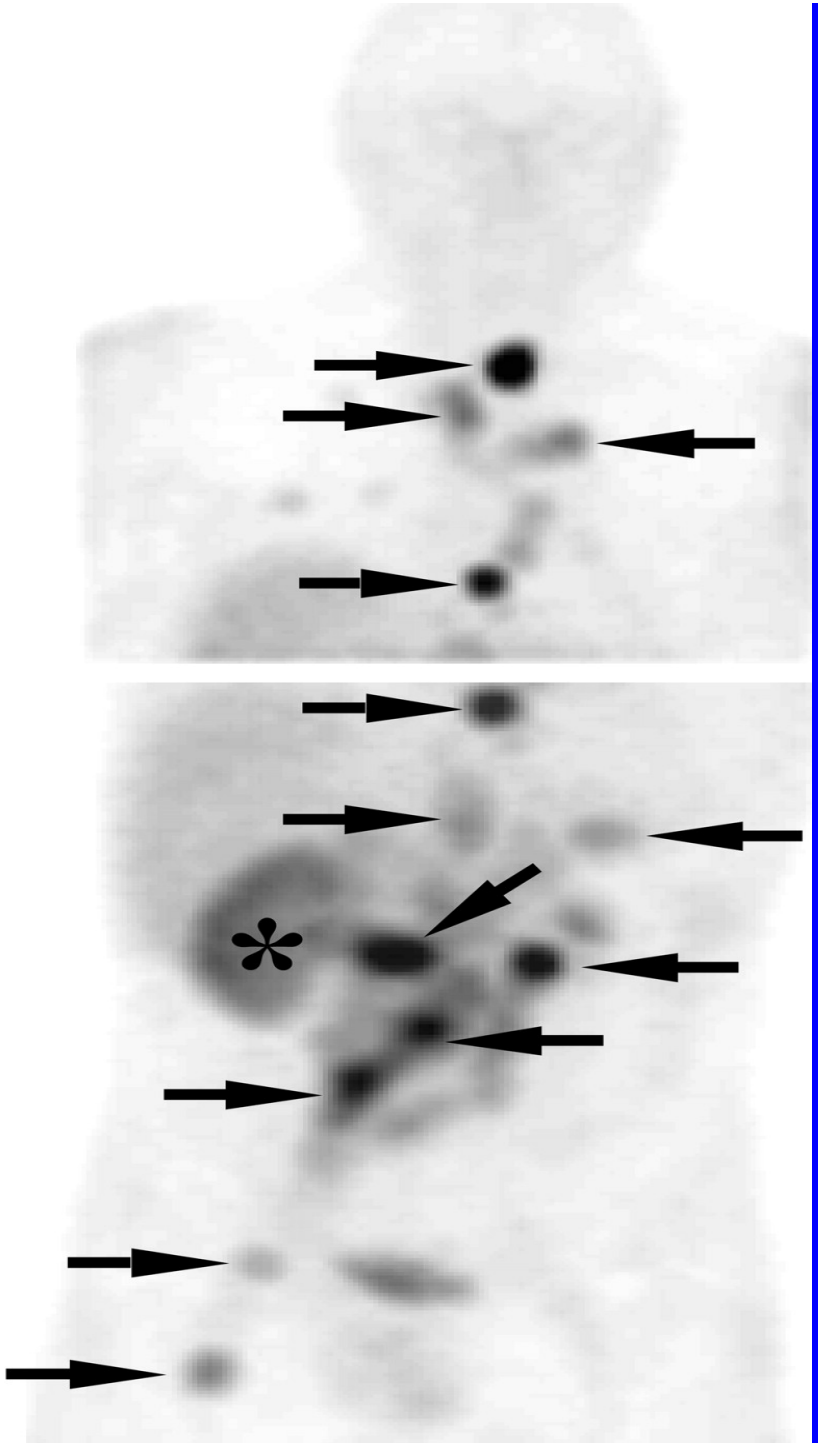
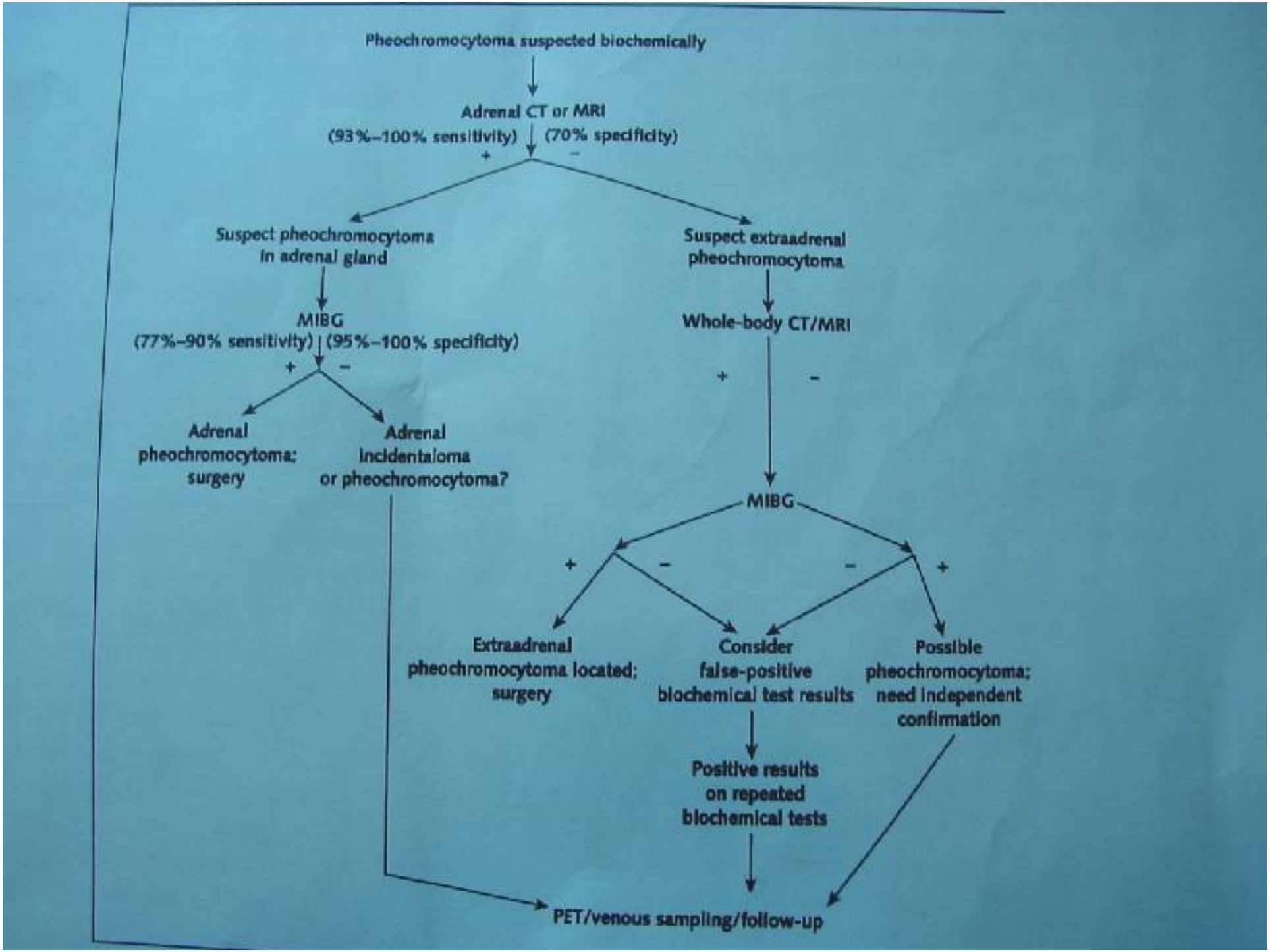
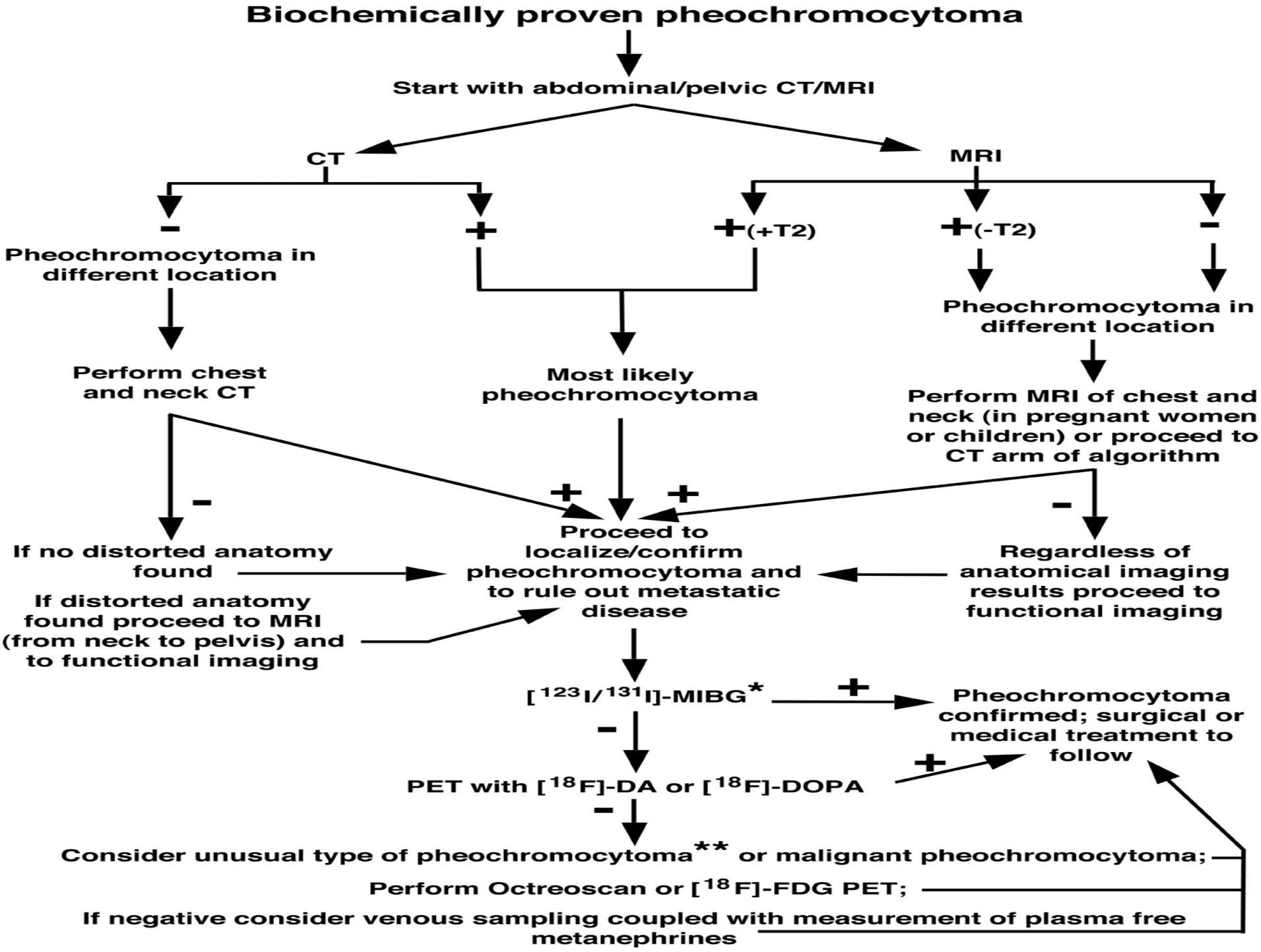



Pheochromocytoma suspected biochemically
Adrenal CT or MRI
(93%–100% sensitivity)
(70% specificity)
+
–
Suspect pheochromocytoma in adrenal gland
Suspect extraadrenal pheochromocytoma
MIBG
(77%–90% sensitivity)
(95%–100% specificity)
+
–
Whole-body CT/MRI
+
–
Adrenal pheochromocytoma; surgery
Adrenal incidentaloma or pheochromocytoma?
MIBG
+
–
–
+
Extraadrenal pheochromocytoma located; surgery
Consider false-positive biochemical test results
Possible pheochromocytoma; need independent confirmation
Positive results on repeated biochemical tests
PET/venous sampling/follow-up


Biochemically proven pheochromocytoma
Start with abdominal/pelvic CT/MRI
CT
MRI
-
+
+(+T2)
+(-T2)
-
Pheochromocytoma in different location
Pheochromocytoma in different location
Perform chest and neck CT
Most likely pheochromocytoma
Perform MRI of chest and neck (in pregnant women or children) or proceed to CT arm of algorithm
-
+
+
-
If no distorted anatomy found
If distorted anatomy found proceed to MRI (from neck to pelvis) and to functional imaging
Proceed to localize/confirm pheochromocytoma and to rule out metastatic disease
Regardless of anatomical imaging results proceed to functional imaging
[123I/131I]-MIBG*
+
Pheochromocytoma confirmed; surgical or medical treatment to follow
-
+
PET with [18F]-DA or [18F]-DOPA
-
Consider unusual type of pheochromocytoma** or malignant pheochromocytoma;
Perform Octreoscan or [18F]-FDG PET;
If negative consider venous sampling coupled with measurement of plasma free metanephrines

PHEOCHROMOCYTOMA/ PERIOP. Mgmnt

3 principles:

1. Rx. Of HTN
2. Expand intravascular volume
3. Control cardiac arrhythmias

PBZ long acting α-antagonists 1-3 wks

Lessens risks of CV collapse when tumor is removed

Selective α-1/Ca^{+2} channel blockers

PHEOCHROMOCYTOMA/ PERIOP. Mgmnt

. B-blockers :arrhythmia/extrasystoles

β blockade should not be started until adequate α-blockade leading to unopposed α effect:

1. worsened vasoconstriction
2. HTN crisis
3. CHF(preexisting myopathy)
4. Pulm. Edema

PHEOCHROMOCYTOMA/ PERIOP. Mgmnt

- Avoid anesthetic drugs that precipitate cathecolamine secretion
- A-line
- CVP-Line
- Nitroprusside :HTN episodes,
- Esmolol:tachy,arrythmias
- Phentolamine

PHEOCHROMOCYTOMA/ PERIOP. Mgmnt

In the past, mortality was high as 50%

Currently :<5%

25 %pt. ,the HTN is essential but may require less medical Rx.

PHEOCHROMOCYTOMA/ Surgical considerations

Pregnancy

Maternal MR 17%

Fetal MR 40%

1st trimester

Late in pregnancy :c-section

PHEOCHROMOCYTOMA/ Surgical considerations

- MEN 2 (Bilateral and hyperplasia precedes development of pheo.)
- If unil.:unil.adrenalectomy and close F/U for devpt. Of metachronous lesions 1/3
- Bil. Adrenalectomy to prevent metachronous leaving pt. With 10-30%risk of addisonian crisis

PHEOCHROMOCYTOMA/ Surgical considerations

Cortical sparing with risk of recurrence of 25% in long term @10 yrs

PHEOCHROMOCYTOMA/ Surgical Approaches

1926 Charles Mayo
Cesar Roux

1989 laparoscopy for cholelithiasis

1991 Snow et al. first transabdominal

1992 Gagner :first lateral lap.adrenalectomy

1995 Mercan posterior ,retrop. laparoscopic

- **Box 37-5. Indications and Contraindications for Laparoscopic Adrenalectomy**

- ***Indications***
- Aldosteronoma
- Cushing's syndrome
- Cortisol-producing adenoma
- Adrenal hyperplasia from failed treatment of ACTH-dependent Cushing's syndrome
- Primary adrenal hyperplasia
- Pheochromocytoma (sporadic or familial)
- Nonfunctioning cortical adenoma (>4–5 cm or atypical radiographic appearance)
- ***Contraindications***
- Any locally invasive adrenal tumor
- Regional lymph node metastases
- Large adrenocortical cancer
- Existing contraindication to laparoscopic surgery
- Prior nephrectomy, splenectomy, liver resection on affected side*
- ***Controversial***
- Suspected primary adrenal malignancy
- Large tumor size
- Adrenal metastasis

PHEOCHROMOCYTOMA/ Surgical Approaches

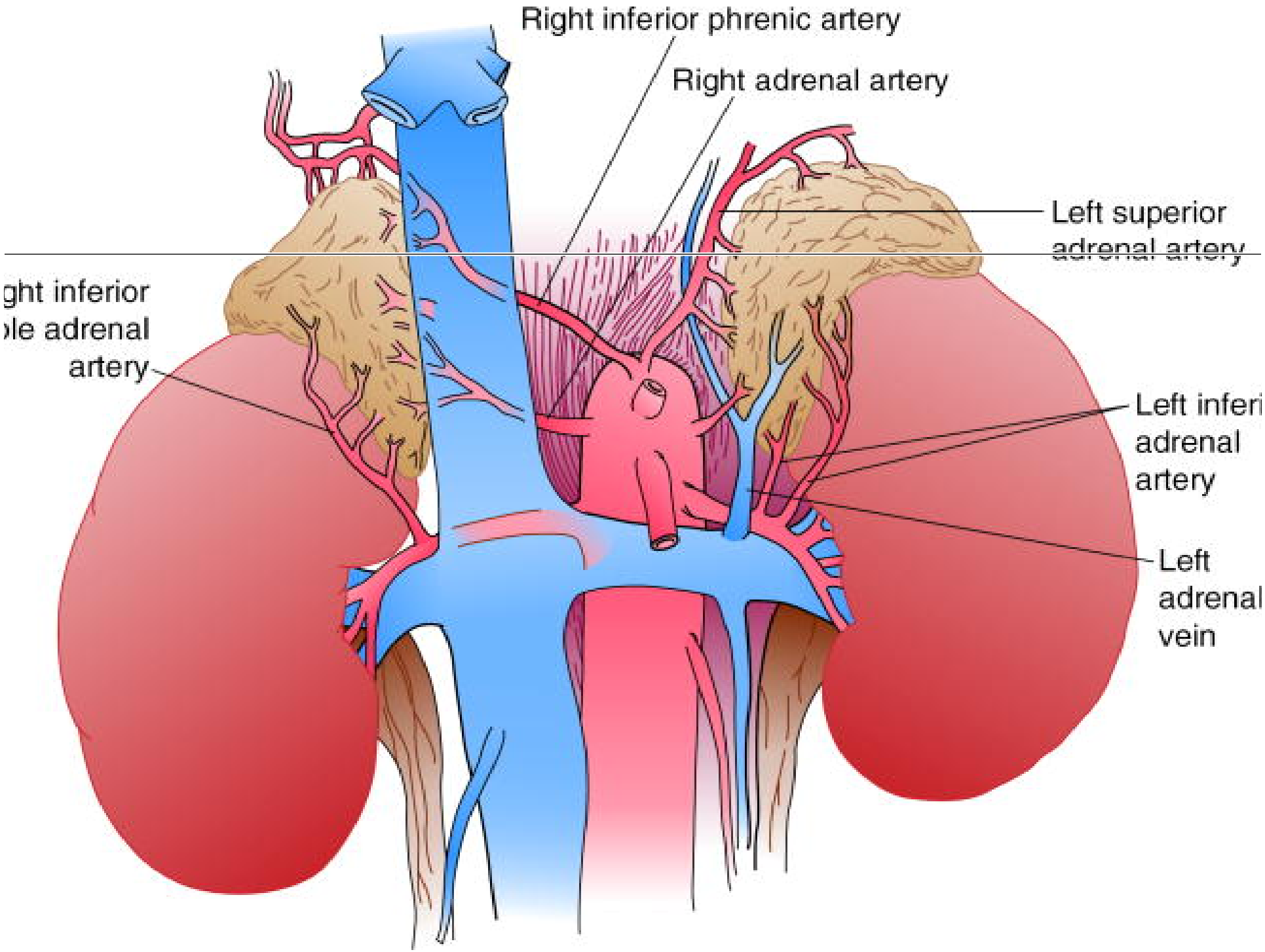
6-8 cm as the limit for lap. Approach

Pre-op or intraop. evidence of malignancy

OPEN APPROACH: Malignant

size

1. **Anterior(extraadrenal,bil.,mets.)**
2. **Thoracoabdominal(large malignant)**
3. **Lateral**
4. **Posterior retroperitoneal**


Right inferior phrenic artery
Right adrenal artery
Left superior
adrenal artery
ght inferior
le adrenal
artery
Left inferi
adrenal
artery
Left
adrenal
vein

PHEOCHROMOCYTOMA/ Surgical Approaches

Very vascular :3 arterial supplies:

- **Inferior phrenic**
- **Aorta**
- **Renal artery**

Venous :single large

right :short,IVC directly

left: left renal vein

PHEOCHROMOCYTOMA/ Surgical Approaches

- Mortality 0-3%
- Morbidity <5%
- Minimize tumor manipulation

PHEOCHROMOCYTOMA/ FOLLOW UP CARE

No reliable method to distinguish benign from malignant:lifelong surveillance

RR benign 6.5 %

½ of malignant have residual disease

Recurrent pheo.may occur late as 20 yrs.

PHEOCHROMOCYTOMA/ prognosis

Nonmalignant pheo. 5 yr survival >95%

RR<10%

Resection cures HTN in 75%

25%better control 2° irreversible vascular and renal damage

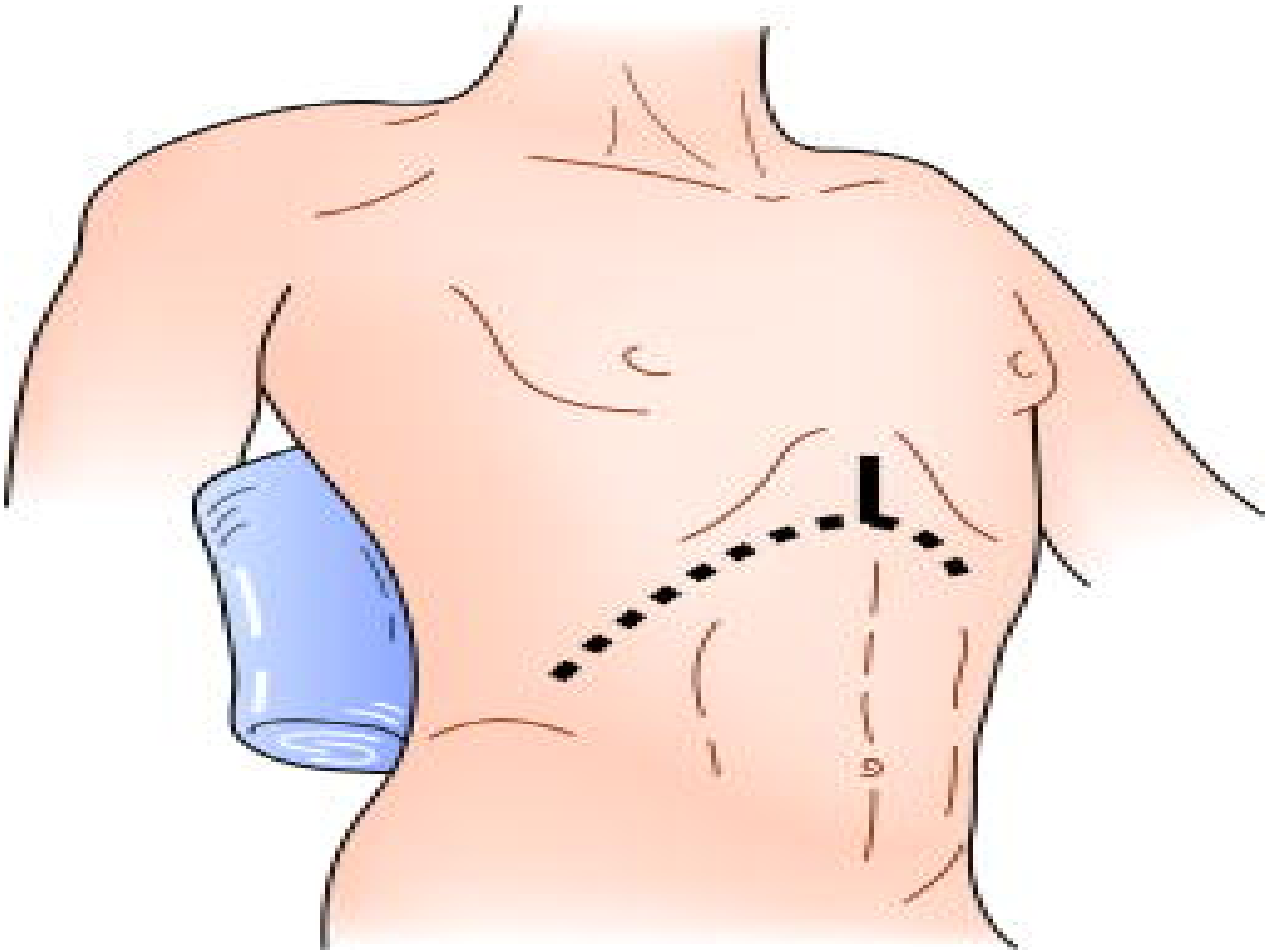
PHEOCHROMOCYTOMA/ Surgical considerations

Malignant :40% 10yr survival

debulked when possible

^{131}I MIBG small soft issue mets.

ERT Bony mets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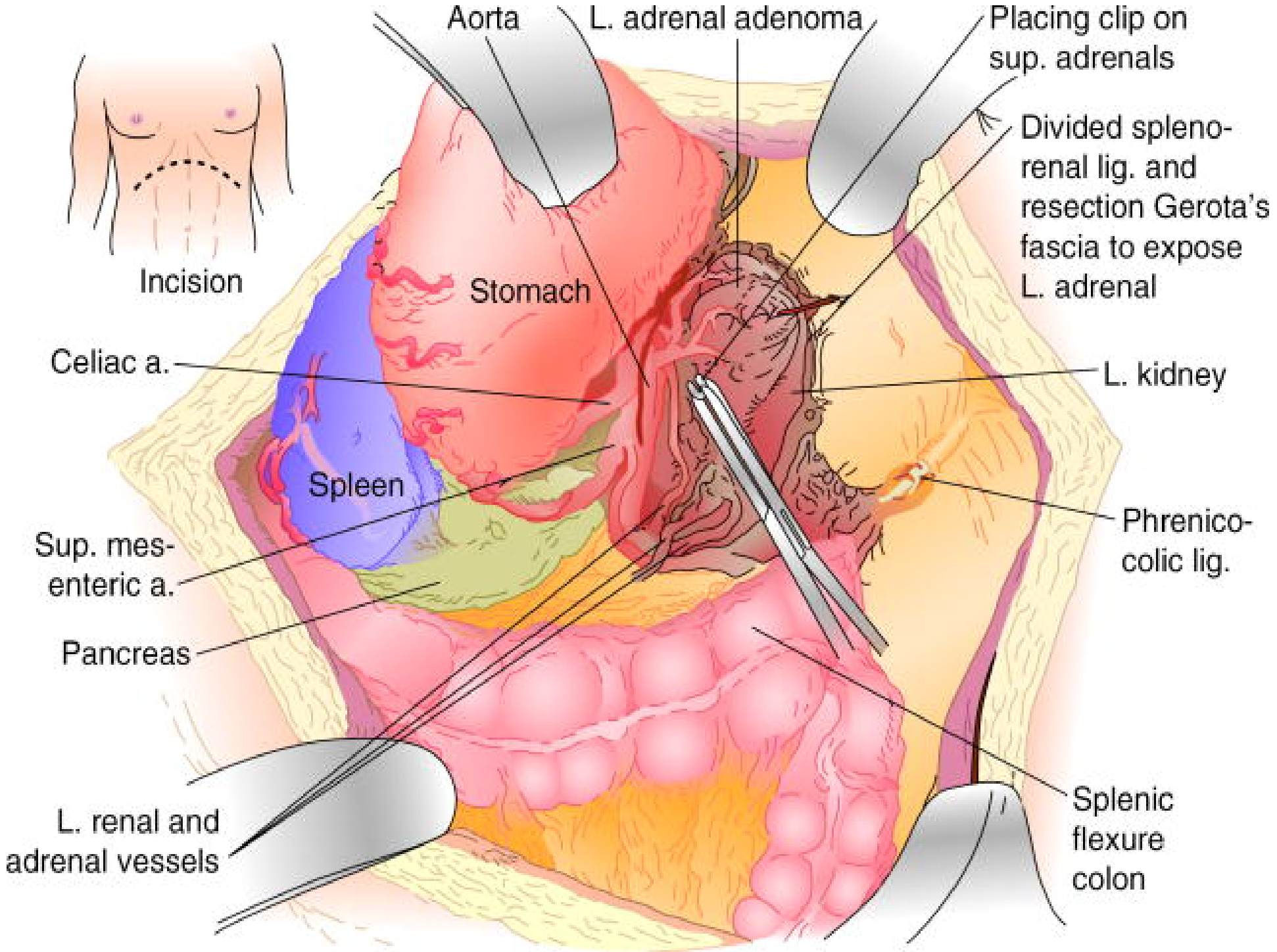
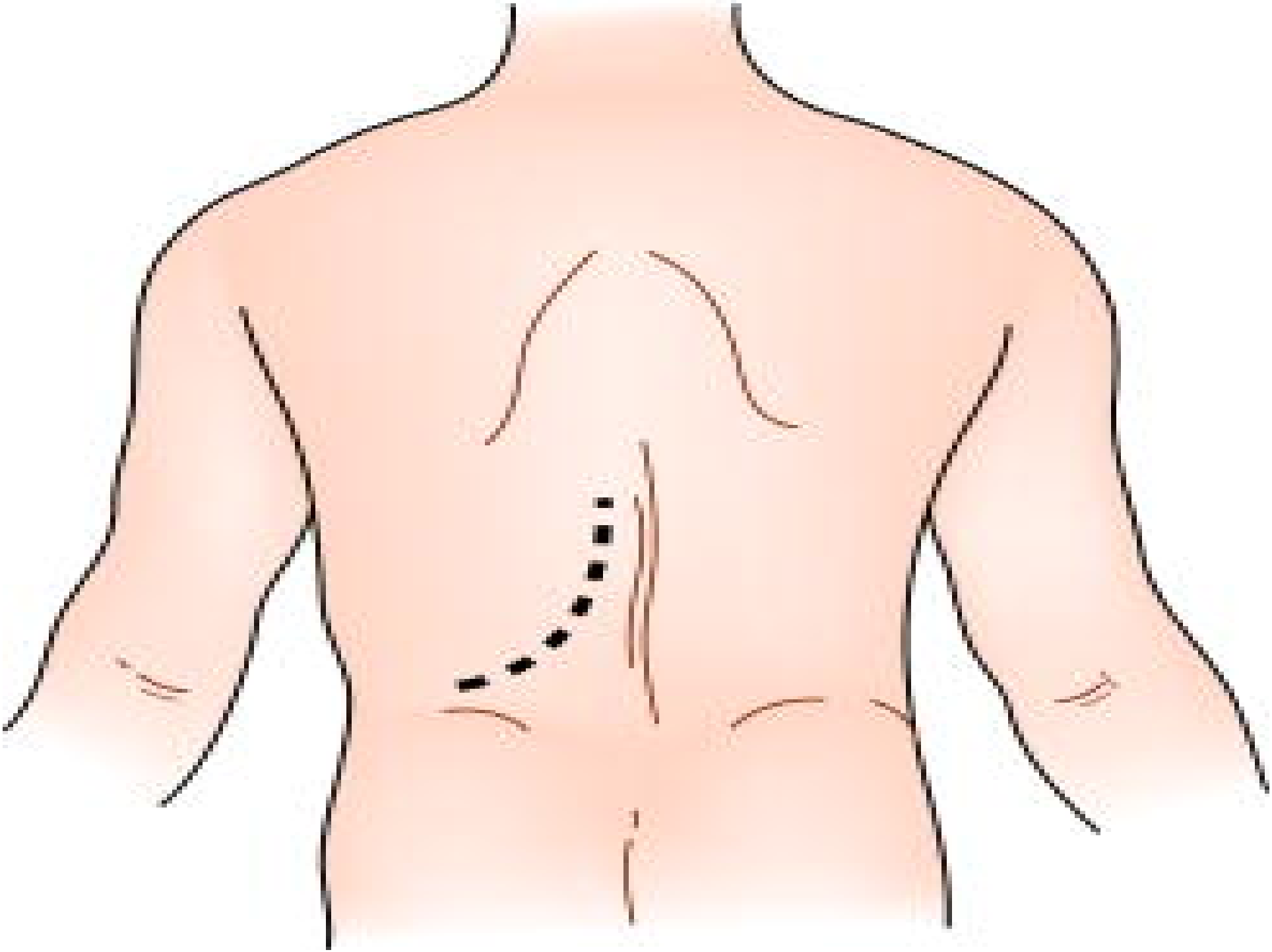
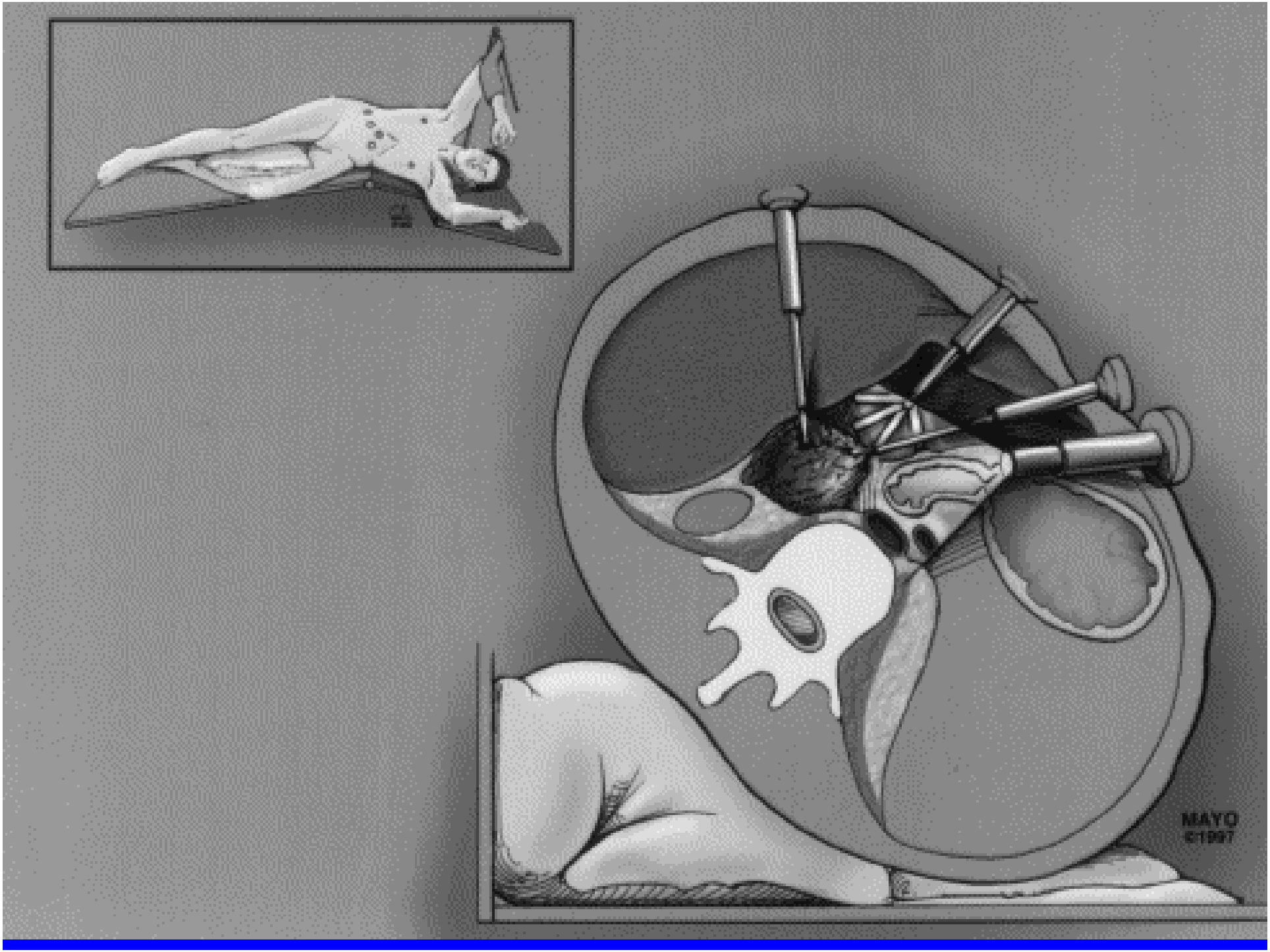
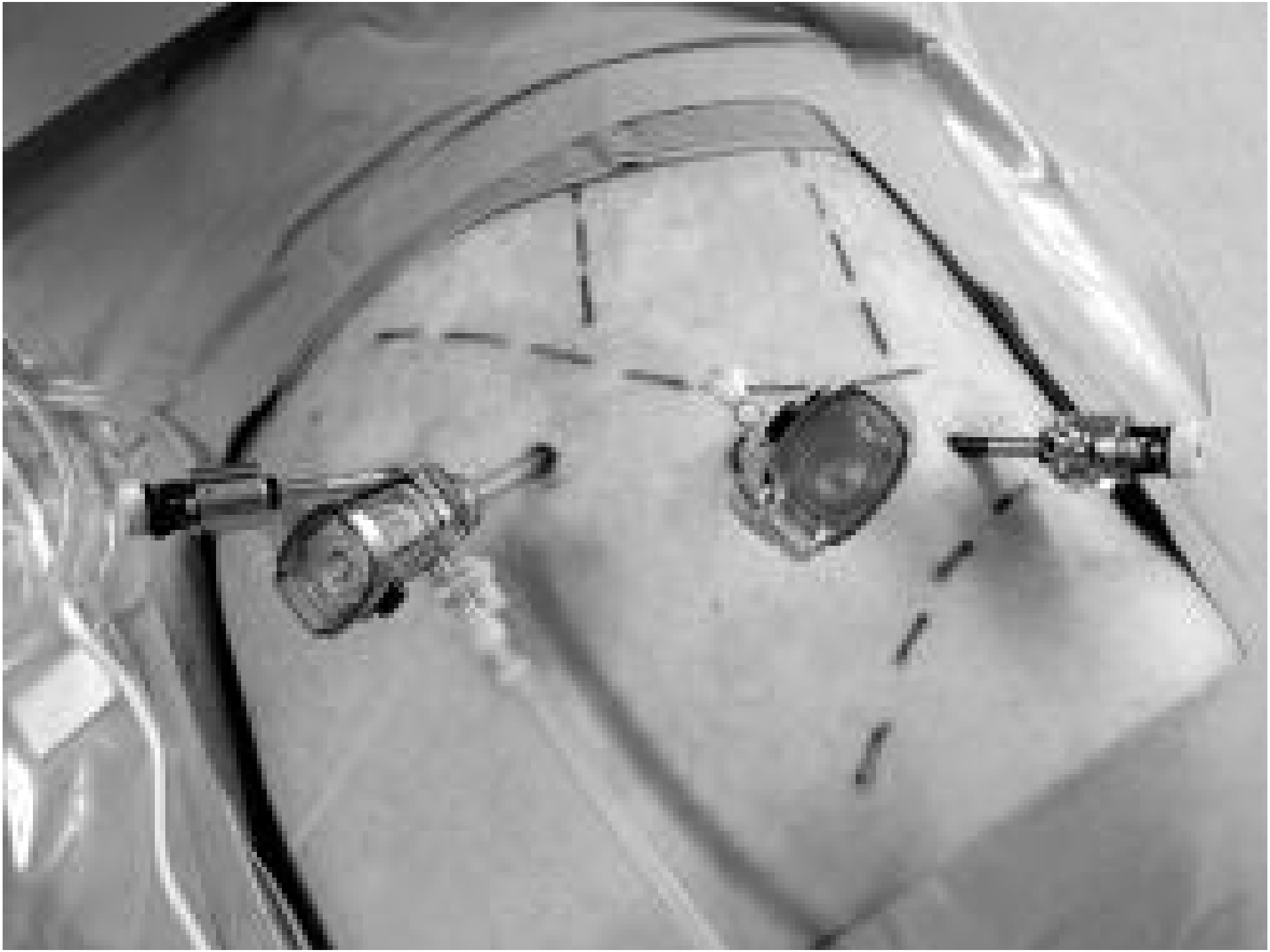
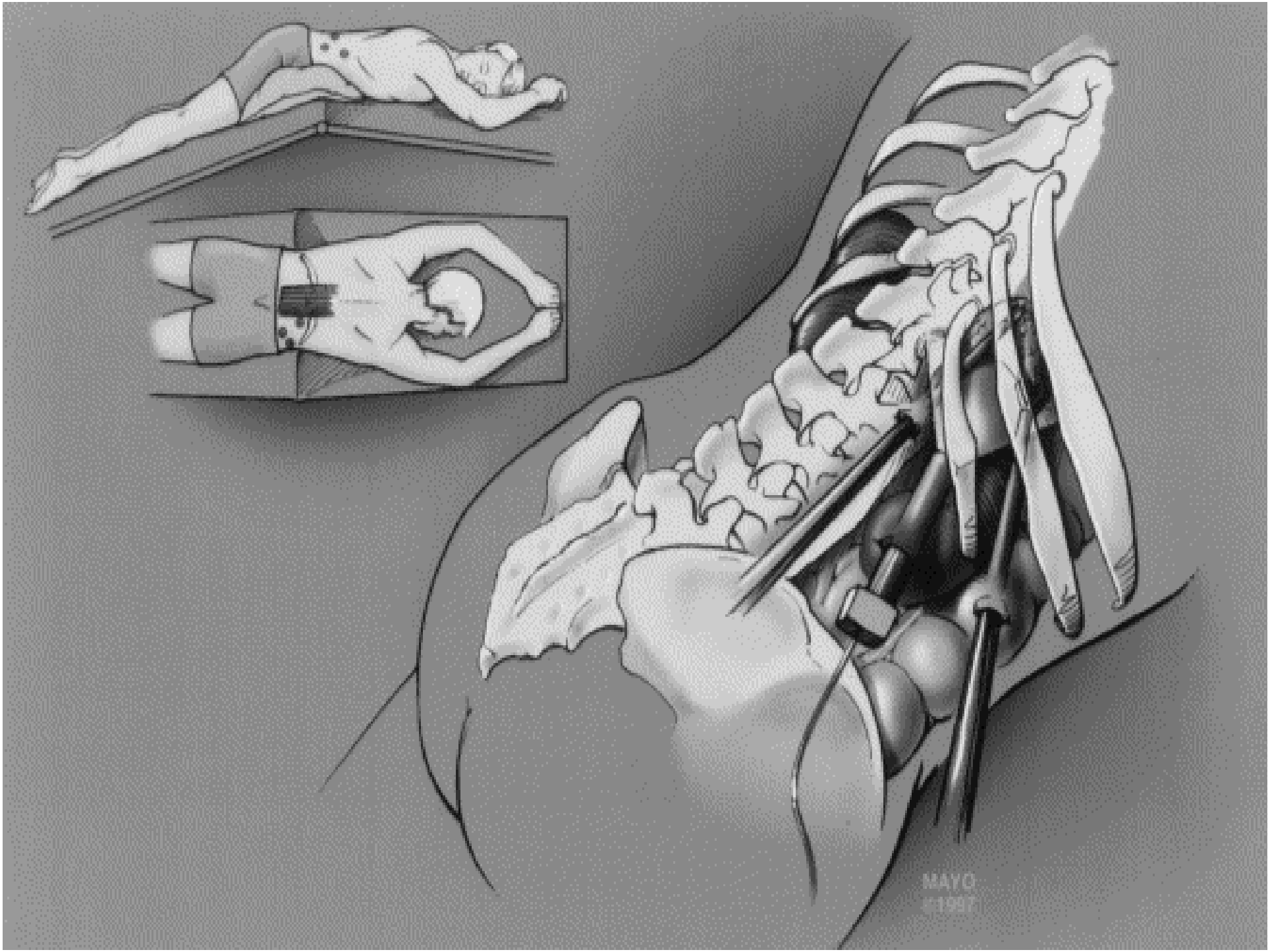
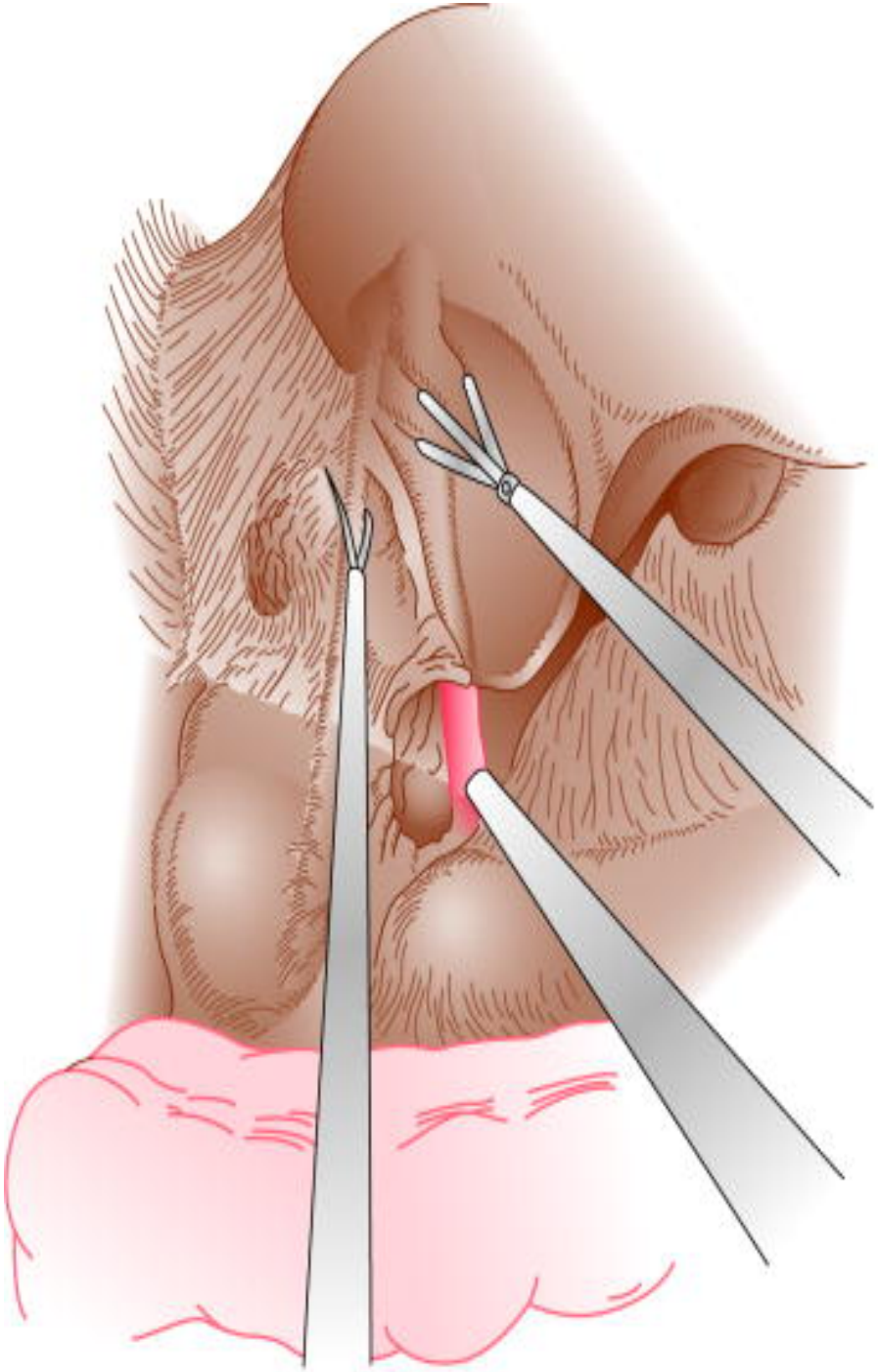

Aorta
L. adrenal adenoma
Placing clip on sup. adrenals
Divided spleno-renal lig. and resection Gerota's fascia to expose L. adrenal
Incision
Stomach
Celiac a.
L. kidney
Spleen
Phrenico-colic lig.
Sup. mes-enteric a.
Pancreas
L. renal and adrenal vessels
Splenic flexure colon

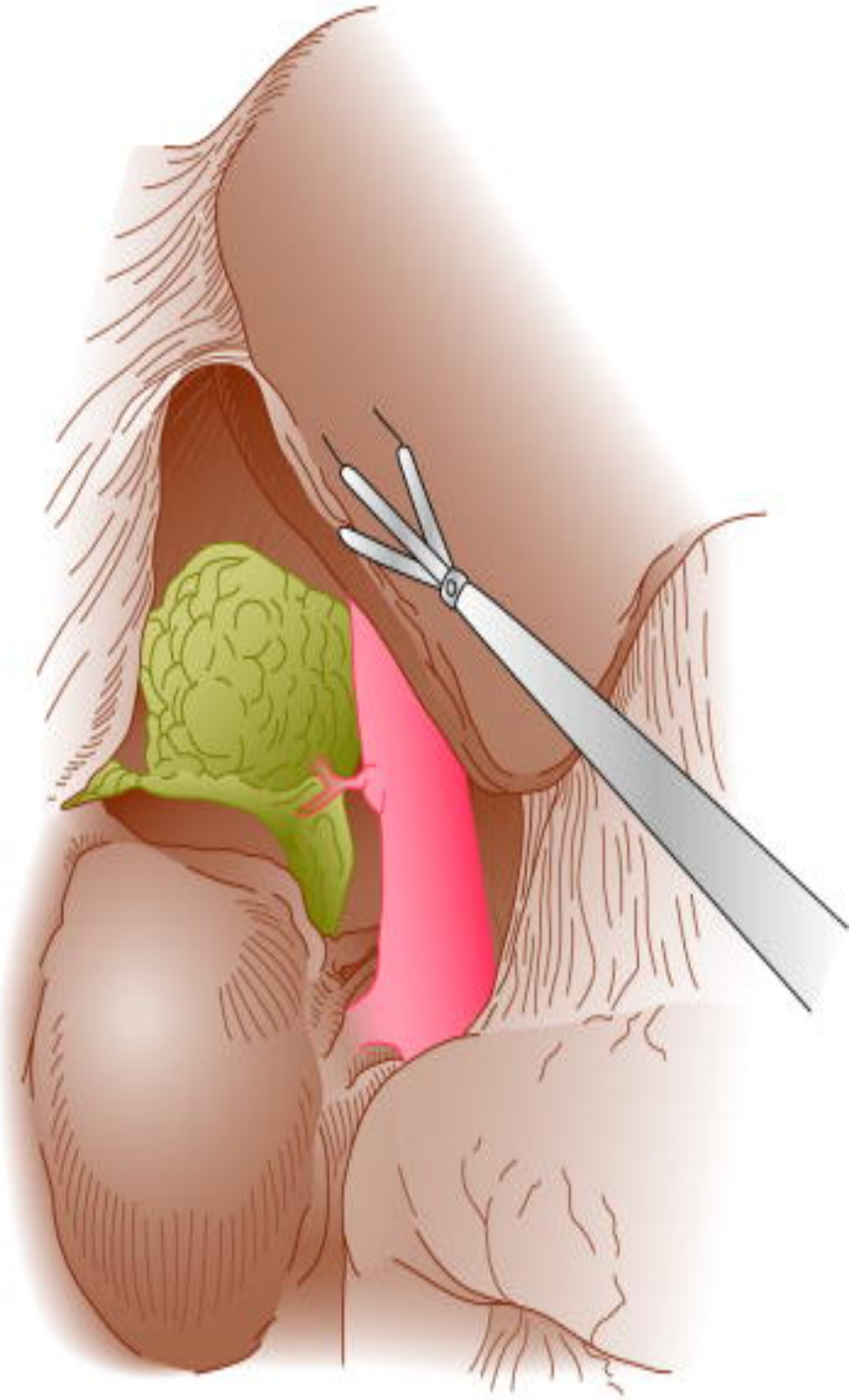


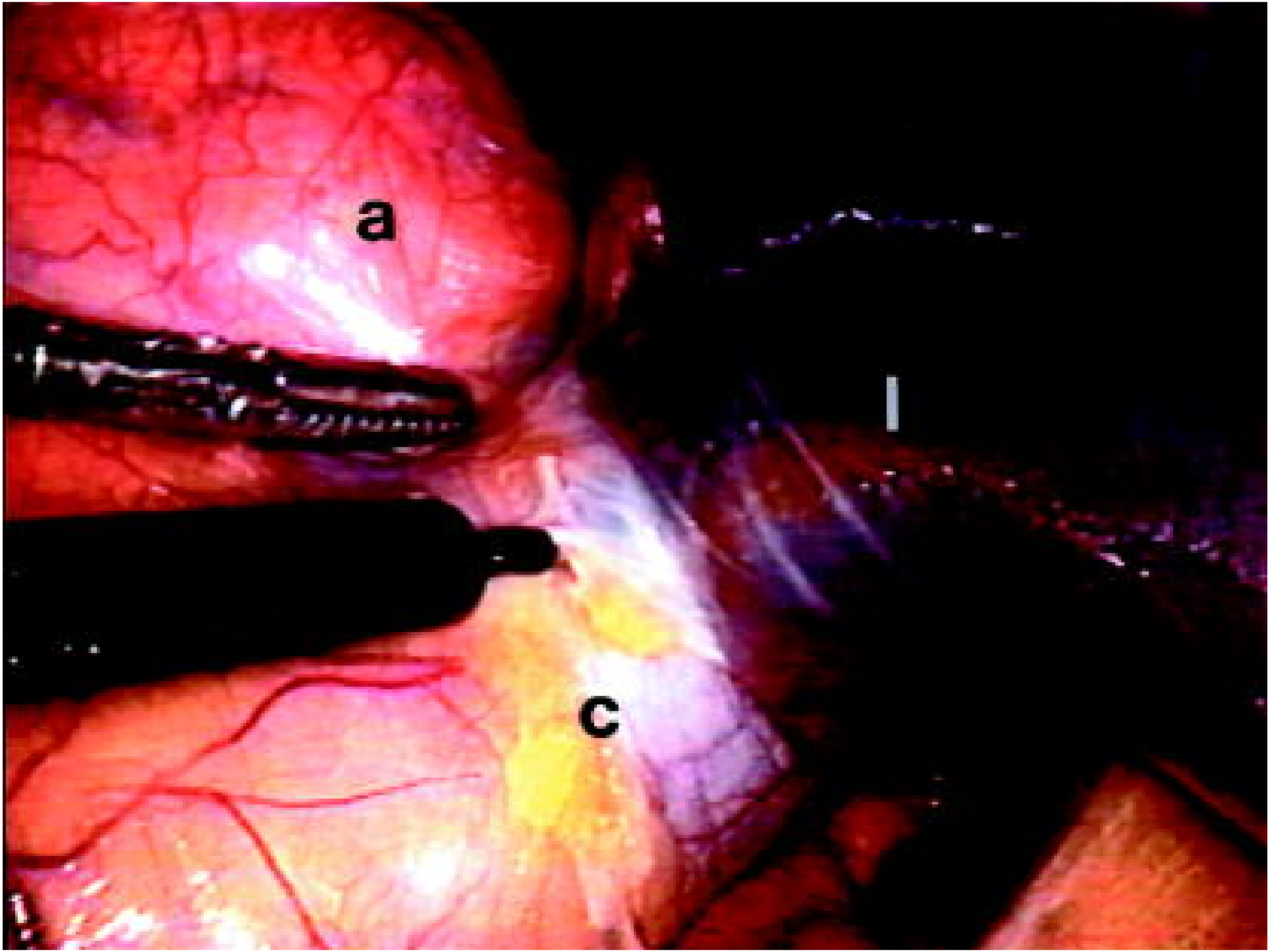

MAYO
©1997




MAYO
©1997



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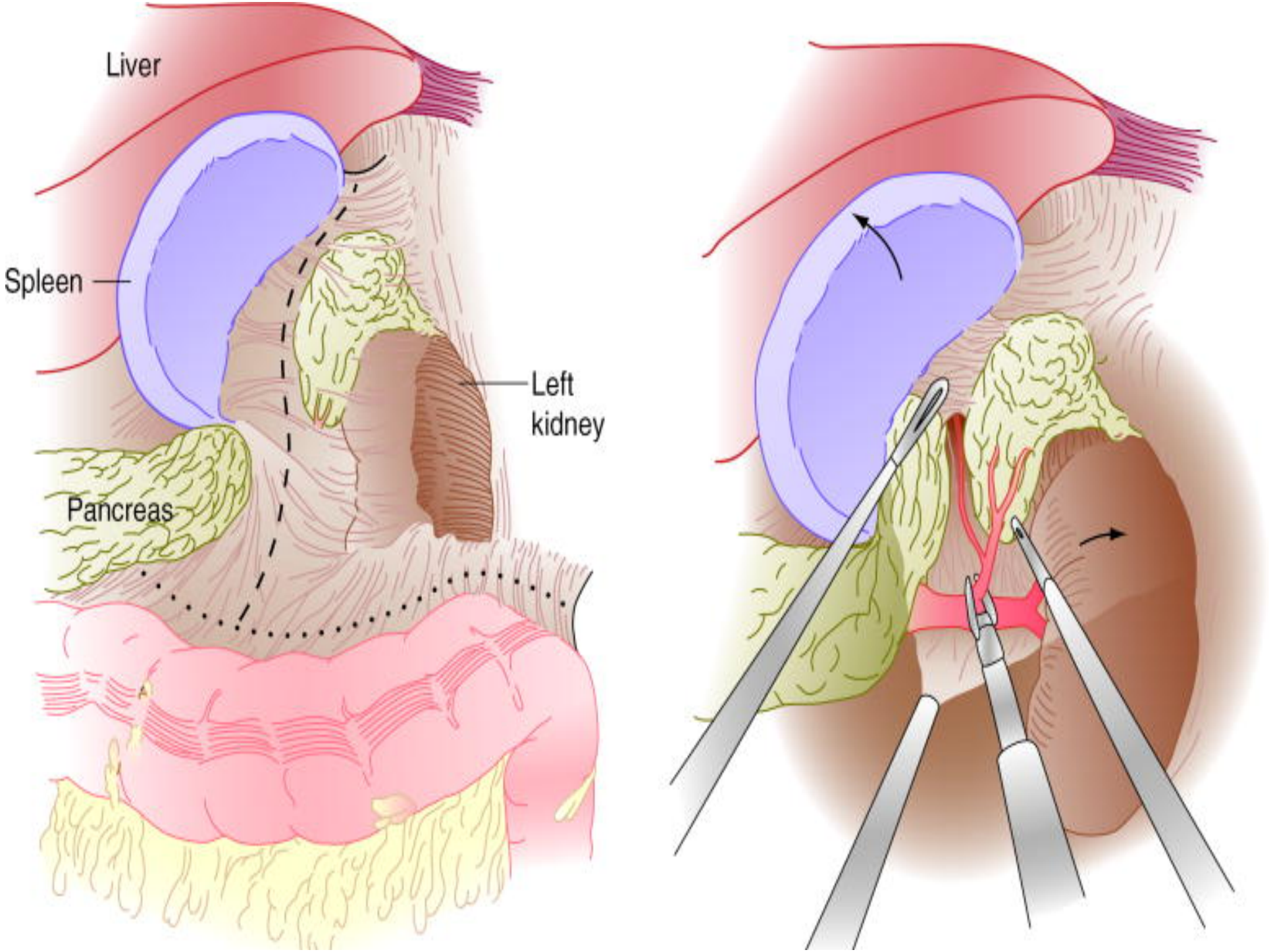
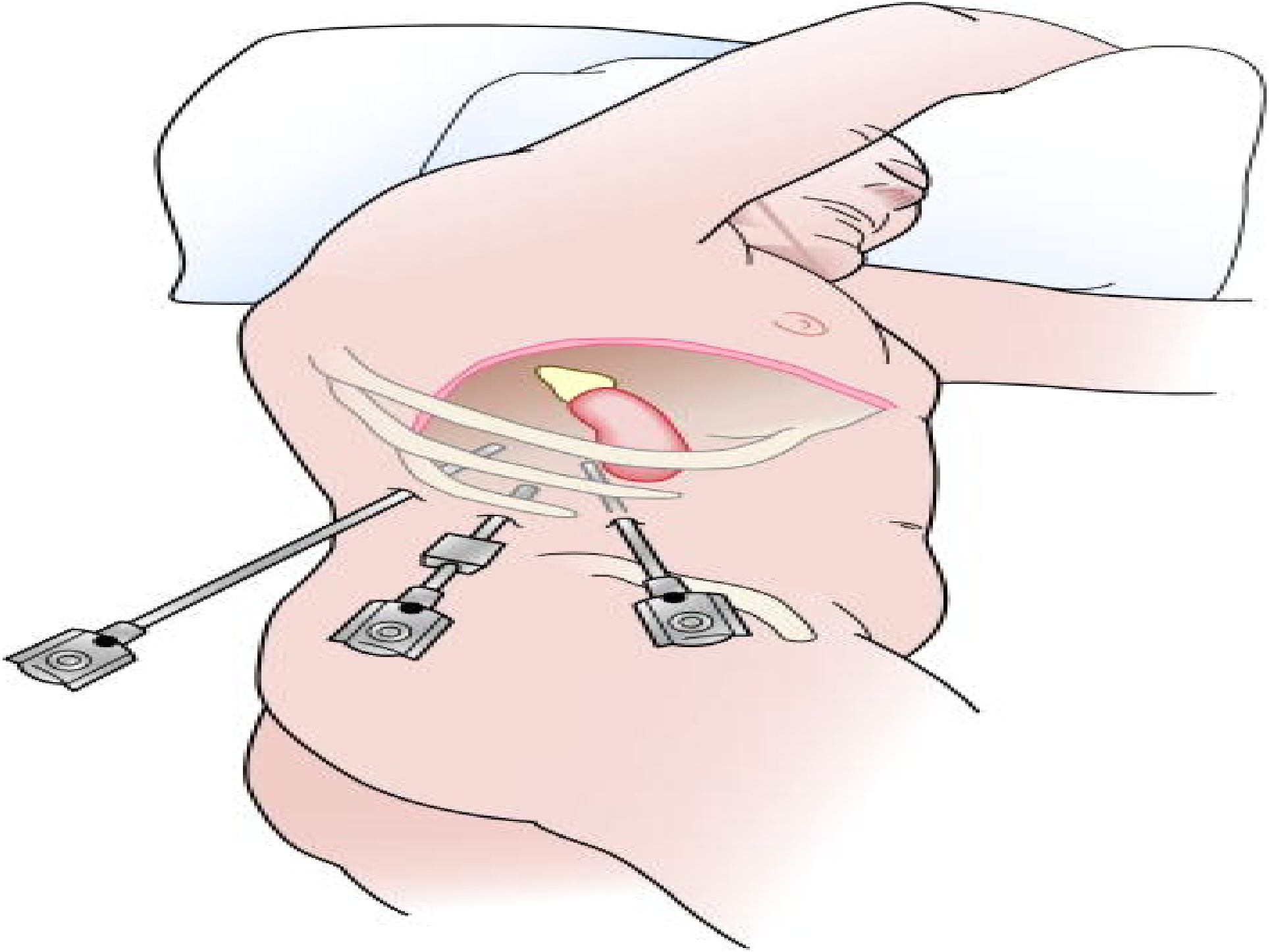

Liver
Spleen
Left kidney
Pancreas



PHEOCHROMOCYTOMA/ Surgical Approaches

"FOCUSED APPROACH"

Laparoscopic adrenalectomy :gold standard

Decreased hospital stay

Less analgesic req.

Short convalescence

< blood transfusion

FEWER **hemodynamic changes**