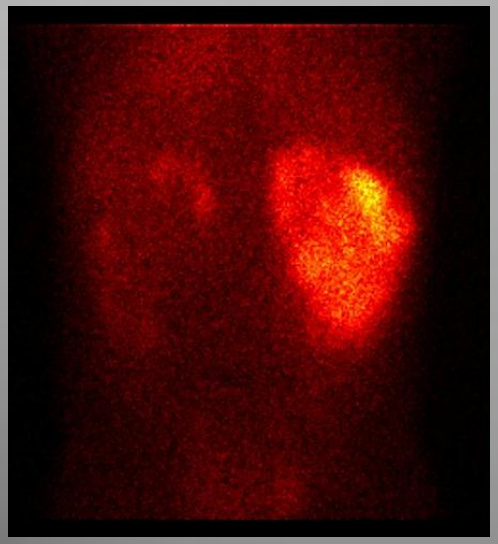
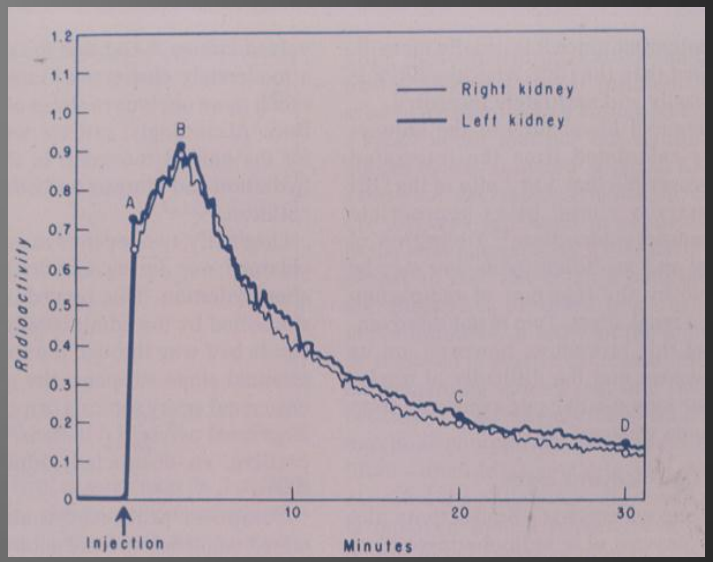
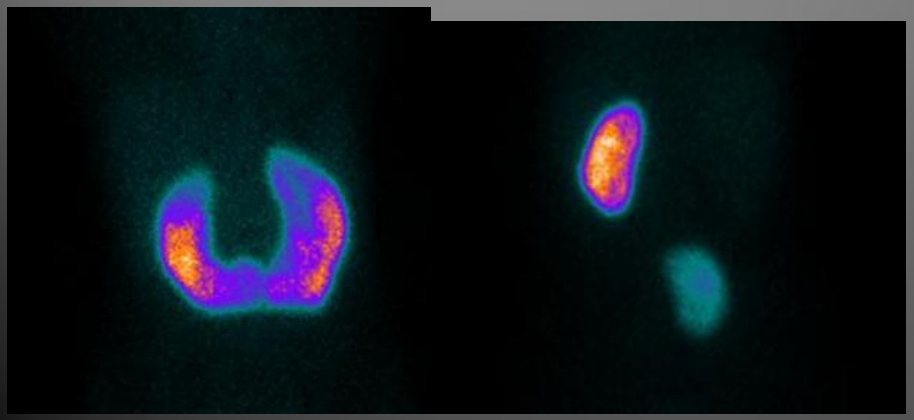
NUCLEAR MEDICINE IN NEPHROLOGY AND UROLOGY







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The most used **radionuclides** in nuclear medicine nephrourology are:

- **Tc-99m** : $T_{1/2}$=6 hours y=140 keV
- **I-131**: $T_{1/2}$= 8 days y=364 keV; $\beta^{-median}$=192keV

Radiopharmaceuticals are pharmacological preparations labeled with radionuclide

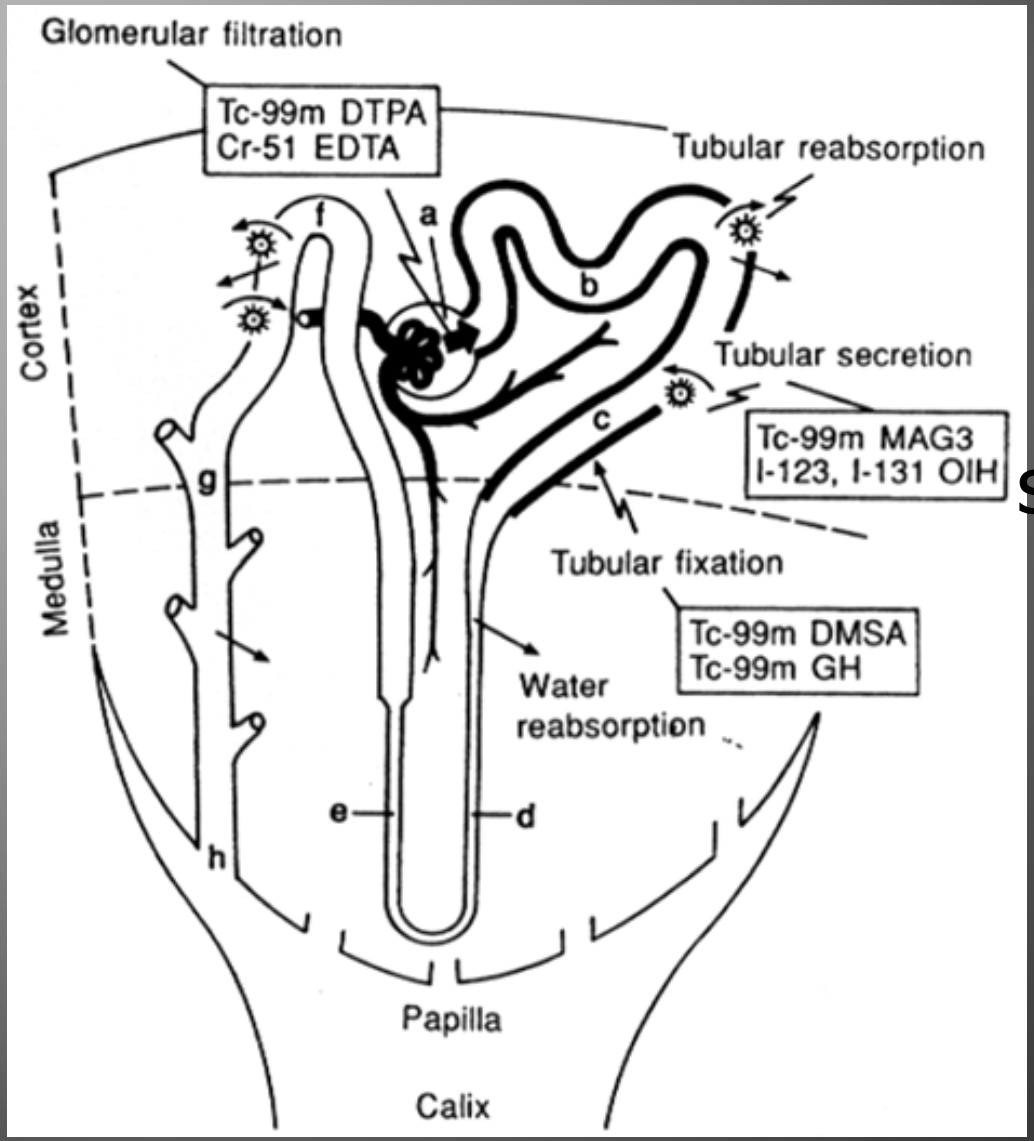
- The most used **radiopharmaceuticals** in nuclearmedicine nephrourology are:

-**Tc-99m-DTPA** (diethylenetriamine-pentaacetic acid)
- **I-131-hippuran** (sodium-ortoiodohippurate)
- **Tc-99m-MAG3** (mercapto acetyl triglycine)
- **Tc-99m-DMSA** (dimercapto-succinic acid)
- **Tc-99m-pertechnetate**

RADIOPHARMACEUTICALS

For dynamic scintigraphy:

HIPPURAN
DTPA
MAG3
EDTA



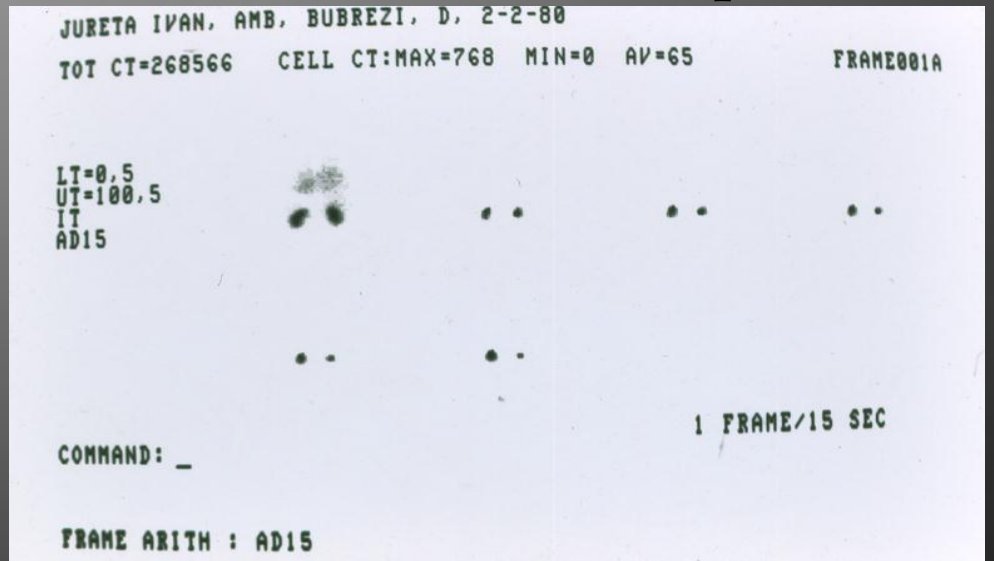
For static scintigraphy:

DMSA
GH

Dynamic renal scintigraphy

- Computerized gamma camera monitors the arrival, uptake (accumulation) and the elimination of radiopharmaceuticals from the kidneys. In computer memory, during the 20-30 minutes are stored sequential scintigrams with optional duration (usually every 20 sec to 1 min).

- After completion of the study the same are displayed on the computer screen as a series of sequential scintigrams.

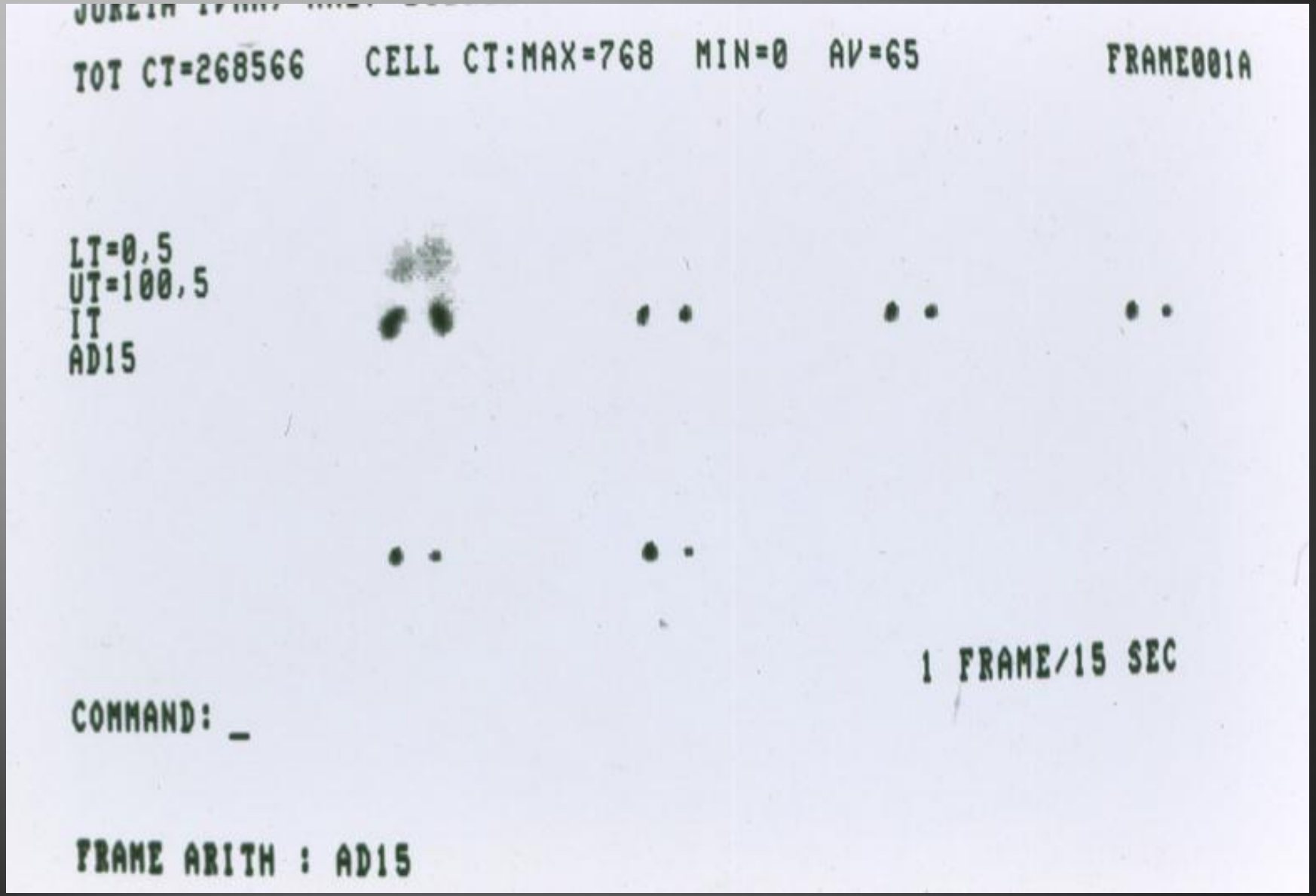


Dynamic renal scintigraphy

- **Analysis:**

  -qualitative- kidney morphology: shape, size, position; **function:** timing and intensity of accumulation, the homogeneity of the appearance; activity **elimination** from kidney.

  - quantification-ROI, generate renogram curves, deconvolution renogram curves and obtain relative separate renal clearance and transit time of radiopharmaceuticals through the kidney, parenchyma and pelvis.


TOT CT=268566 CELL CT:MAX=768 MIN=0 AV=65 FRAME001A
LT=0,5
UT=100,5
IT
AD15
1 FRAME/15 SEC
COMMAND: _
FRAME ARITH : AD15

TOT CT=268566

LT=0,5
UT=100,5
IT
AD15

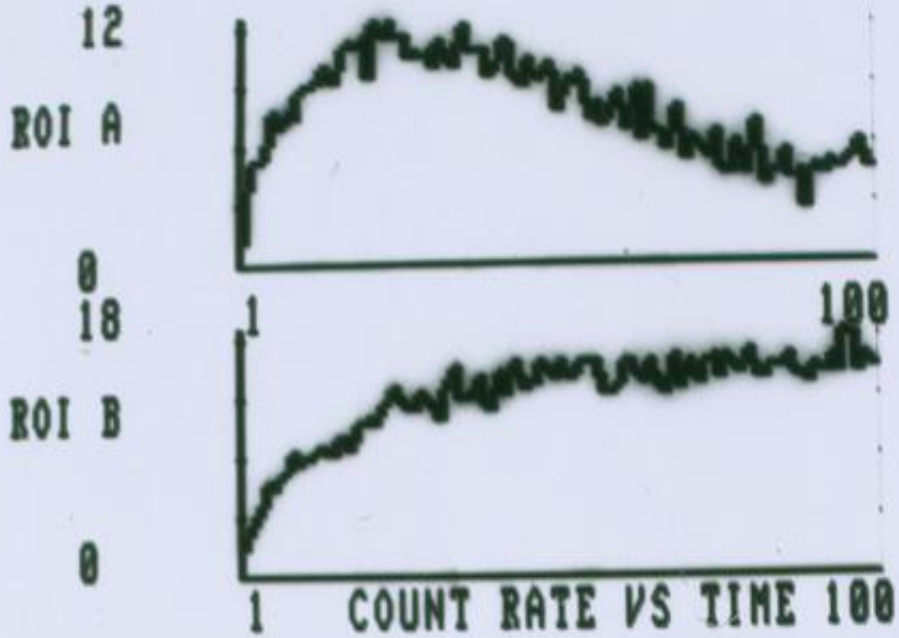
CELL CT:MAX=768 MIN=0 AV=65

FRAME001A

	COUNTS	CELLS	AVE
A:	25780	69	373
B:	27381	71	385

1 FRAME/15 SEC

FRAME ARITH : AD15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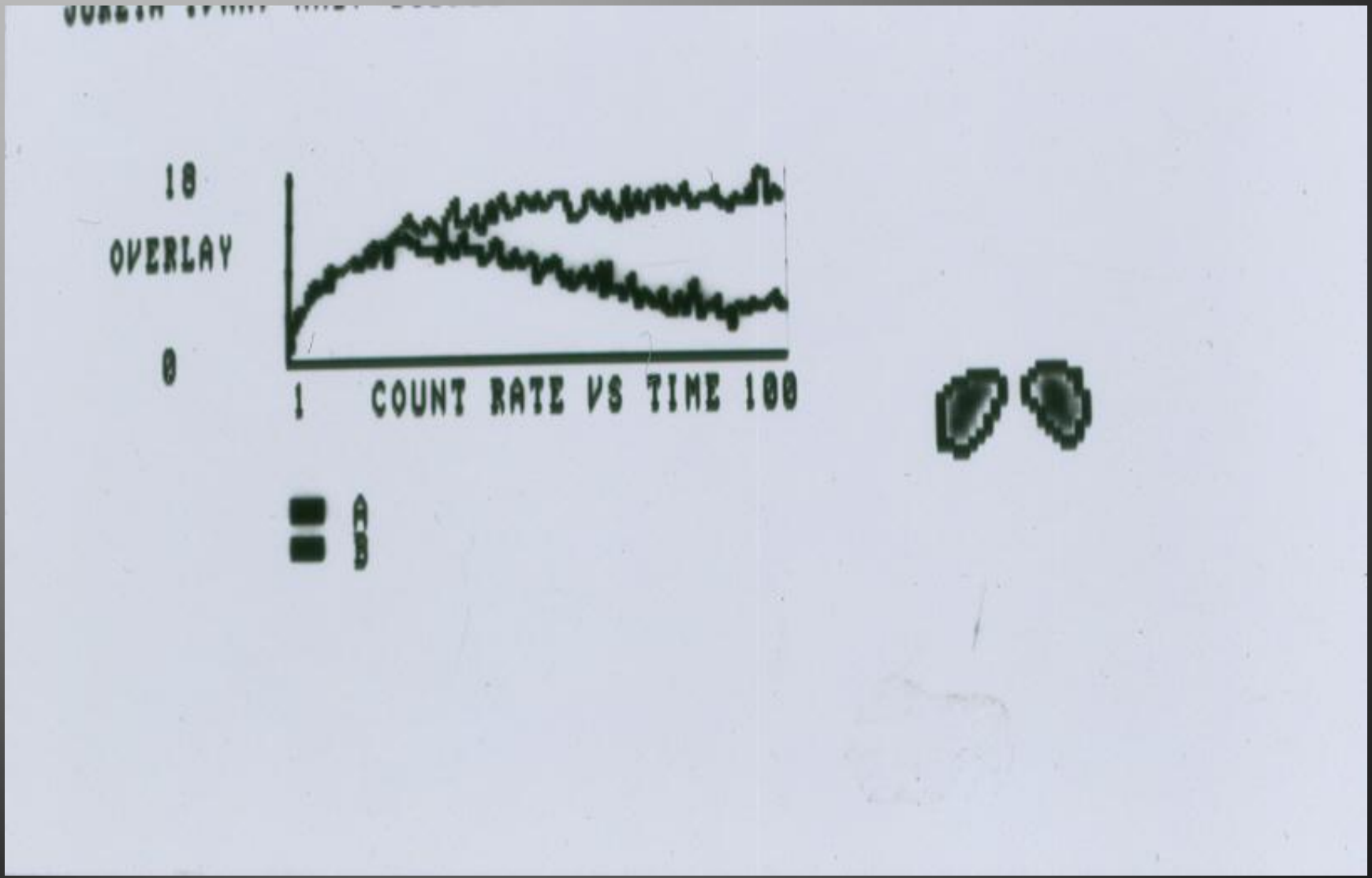
ROI A
0
18
ROI B
0
1
100
1
COUNT RATE VS TIME 100


18
OVERLAY
0
1
COUNT RATE VS TIME 100

Dynamic renal scintigraphy can be done with several radiopharmaceuticals

1. Tc-99m-DTPA (diethylenetriamine-pentaacetic acid)
2. Tc-99m-glucoheptonat
3. I-131 (I-123)-hippuran (sodium-ortoiodohippurate)
4. Tc-99m-MAG3 (mercapto acetyl triglycine)

Renogram curve

- **Renogram curve** is time activity curve which reflects :

  - arrival of radiopharmaceuticals in kidney- initial, ascending deflection - **circulatory or vascular segment**

  - accumulation, uptake or ascending phase- **filtration or secretory segment**

  -elimination of radiopharmaceuticals from kidney- descending part of the curve - elimination **or excretory segment**

  - It can be obtained in two ways:
    - Scintillation probe- renography
    - Computerized gamma camera

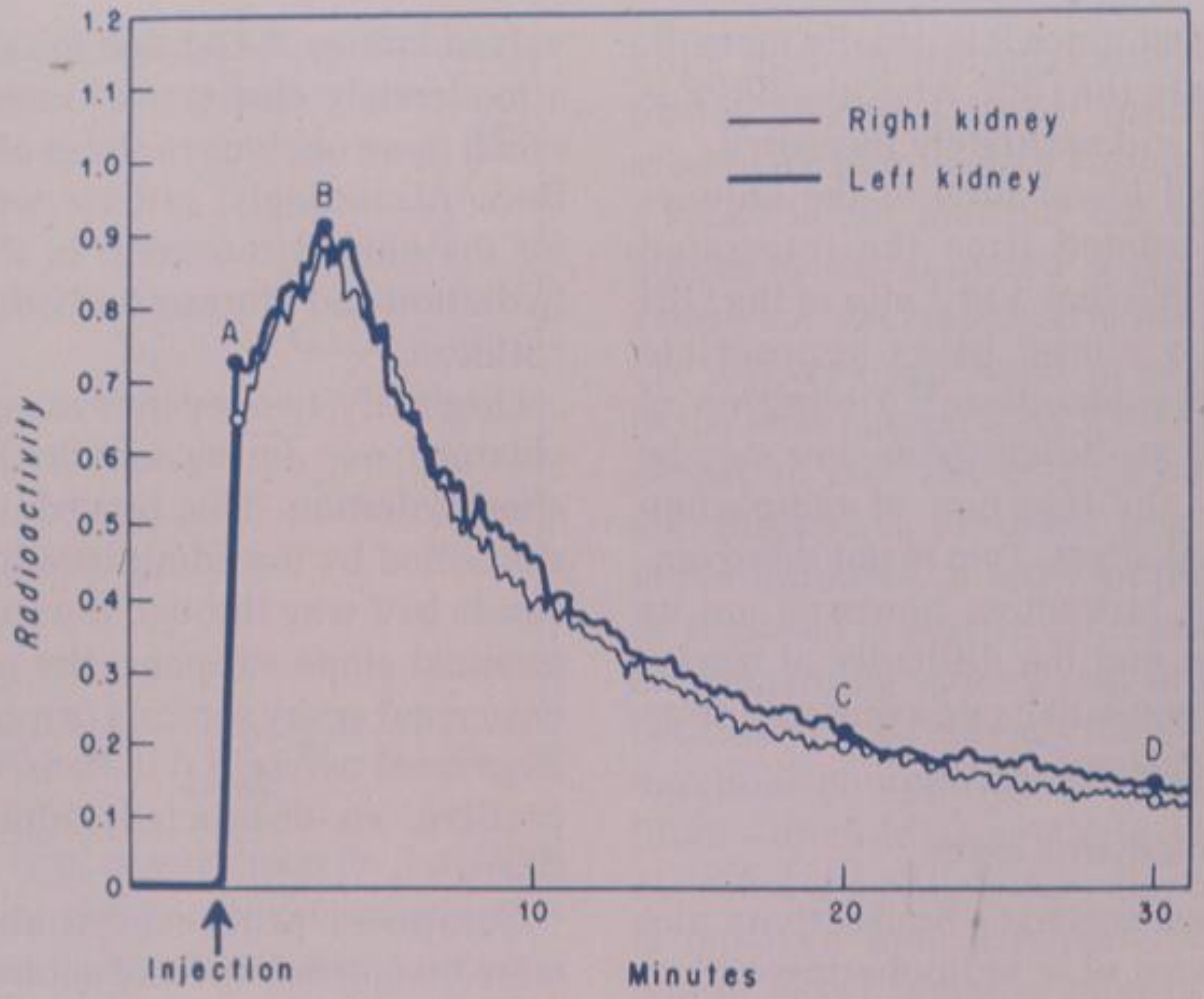
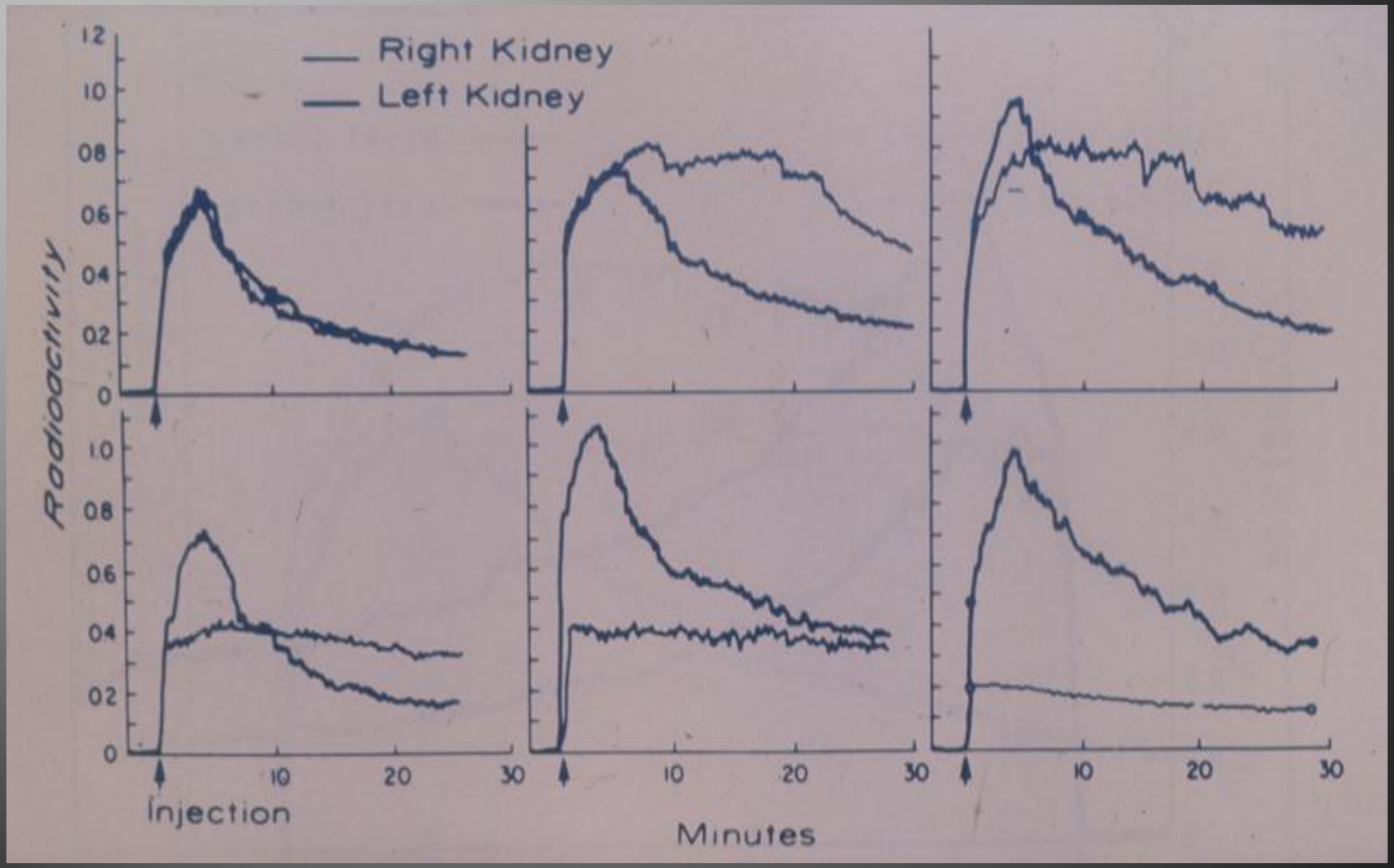


Fig. 21–7. Normal OIH time-activity curve, or renogram. *A* is the initial deflection, *B* is the point of maximum intensity and C and D are the 20- and 30-min activities, respectively.


Right Kidney
Left Kidney
Radioactivity
12
10
08
06
04
02
0
10
08
06
04
02
0
10
20
30
Injection
Minutes

Renogram curve deconvolution

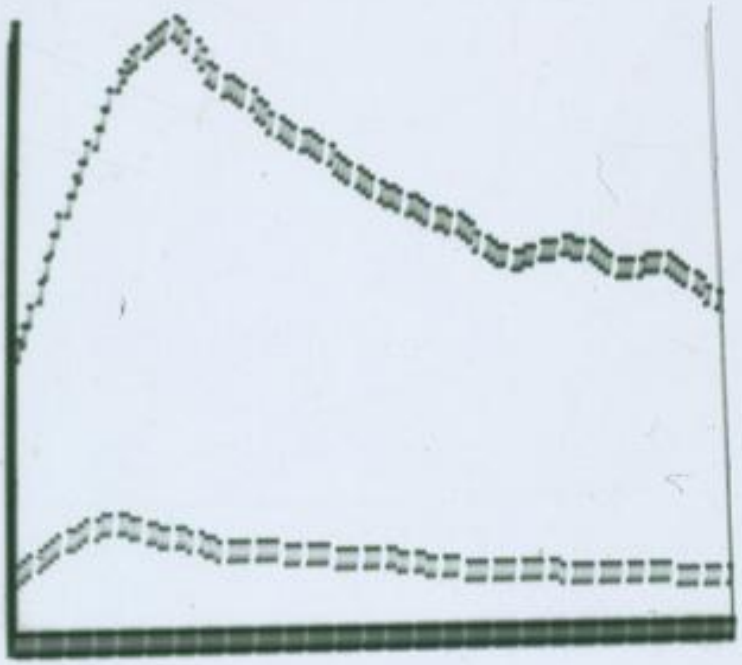
- Curve that reflects activity changes in the circulation (cardiac curve) represents **input renal curve.** It can be obtained, analogously to renogram curve, by recording with scintillation probe or with computerized gamma camera of vascular area of the heart.
- Renogram curve, with mathematical processing, **deconvolution**, with the help of **input renal curve**, becomes **impulse retention function**, and represents a kidney response to a hypothetical injection of the radiopharmaceutical directly into the renal artery.

- It allows us to obtain:

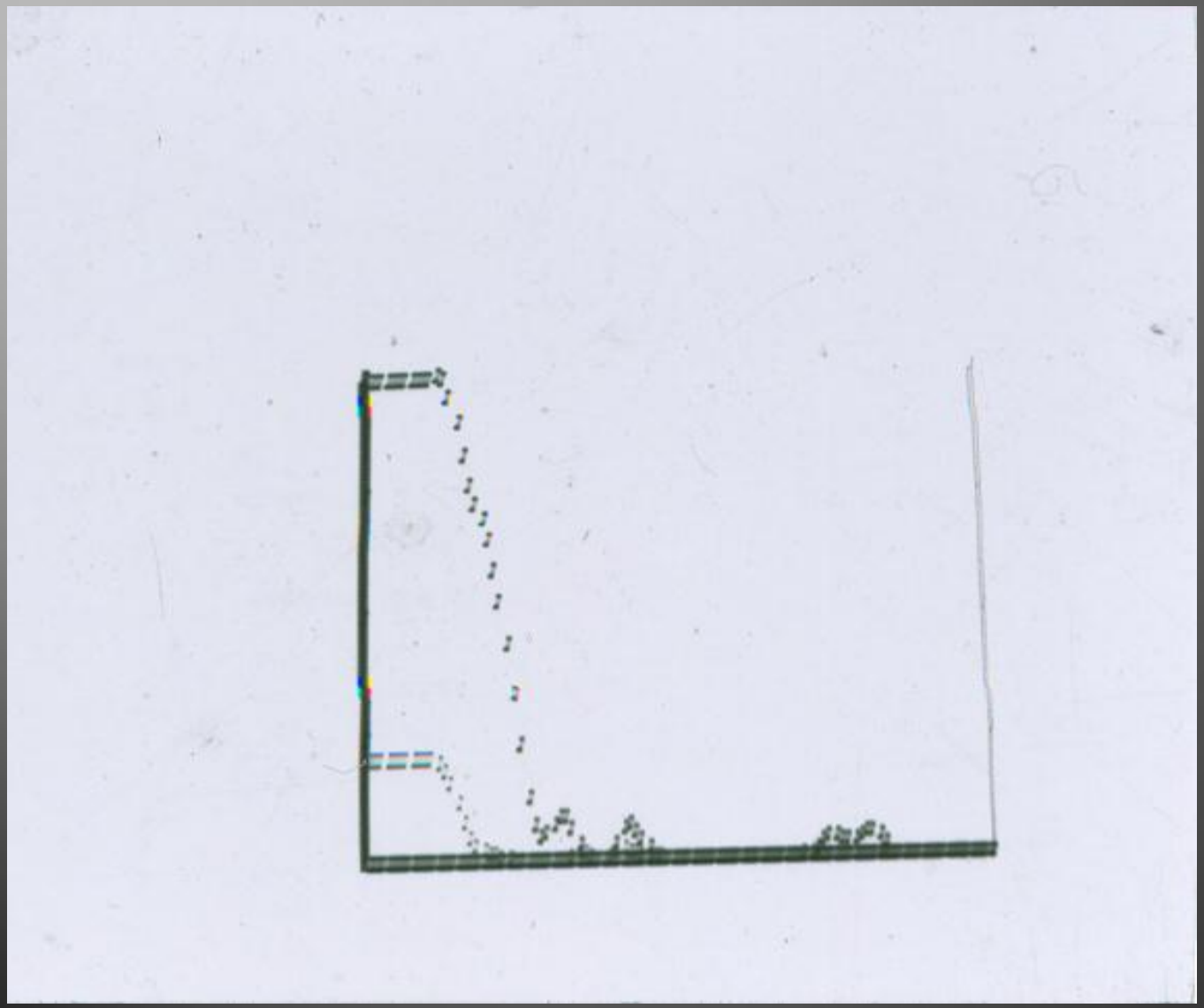
  - Relative, separate renal function

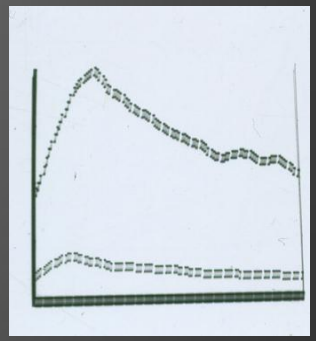
  - Minimum, medium and maximum
    transit time of the radiopharmaceutical through the
    kidney, kidney parenchyma and pelvis

Renogram curve



Retention function: separate clearance





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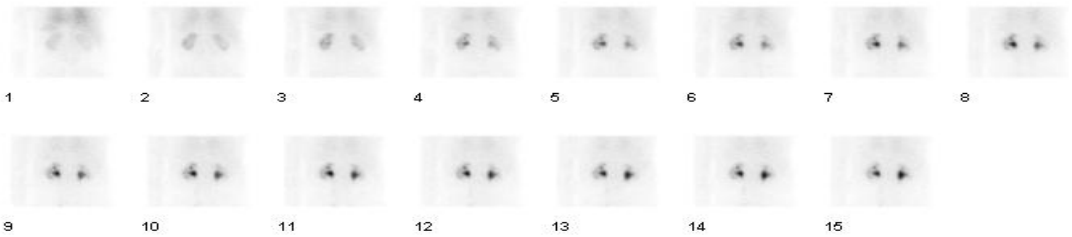
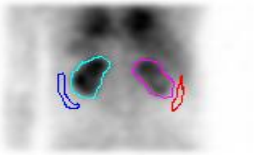


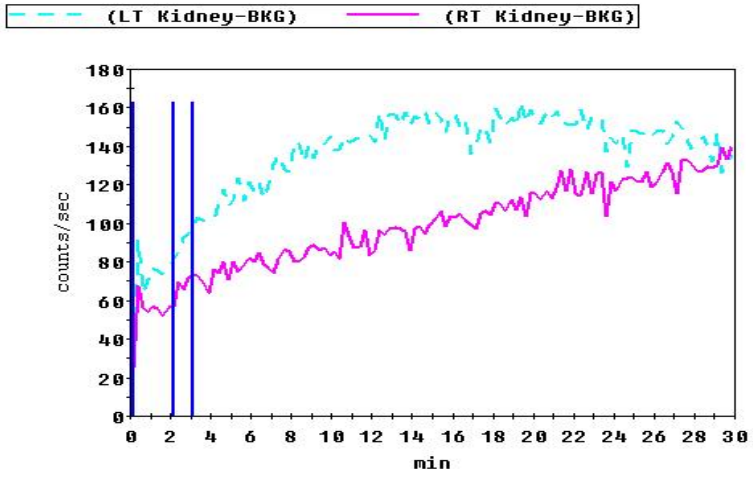
Age: 55. Years
Height (cm): 169.
Weight (kg): 83.
Radiopharmaceutical: TcDTPA

Kidney	Left	Right
Kidney Area (cm^2)	75.	68.8
Kidney Depth (cm):	7.2	7.2
Uptake% (Int):	57.	43.

Time to Peak:	19.2	29.8
Peak to 1/2 Peak:	21.6	NA



Uptake Interval



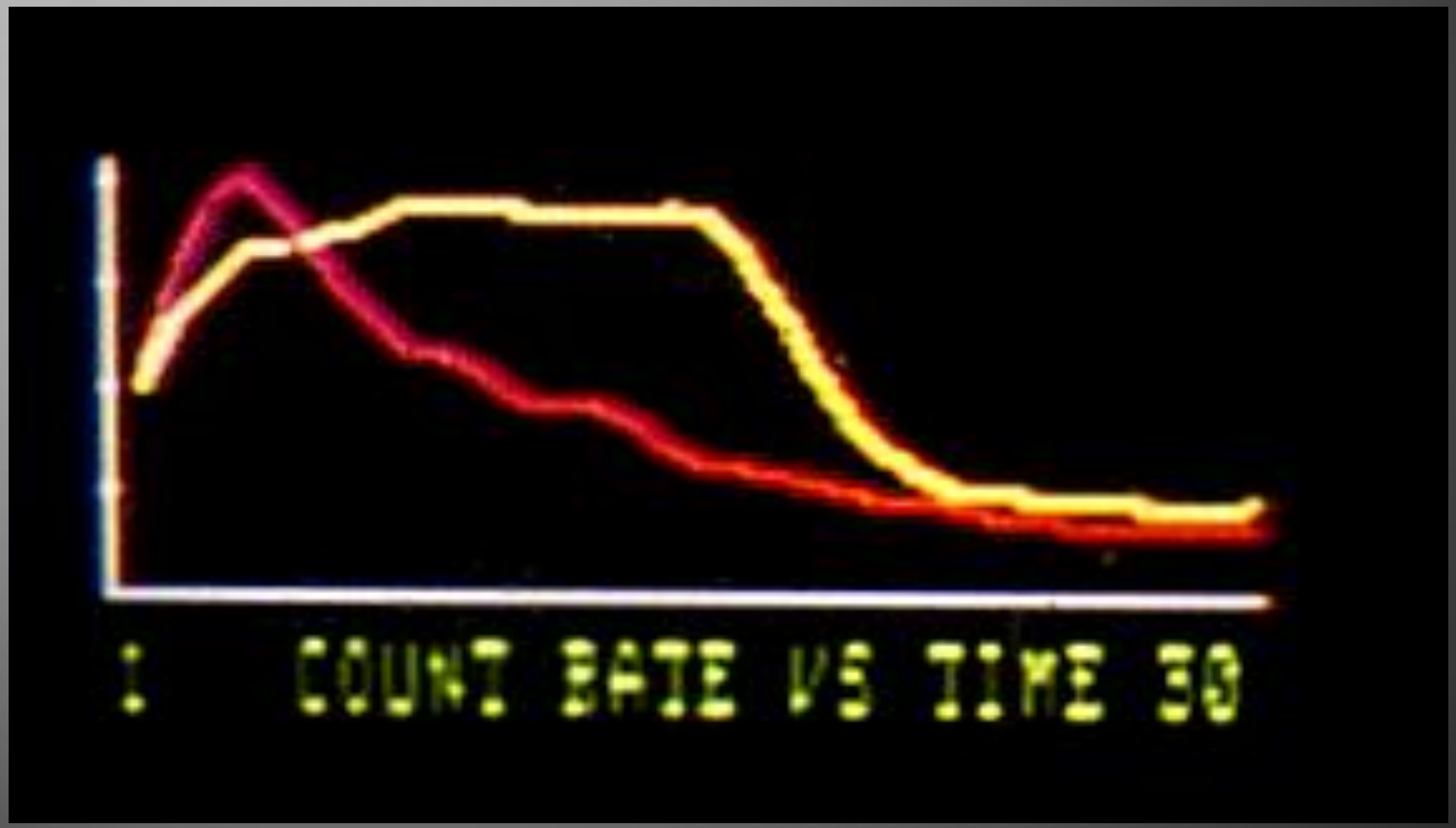
Function

- **Indications: functional testing** of inflammatory, obstructive, vascular disease, kidney transplantation.

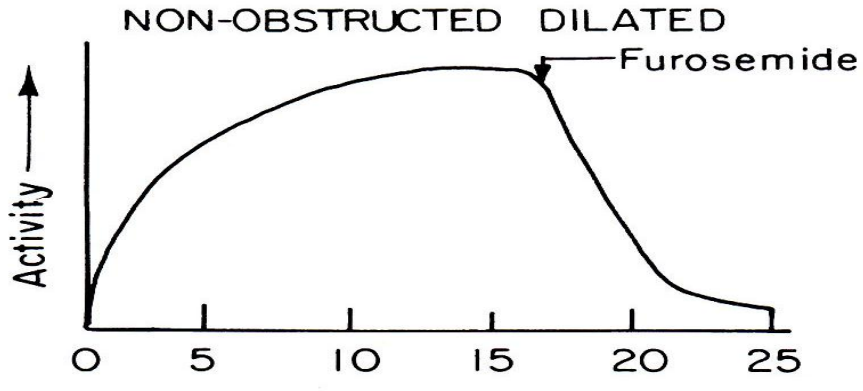
- **Variants:**
  - Diuretic DSB

  - DSB at renovascular hypertension (without and with captopril).

Diuretic dynamic renal scintigraphy



Diuretic dynamic renal scintigraphy



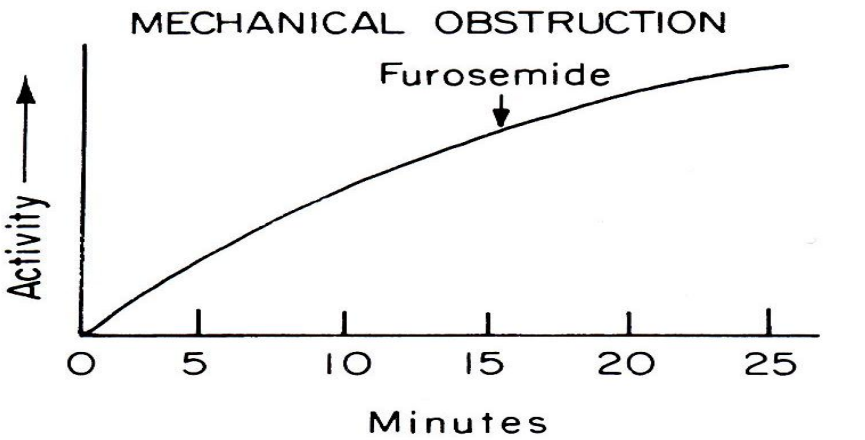


FIGURE 10–8. Characteristic time-activity curves in a diuretic renogram.

Captopril scintigraphy

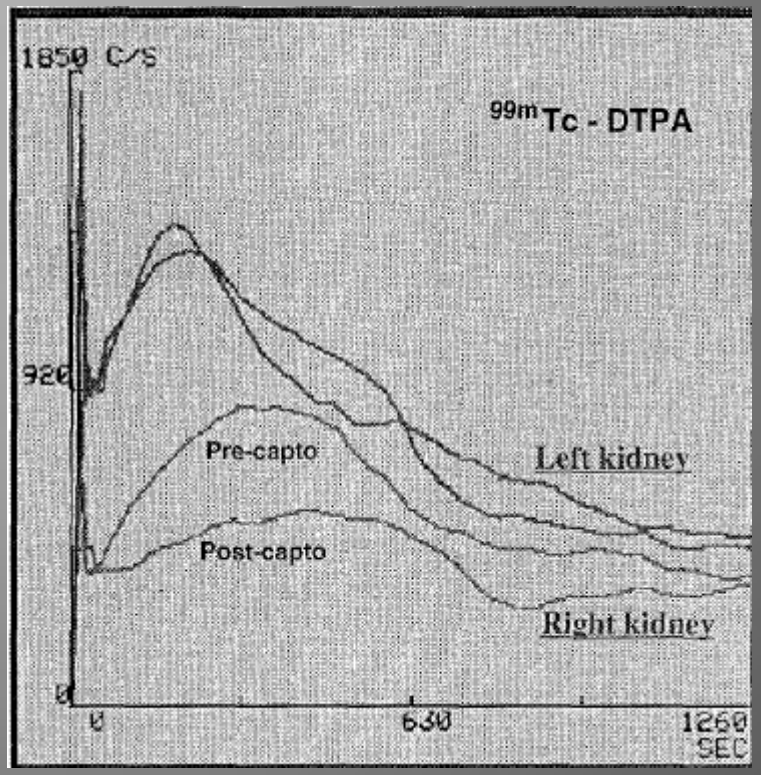
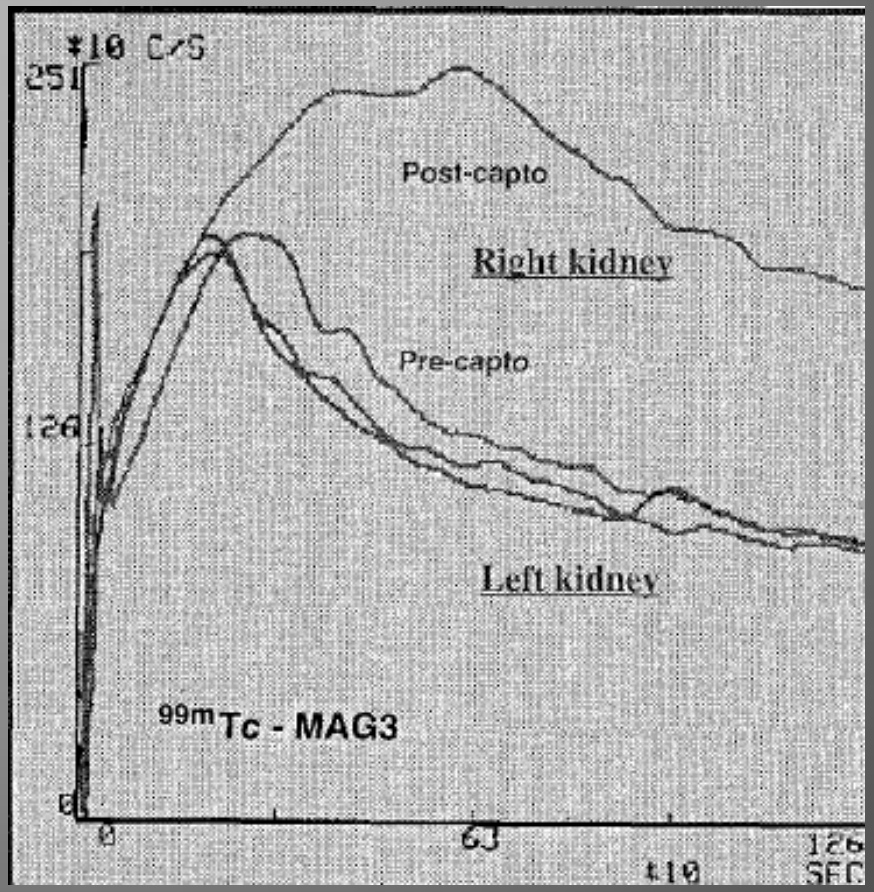


Fig. 3. a ^{99m}Tc-DTPA CRS in a 20-year-old male with recent onset of hypertension (172/118) and normal renal function. The pre-captopril renogram shows asymmetry of function [upslope (F): right, 34% and left, 66%] and excretion [peak time (T_{max}): right, 5 min 50 s and left, 3 min 10 s; residual cortical activity (RCA): right, 45% and left, 32%]. The post-captopril renogram, 4 h later, exhibits worsened function (F: right, 26% and left, 74%) and increased cortical retention (T_{max}: right, 8 min and left, 3 min 25 s; RCA: right, 70% and left, 35%) on the right side. After successful PTRA of a right fibrodysplastic RAS, hypertension was cured and CRS no longer showed captopril-induced changes. The renograms

Captopril scintigraphy



parallel; however, the post-captopril downslope of the right kidney is modified, with delayed T_{max} (3 min 15s vs 10 min, pre- and post-captopril respectively) and increased RCA (52% and 73%, pre- and post-captopril, respectively). Angiography demonstrated bilateral atheromatous RAS (right = 70%, left = 50%) and successful PTRA of the right RAS partially improved the hypertension

Clearances

- Renal clearance of certain substance is the **amount of plasma** which was purified (cleared) by passing through the kidneys in one minute.

$$\text{Clearance} = \frac{U \times V}{Pa}$$

- U= the concentration of the substance in the urine (mg/ml).
- V = vol. of urine excreted from the kidneys in the min. (ml/min.).
- Pa = conc. of the substance in the renal artery ie. plasma (mg/ml).

GFR-glomerular filtration rate

- If the substance filtered at the glomerulus as effective as water, and when passing through the tubular system of the kidney none of these substance is either secreted from the tubular cells into the lumen of the tubules, nor reabsorbed in the tubular cells, then the clearance of this substance is a measure of **glomerular filtration -GFR.**

  ● Tc-99m-DTPA is secreted by glomerular filtration and measuring its clearance the GFR is determined.

  ● Normal values:
  - Men 124 ± 26 ml / min.
  - Women: 110 ± 13 ml / min.

ERPF-Effective Renal Plasma Flow

- If the substance is completely removed from the blood or plasma by passing through the kidneys (glomerular filtration and tubular excretion), then the clearance of this substance is equal to the flow of blood or plasma through the kidneys, respectively, equal to the **effective renal plasma flow (ERPF).**

- Because I-131-hippuran is practically completely cleared from the plasma passing through the kidney, its clearance represents ERPF.

- Normal values: 623 ± 112 ml /min.

Classical methods for the measurement of GFR and ERPF are measurements of the clearances of inulin and para-aminohippuric acid

- These classic methods include:
  - Continuous intravenous infusion
  - Multiple blood samples
  - Catheterization of the bladder due to urine samples.

Radionuclide techniques for clearences determinations

1. Methods based on measurements of activity in samples of plasma and urine
   - The method of continuous infusion
   - Single injection method with urine and plasma samples
   - Single injection method by taking only plasma samples
   - Method of the one sample
   - Methods of external measurements: vascular, bladder, renal

2. Methods based on measurements with gamma cameras

Method of constant infusion

$$\text{Clearance} = \frac{U \times V}{P \times t}$$

U and P (**imp**./ml/min.)= conc. (**activity**) of substance in blood and urine.

V (ml)= vol. of urine in the time period "t".

Improvement: until equilibrium, it is not necessary to take blood samples. Someone can monitor, with external measurements, the increasing concentration of the radiofarmaceutical, and only after reaching the equilibrium we can take samples of blood and urine.

Single injection method with urine and plasma samples

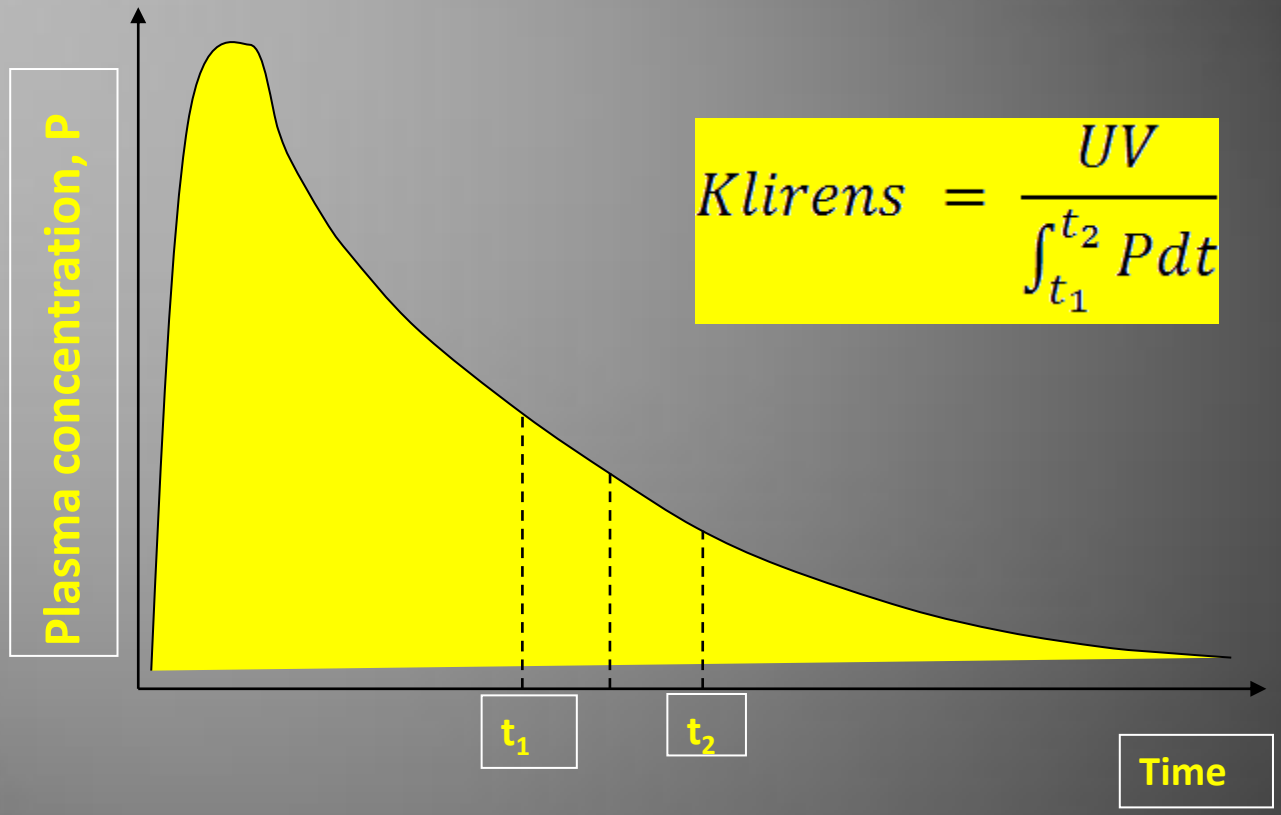
- $$Cl = \frac{U \times \Delta V}{P \times \Delta t}$$ integrating the numerator and denominator we get:

$$Klirens = \frac{UV}{\int_{t_1}^{t_2} Pdt}$$

After a single injection, there is a sudden rise in tracer conc. in the plasma and exponential decline. Equation for calculating the clearance is applied for a very short period of time Δt during which the concentration (activity) in the plasma is constant. If the vol. of urine resulting in this time equals ΔV and has a conc. of the tracer, U, then the clearance is equal to the first formula.

The clearance is calculated by dividing the amount of tracer excreted in given time interval divided by the area under curve which represents tracer conc. in plasma for that interval.

Improvement: there is no continuous infusion of the radiopharmaceuticals- only single injection.



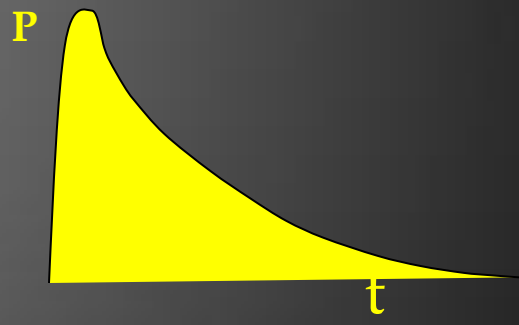
Single injection method with urine and plasma samples

Single injection method by taking only blood ie. plasma samples- Vλ method (GFR)

- If the tracer is secreted only by kidneys, then in some "infinite" time all the tracer will be excreted ie. the total amount of excreted tracer will be equal to the total amount of a given tracer.

$$U \times V = Q_0$$

$$K = \frac{U \times V}{\int_{t2}^{t1} P \, dt} \longrightarrow K = \frac{Q_0}{\int_0^{\infty} P \, dt}$$



- Clearance is therefore calculated so that the injected dose is divided by the area under curve of tracer conc. (for which we need only plasma samples).

Improvement: in this way we avoid the collection of urine samples.

The tracer disappearance curve from plasma has two component : fast component corresponds to the transition of the tracer into the extravascular and extracellular space, and the slow component corresponds to secretion of the tracer from the kidney (required eight plasma samples).

- Approximation of the tracer disappearance curve as monoexponential one, leads to:

$$\int_0^{\infty} P x dt = C_0 \times 0{,}693 / t_{1/2} = C_0 \times \lambda^{-1}$$

$$K = \frac{Q_0}{C_0} \times \lambda$$

- Injected dose (Q_0) divided by the concentration in the "zero" time (C_0) is equal to the volume of tracer distribution (V) in the "zero" time.

$$\frac{Q_0}{C_0} = V \longrightarrow K = V\lambda$$

- **λ represents the rate of disappearance of tracer from the plasma.**
- **The method calculates clearance as the product of vol. of tracer distribution in the "zero" time and constant λ (Vλ method).**

One sample method

- Taking a single plasma sample after a time of dosing, and by dividing the injected dose by the concentration (activity) of that sample, distribution volume of injected tracer is obtained.

  By correlating these results with the clearance of these substances determined by classical methods, a formula for calculating clearance is obtained.
- For ERPF it is proposed an exponential relationship with taking a plasma sample in 44 th minute.

- ERPF (hippuran)=1126 $(1-e^{-0,008(V44-7,9)})$ ml/min

- **V_{44}= distribution vol. of tracer in 44-th minute.**

- GFR (DTPA) for adults is calculated by the following formula (Tauxe):

$$GFR_{120}\ (ml / min) = 361{,}8\ (1 - e^{-0{,}0124(V120-10{,}12)}),$$

if the sample is taken at 120 min after injection.

- V_{120} (l) is the virtual volume of distribution of radiopharmaceutical, and is obtained from the ratio of the activities of the injected dose and the activity of 1 ml of plasma of the blood sample taken in 120. min after injection.

Formula for calculating GFR in children has different form (Hamm and Piepsz):

- $Cl\ (GFR)\ (ml\ /\ min) = (2.602 \times V_{120}) - 0.273$

V_{120} (l) is a virtual vol. of tracer distribution in 120 min.
and is obtained from the ratio of the activities of the injected dose and the activity of 1 ml of plasma of the blood sample taken in 120 th min after injection.

- Within the dynamic renal scintigraphy with deconvolution, the Department of Nuclear Medicine, Split started 30 years ago with the determination of ERPF and GFR.
- By 1998 GFR was estimated from "two plasma sample" (Vλ method).
- From 1998 "one plasma sample" method or method "volume of distribution“ is used. A sample is taken at 120 th minutes after the injection. This method is less reliable for the GFR values <30 ml / min / 1.73 m2 , but is reliable enough for clinical use with the advantage of taking only a single sample.
- In average, every year at our Department complete 800 tests in patients referred by nephrologists (pediatricians and internists) and urologists are done.

Patient Preparation:

The patient is well hydrated: 1 dcl of water or tea /10 kg body weight, one hour before the recording.

Babies need to drink an extra bottle one hour before the recording and older children 250-500ml of liquid (water, juice ...).

Radiation Burden

For ^{99m}Tc-DTPA, Effective Dose is approximately 0.1mSv/examination [21].

External measurement methods

- Detector measures the disappearance of activity from plasma (above the heart, bladder ..) after a single injection, then the "peeling" of the curve is made and λ1 and λ2 respectively C1 and C2 are determined, ie. intersections of lines on the y-axis. For the calibration of curve it is required at least one blood sample.

Excretion index-EI

- EI is **ratio** of actually excreted amount of radiopharmaceuticals (%) and the amount of radiopharmaceutical (%), which should be excreted for the given ERPF.

$$EI = \frac{\text{voided dose (\%) + a residual dose (\%)}}{\text{predicted dose excretion for given of ERPF (\%)}}$$

- If the excreted amount of radiopharmaceutical (excreted plus possibly residual urine) is equal to the expected for the given ERPF, EI = 1.
- If the excreted amount is less than expected, then the transit of the hippuran is slowed ie. the same somewhere remains, that can be differentiated from the sequential scintigrams.

- Predicted excretion (in 35 th min) = 79 (1-e (0.0048 x ERPF).

$$\textbf{Residual urine} = \frac{\text{voided urine x counts of bladder after urination}}{\text{counts "full-empty" bladder}}$$

$$\textbf{The residual dose } (\%) = \frac{\text{\% of voided dose x RU}}{\text{volume of voided urine}}$$

$$\text{EI} = \frac{\text{voided dose (\%) + a residual dose (\%)}}{\text{predicted dose excretion for given ERPF (\%)}}$$

- **EI is an index of transit time radioindicators through the kidney.**
- EI <0.9 means a significant retention of activity in the parenchyma or pelvis.

This comprehensive functional renal study (dynamic renal scintigraphy, renogram curves, deconvolution, total and separate renal clearance, radioindicators transit times through the parenchyma, pelvis, total kidney, RU and EI) for patients is very simple:

- The measured dose is injected to the patient and the dynamic study is recorded for 25 min
- Immediately before and after urinating in the 35th min the recording of the bladder is made
- In the 44th min the blood sample is taken

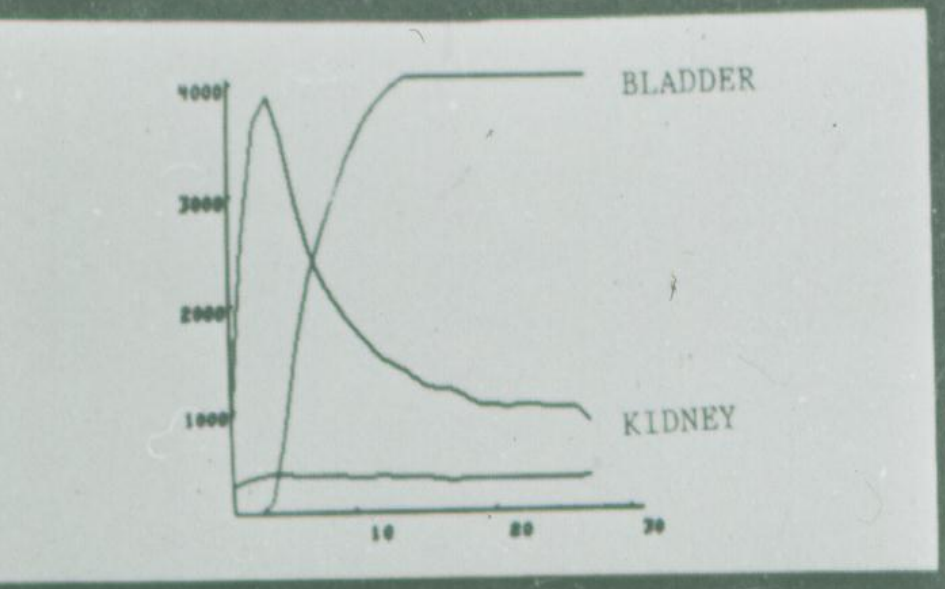
Table 1. Problems After Transplantation Pertinent to Nuclear Medicine

Complication	Most Frequent Time of Occurrence	Comments
Ischemic damage (ATN)	Present at time of transplantation	Cadaveric kidney
Immunologic		
Hyperacute	Within minutes and/or a few hours	Preformed antibodies, irreversible process
Acute	Rapid development after five days, most common during first 3 months	Predominantly cell-mediated, reversible with therapy
Accelerated	Occurring earlier, from day 1 to day 5	LRD after donor-specific transfusions
Chronic	Usually after a few months or years, slowly developing	Humoral, irreversible
Cyclosporin toxicity	While on medication	Improvement after withdrawal
Surgical		
Urine leak	Within days or a few weeks	
Hematoma	Within first few days	Drainage
Wound infection	Within first few days	Surgical and medical treatment
Intrinsic obstruction	Days, months, years	Clots, scars, calculi
Extrinsic pressure leading to obstruction	Second to fourth month	Lymphocele-drainage
Renal artery stenosis	Usually after first month	Medical or surgical treatment

Abbreviation: ATN, acute tubular necrosis.

Normal

0-3 3-6 15-18 24-27



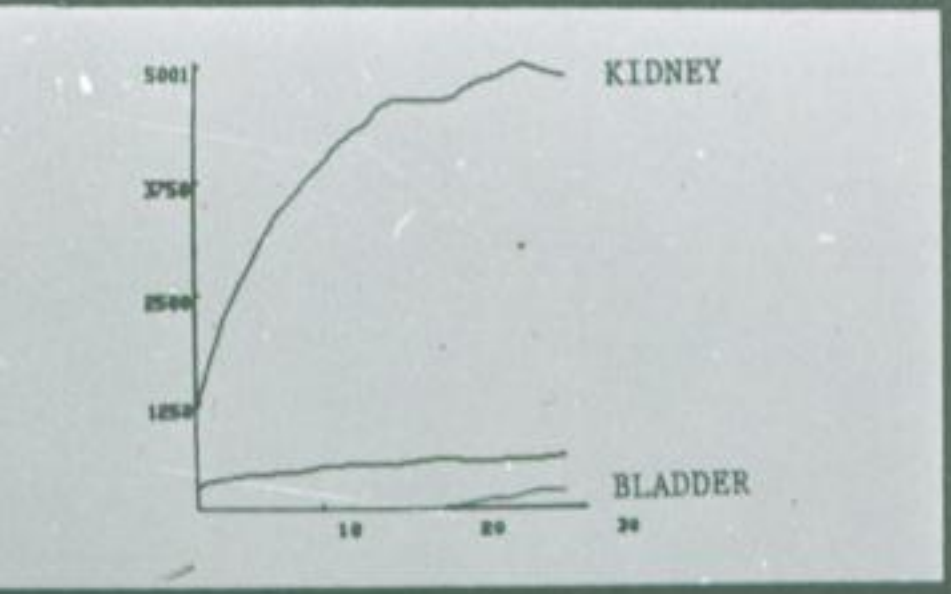
Pre-void Post-void

ERPF ml/min	423
Bladder residuum ml	6
EI	.96

Predicted excretion	68
Actual excretion	60
Total excretion	65

Acute Tubular Necrosis

0-3 3-6 15-18 24-27



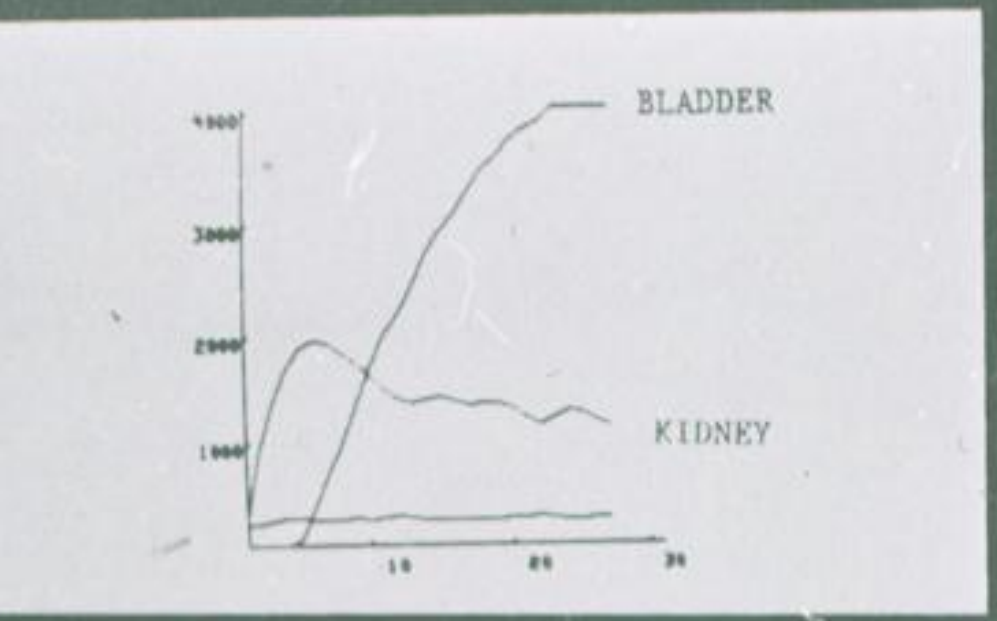
Pre-void Post-void

ERPF ml/min	226
Bladder residuum ml	2
EI	.15

Predicted excretion	53
Actual excretion	7
Total excretion	8

Acute Rejection

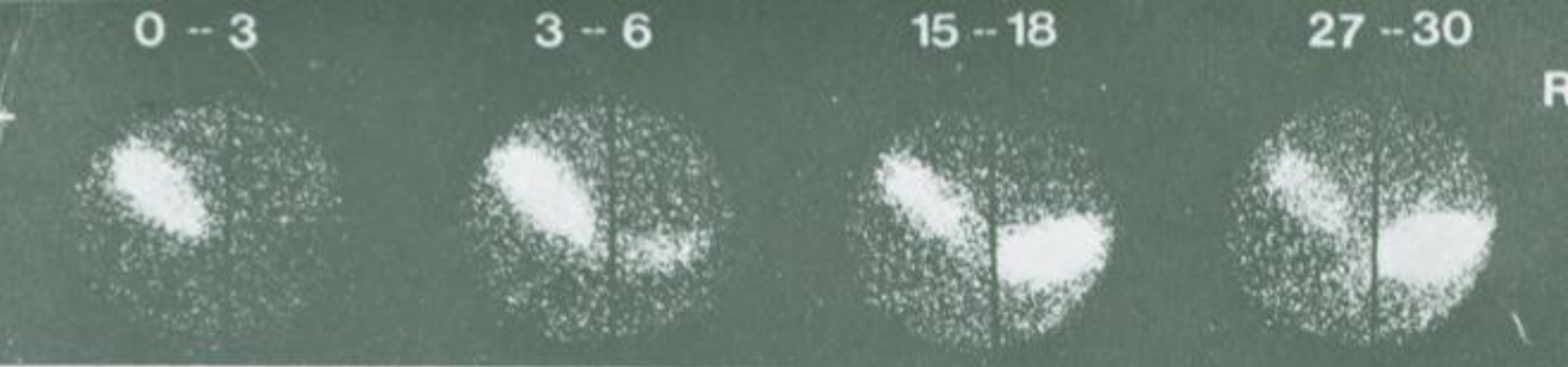
0-3 3-6 15-18 24-27



Pre-void Post-void

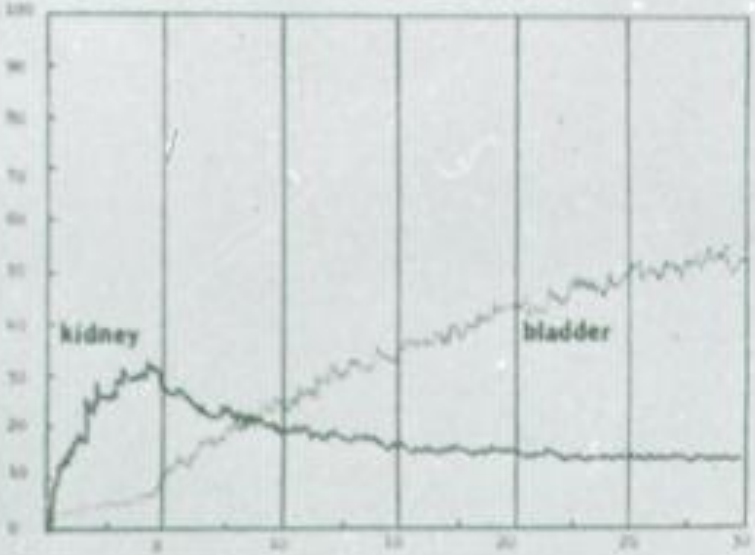
ERPF ml/min	207
Bladder residuum ml	4
EI	.75

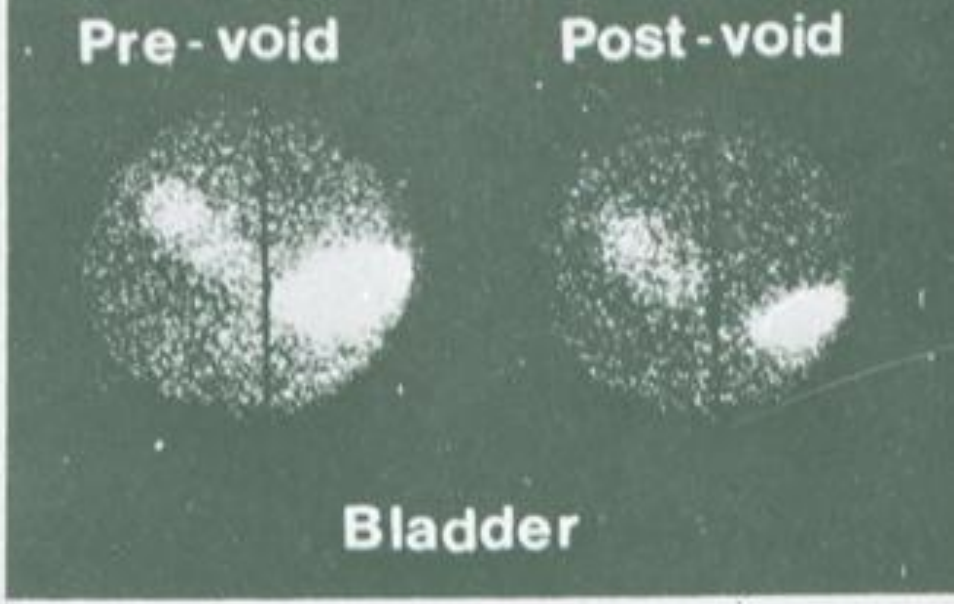
Predicted excretion	51
Actual excretion	39
Total excretion	38



STABLE

CHRONIC REJECTION

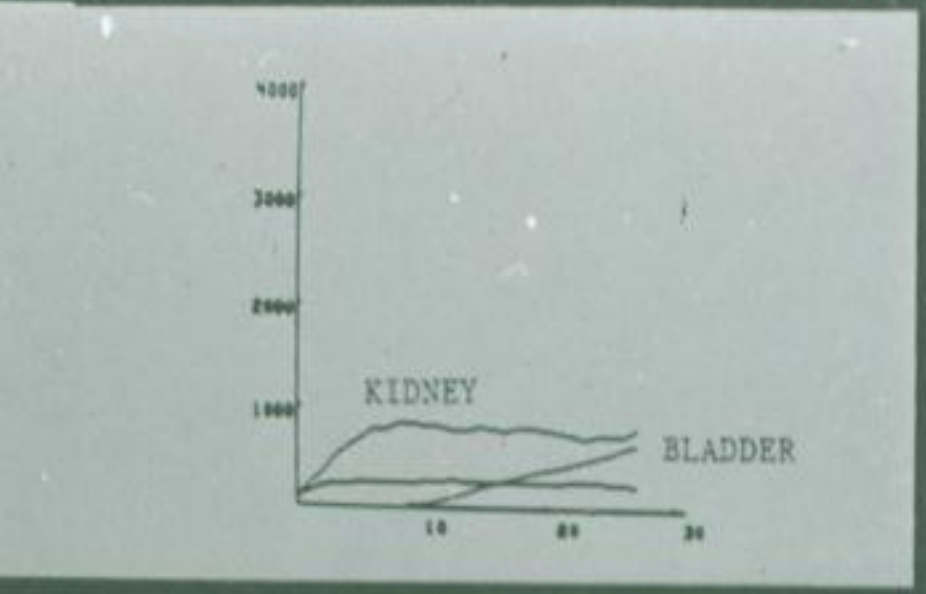




ERPF ml/min	165	Predicted excretion	45%
Bladder residuum ml	25	Actual excretion	47%
EI	1.2	Total excretion	54%

Terminal Chronic Rejection

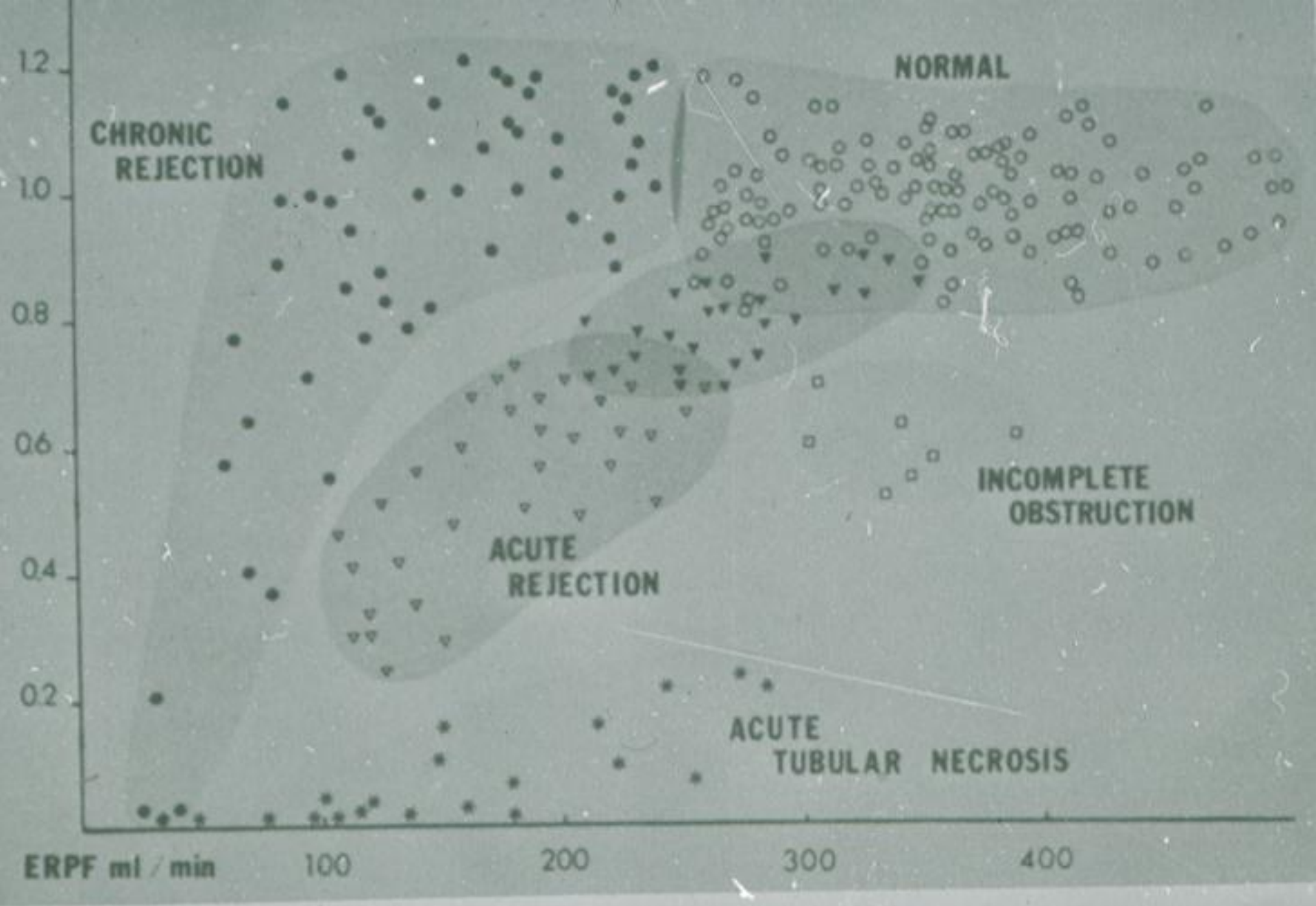
0-3 3-6 15-18 24-27



Pre-void Post-void

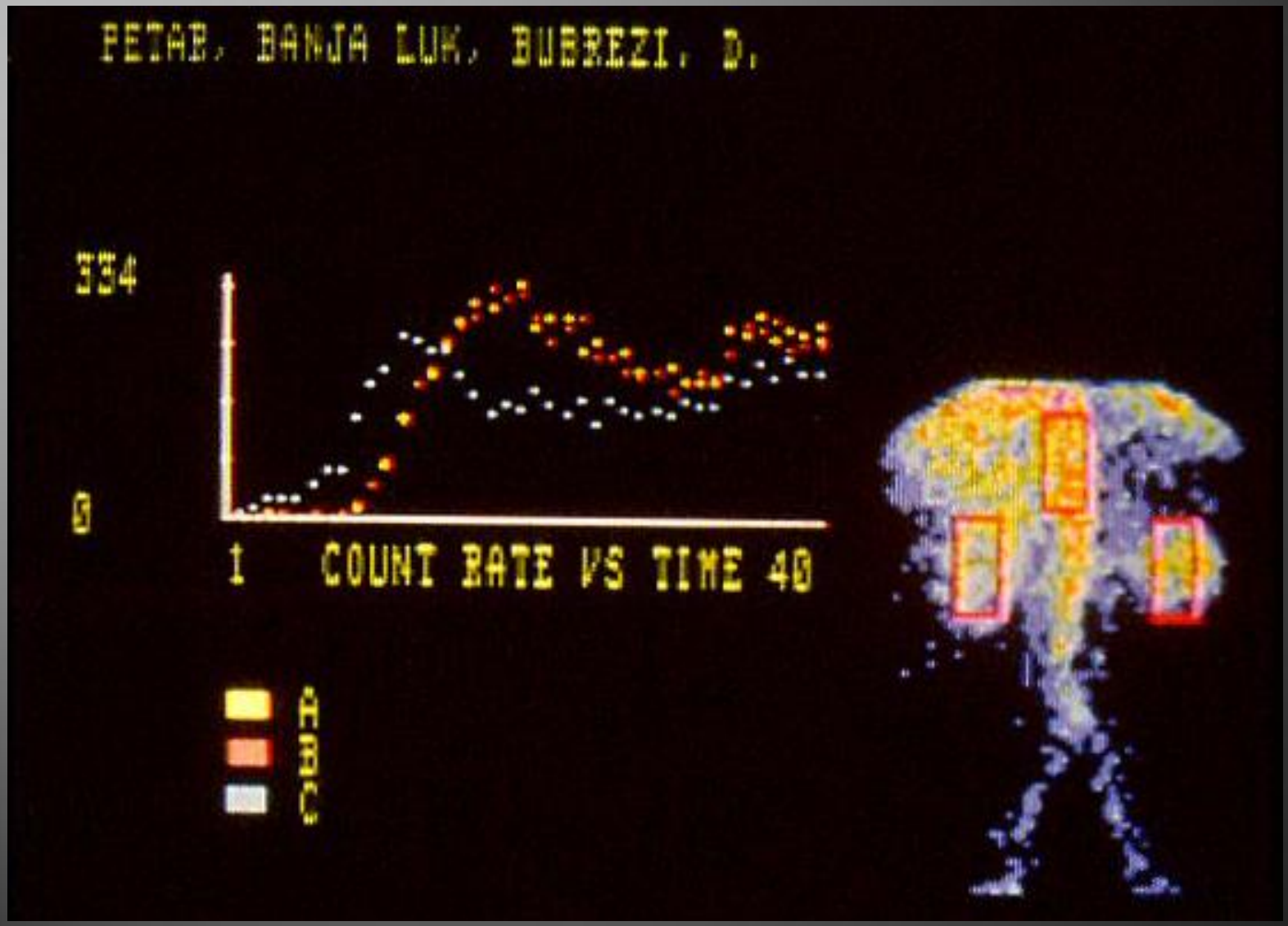
ERPF ml/min	81
Bladder residuum ml	12
EI	.28

Predicted excretion	32
Actual excretion	8
Total excretion	9

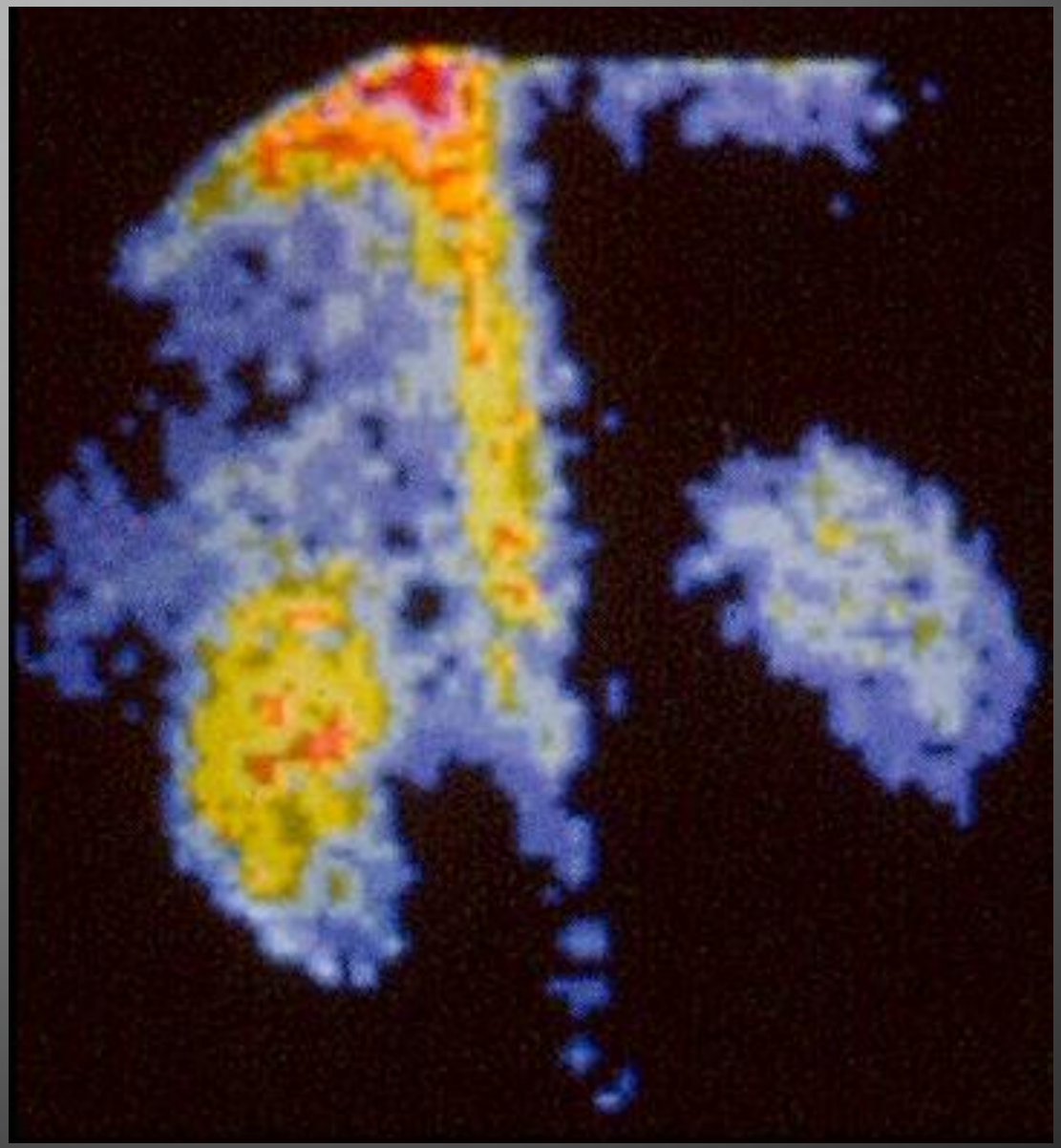


–16. Plot of EI versus ERPF data from transplanted kidney patients with various cl

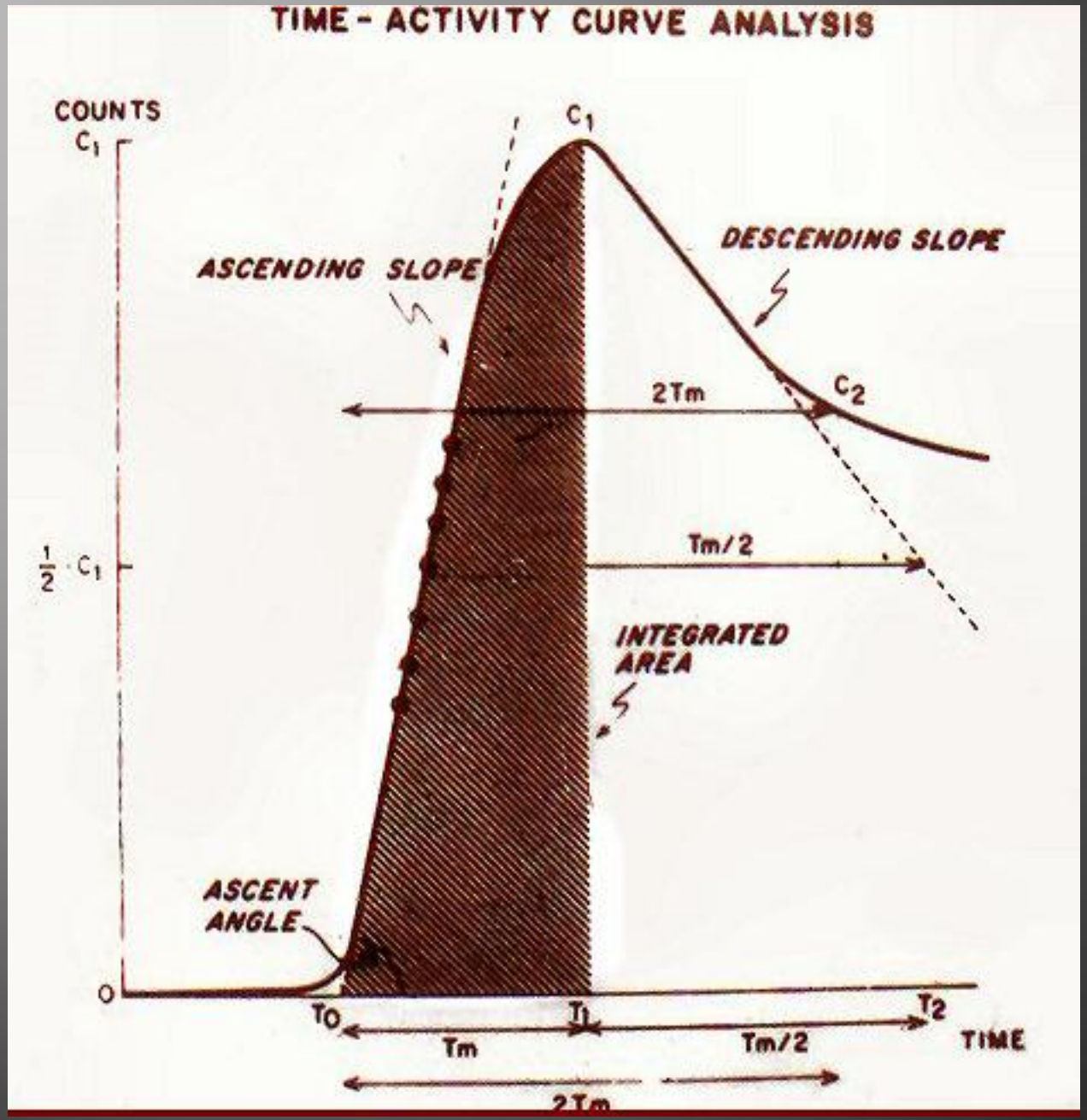
Renal perfusion -angioscintigraphic study



Renal perfusion scintigraphy



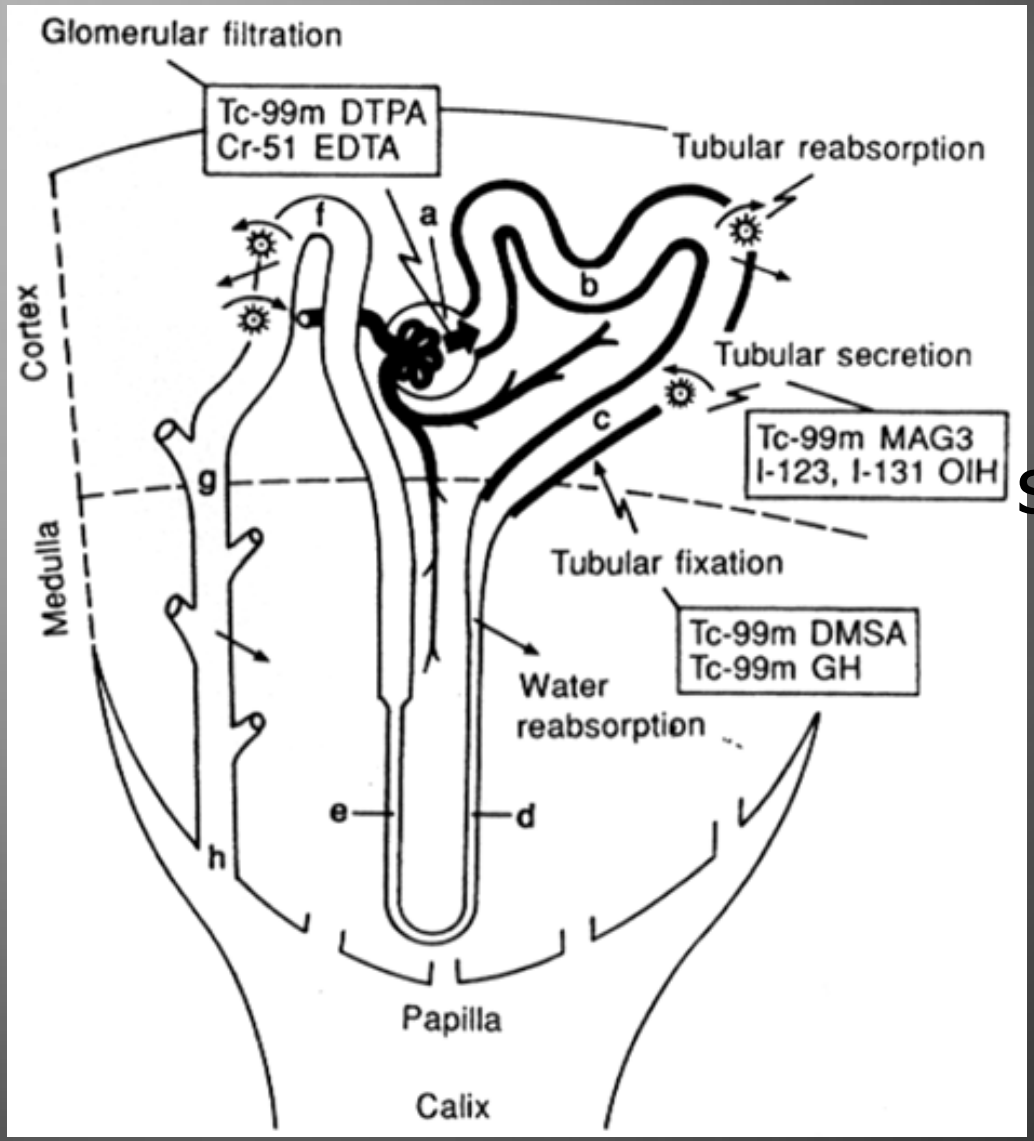

560
0
1 COUNT RATE VS TIME 40


TIME - ACTIVITY CURVE ANALYSIS
COUNTS
C1
C1
ASCENDING SLOPE
DESCENDING SLOPE
2Tm
C2
1/2 · C1
Tm/2
INTEGRATED AREA
ASCENT ANGLE
0
T0
T1
T2
Tm
Tm/2
TIME
2Tm

RADIOPHARMACEUTICALS

For dynamic scintigraphy:

HIPPURAN
DTPA
MAG3
EDTA



For static scintigraphy:

DMSA
GH

Renal static scintigraphy

- Tc-99m-DMSA is accumulated in the renal parenchyma (the cells of the proximal and distal tubular part).
- 3 hours after injection > 40% of the injected activity is bounded in the kidney, while 15% is excreted
- dose is 74 MBq (2 mCi).
- analogic and digital scintigrams are recorded in multiple projections, SPECT if possible and, if necessary, in two positions.
- application: assessment of size, shape, position, hypermobility of the kidney and localized lesions.

Indications:

- **Anomalies of number:**
  - **Unilateral agenesis** (1/1000 newborns, usually on the left side).
  - **Supernumerary kidney** extremely rare, usually small, below the normal kidney, drained independently in the ipsilateral ureter or bladder, prone to infections.

- **Anomalies of position:**

- **renal ectopia**: more common in men, often to the left.
- **crossed ectopia**: one kidney is found on the other side, usually below normal kidney.
- **connected kidney** (renal fusion), horseshoe kidneys: connecting part may contain functional parenchyma, record in the AP projection.

- **Cystic Disease:**

- **simple cyst**- often small, asymptomatic, in the cortex.
- **multilocular cysts**: rare, usually unilateral.

- **polycystic disease**: often bilateral, kidneys are enlarged,in infants poor prognosis, in adults is usually a family, cysts up to 5 cm, long held renal function.
- **spongy kidneys**: medullary cysts in adults, 2 more often in men, bilateral in 75% of cases, the cysts are small, moderately damaged renal function.

- **Inflammation:** acute and chronic pyelonephritis, reflux nephropathy, scars.

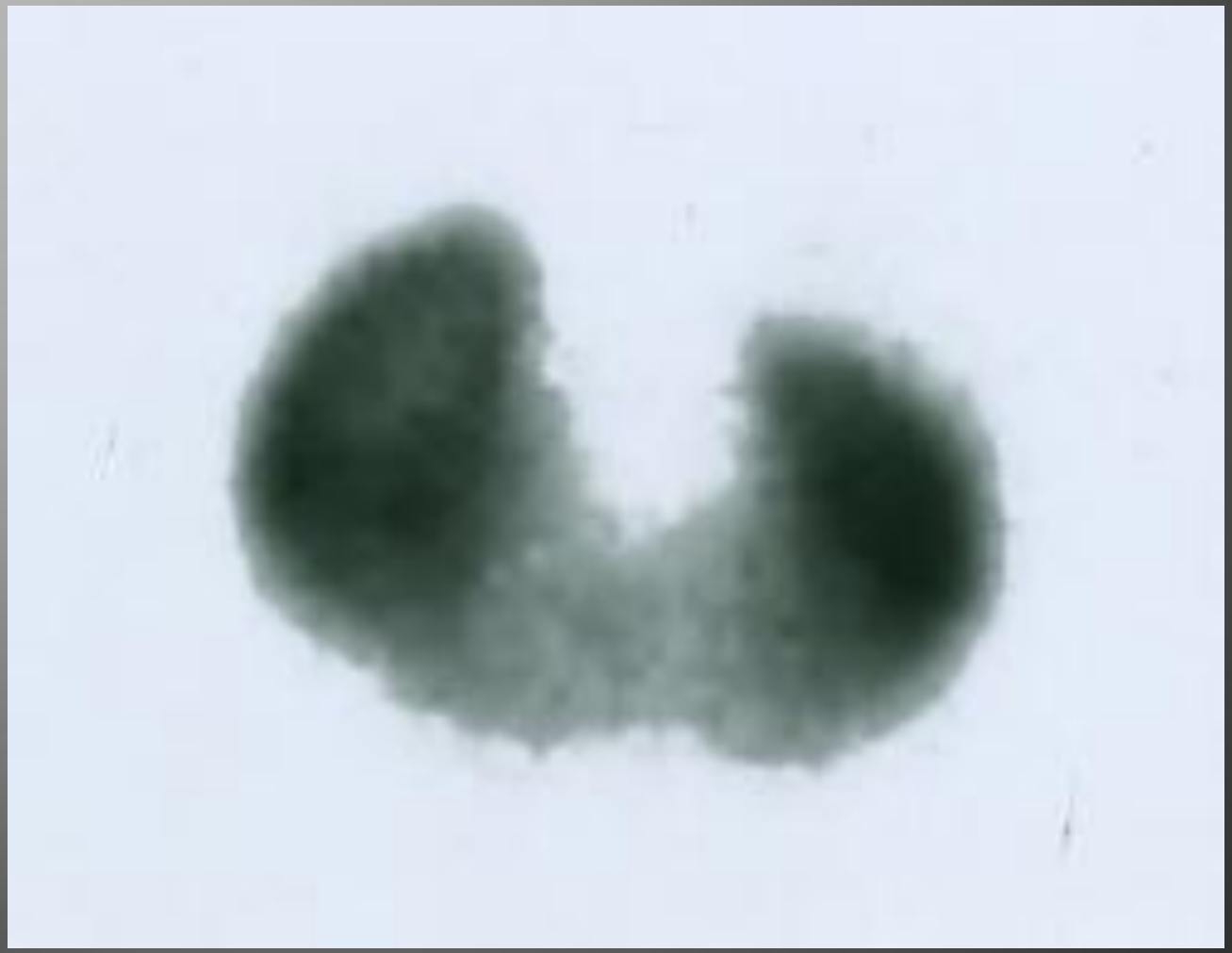
- **Tumors:** benign (cortical adenomas, ev. subcapsular leiomyomas) and malignant (Wilms tm.-20% of pediatric tumors), hypernephroma in adults.

- **Obstructive disease:** nephrolithiasis, hydronephrosis.

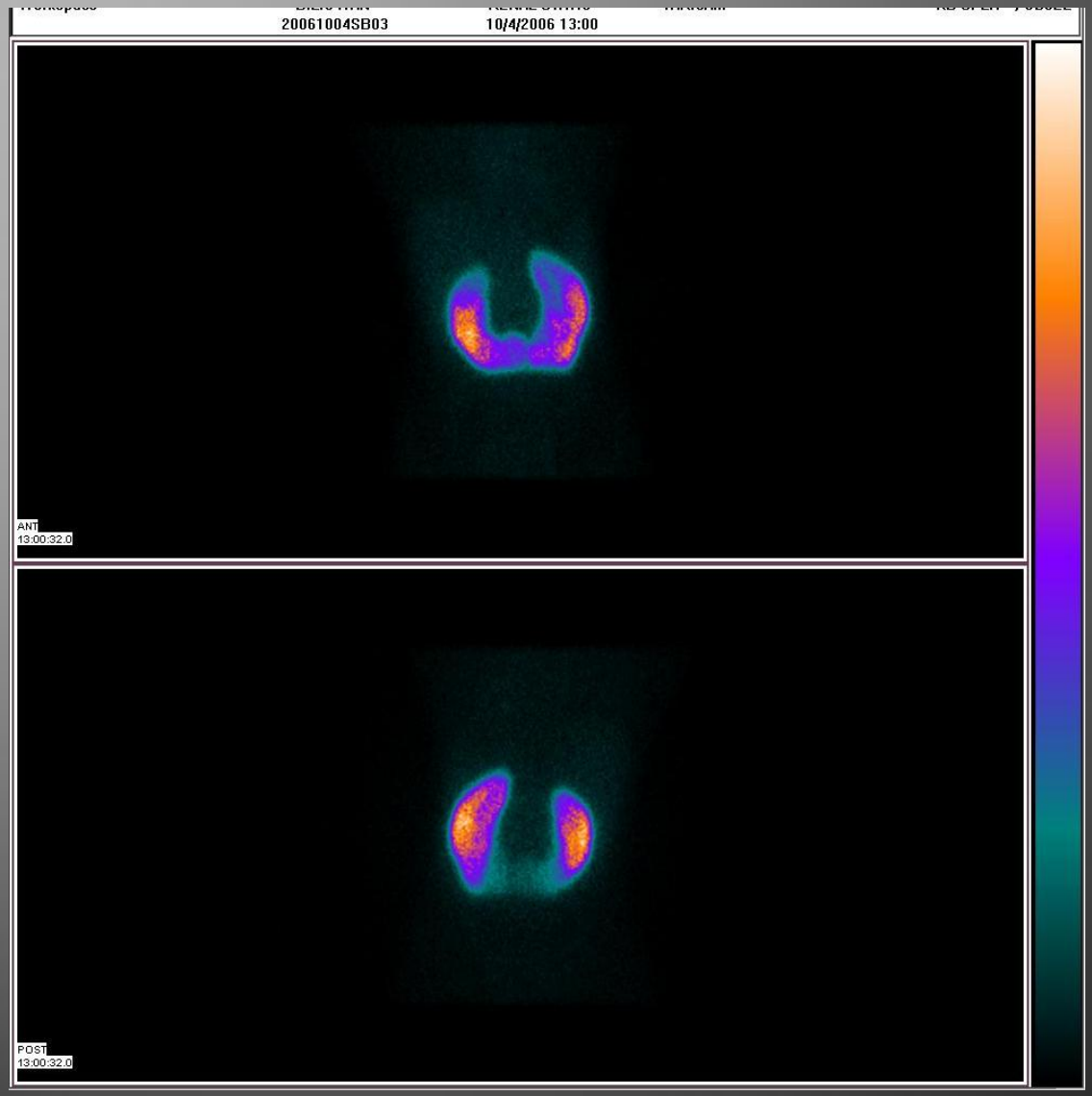
- **Vascular disease:** renal infarctions.

- **Trauma.**

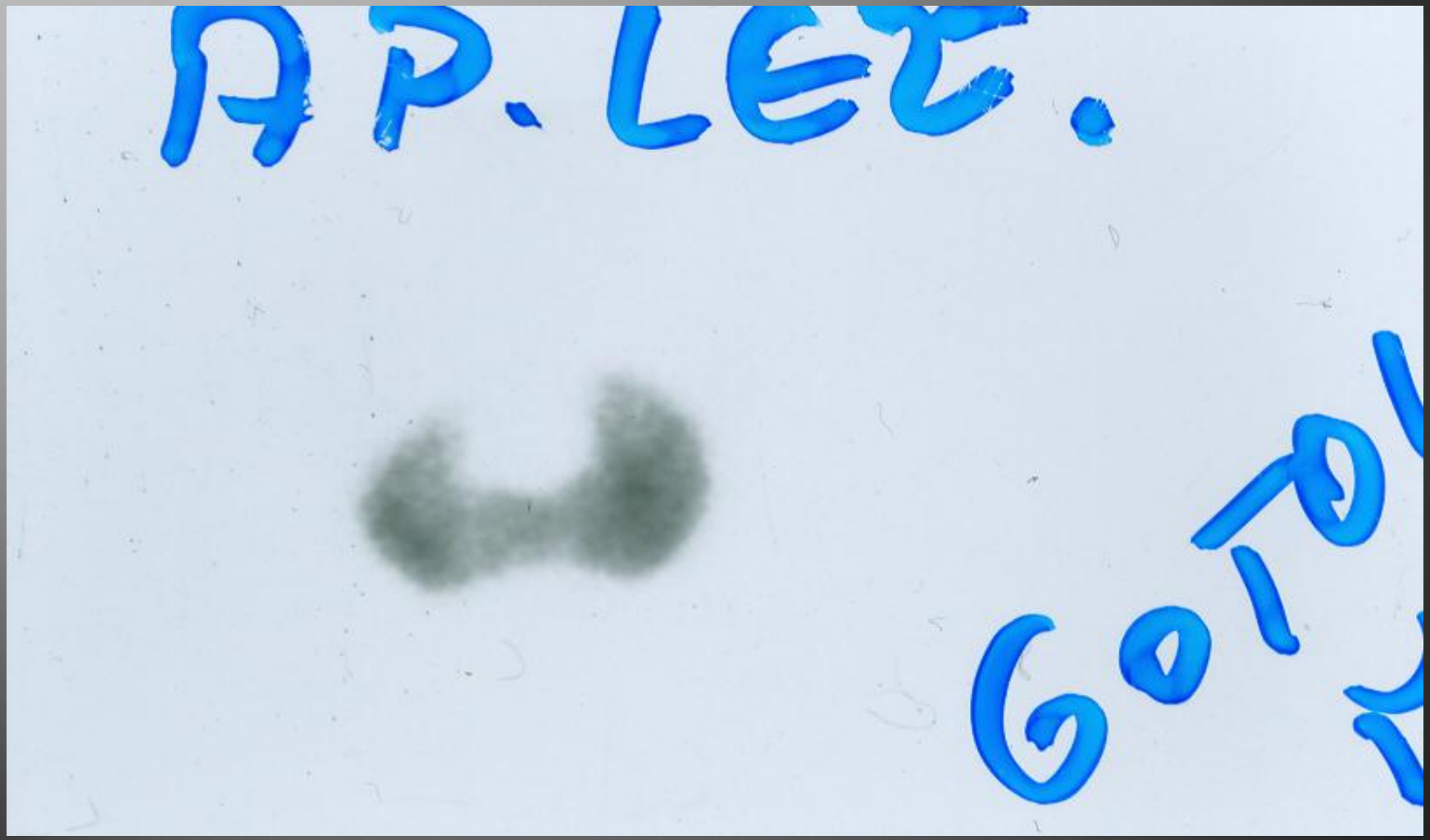
Horseshoe kidney- anterior projection



Horseshoe kidney- anterior and posterior projection

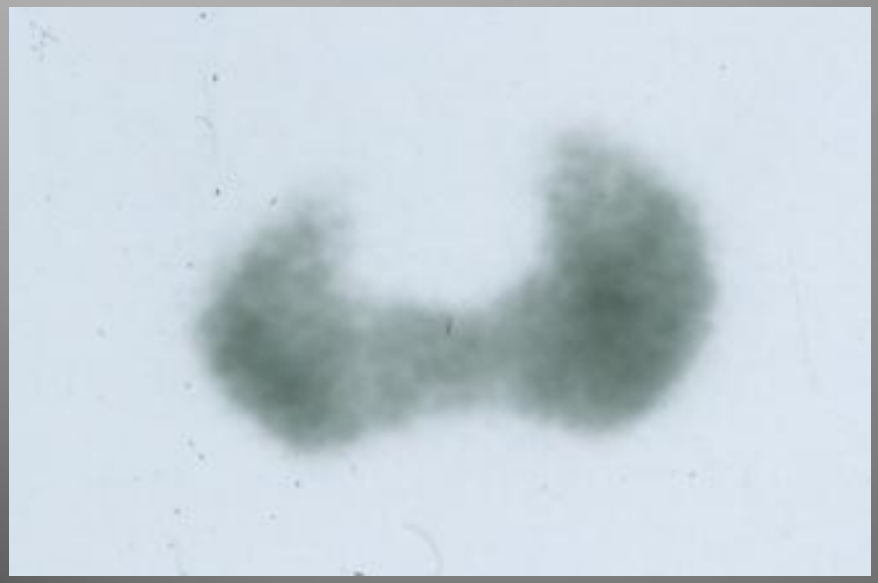


Horseshoe kidney- anterior projection

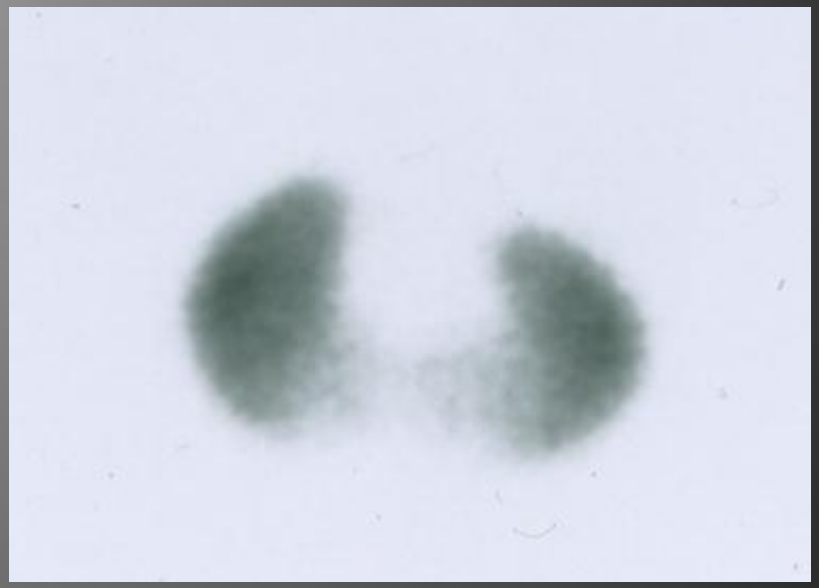


Horseshoe kidney- posterior projection

Horseshoe kidney

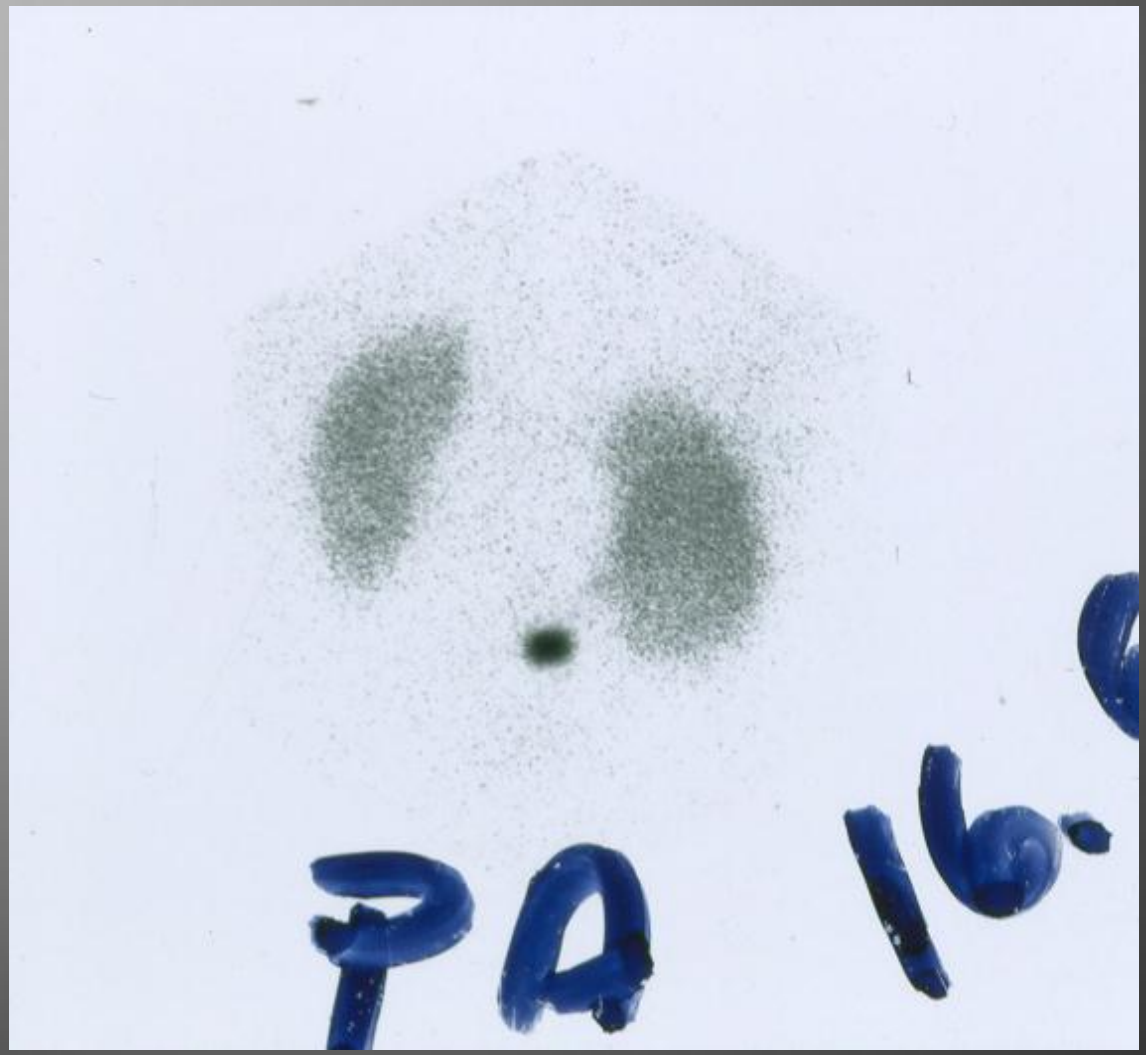


AP

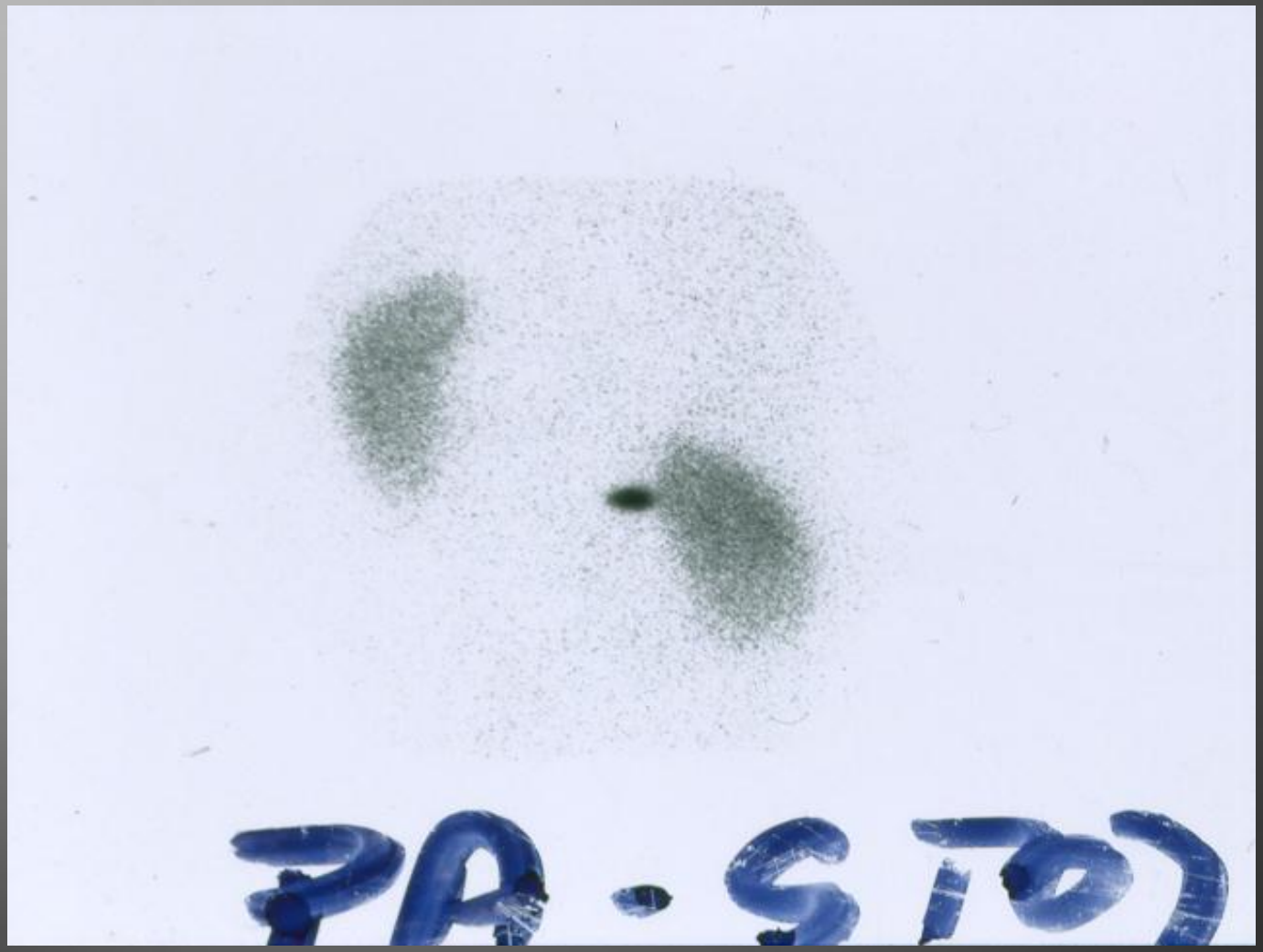


PA

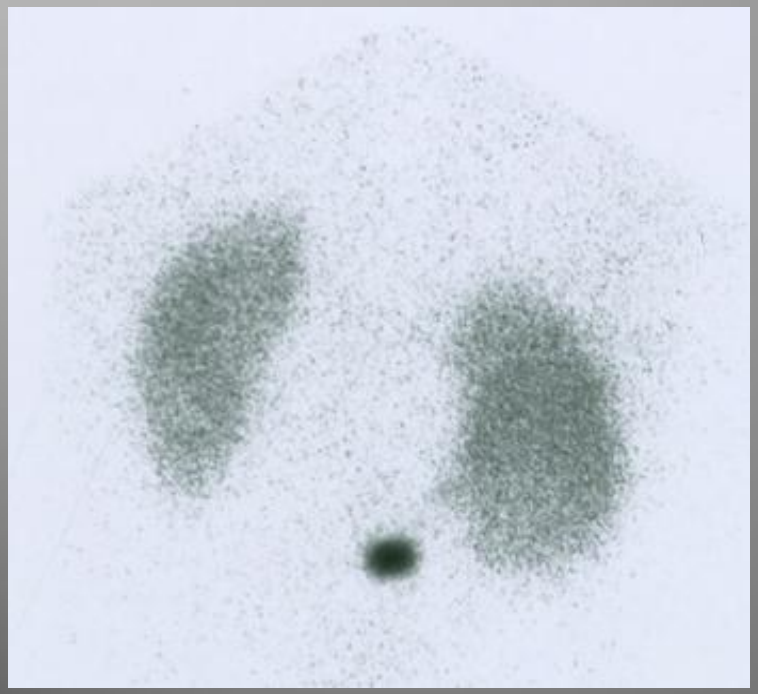
Movable, migrating kidney- lying, supine position



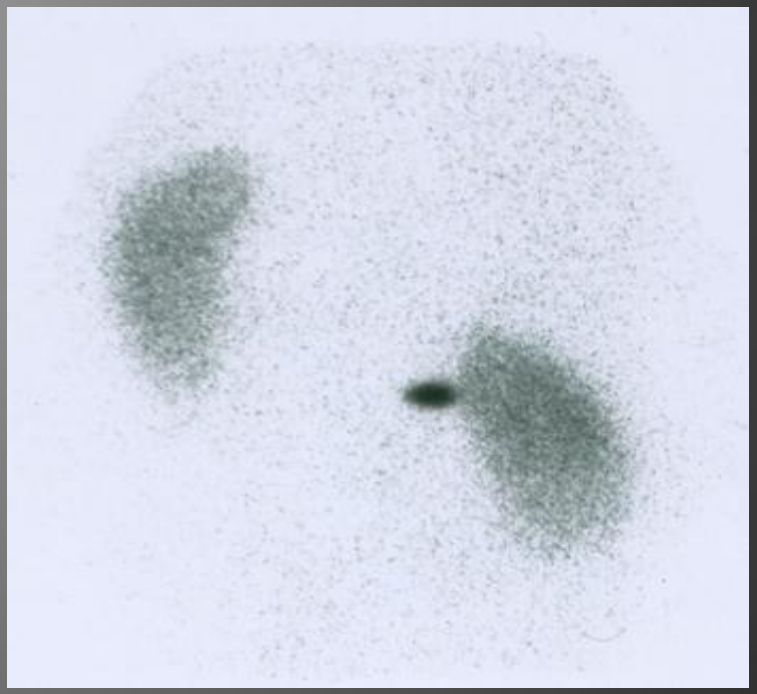
Movable, migrating kidney- standing position



Movable, migrating kidney

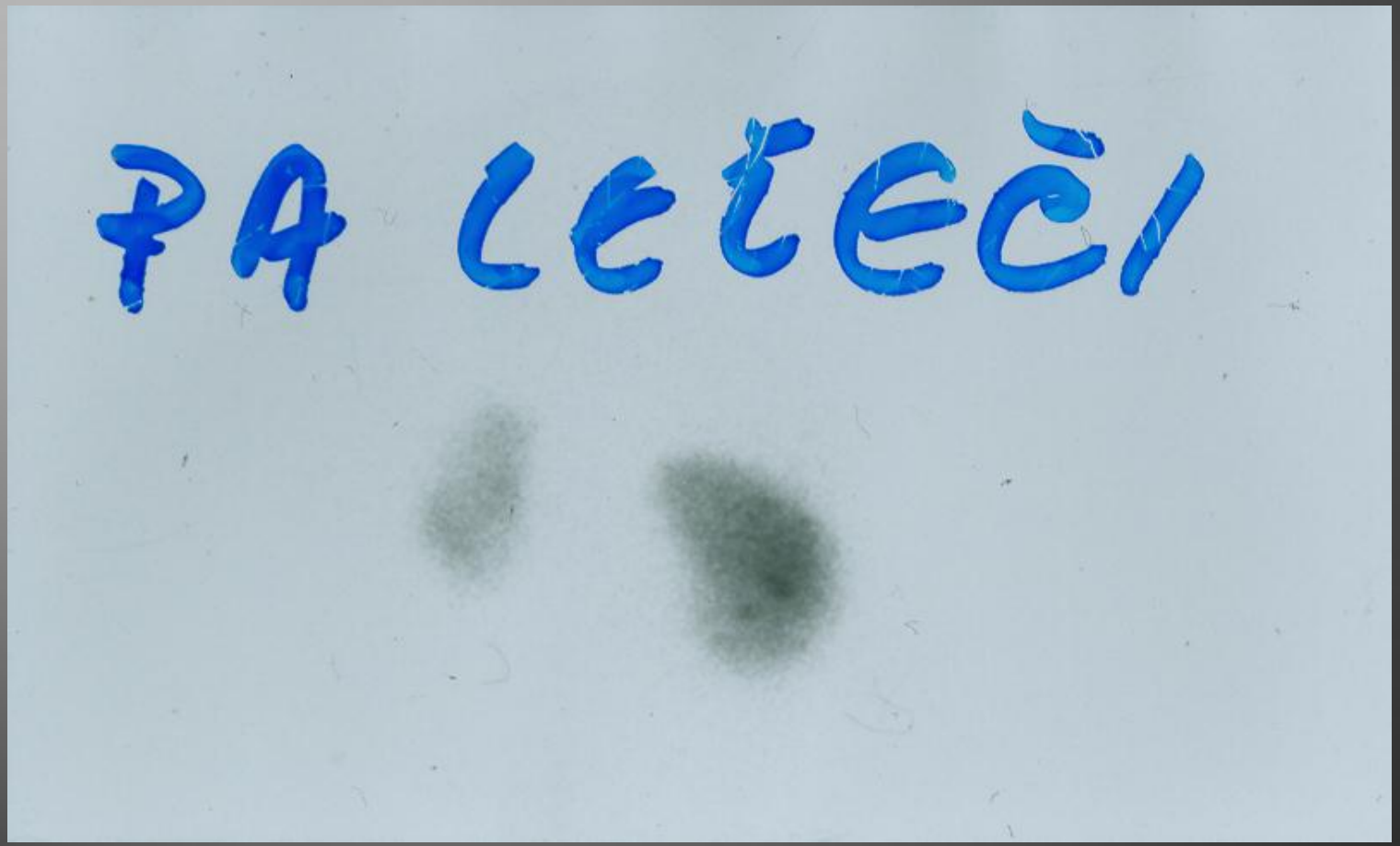


PA supine-lying position

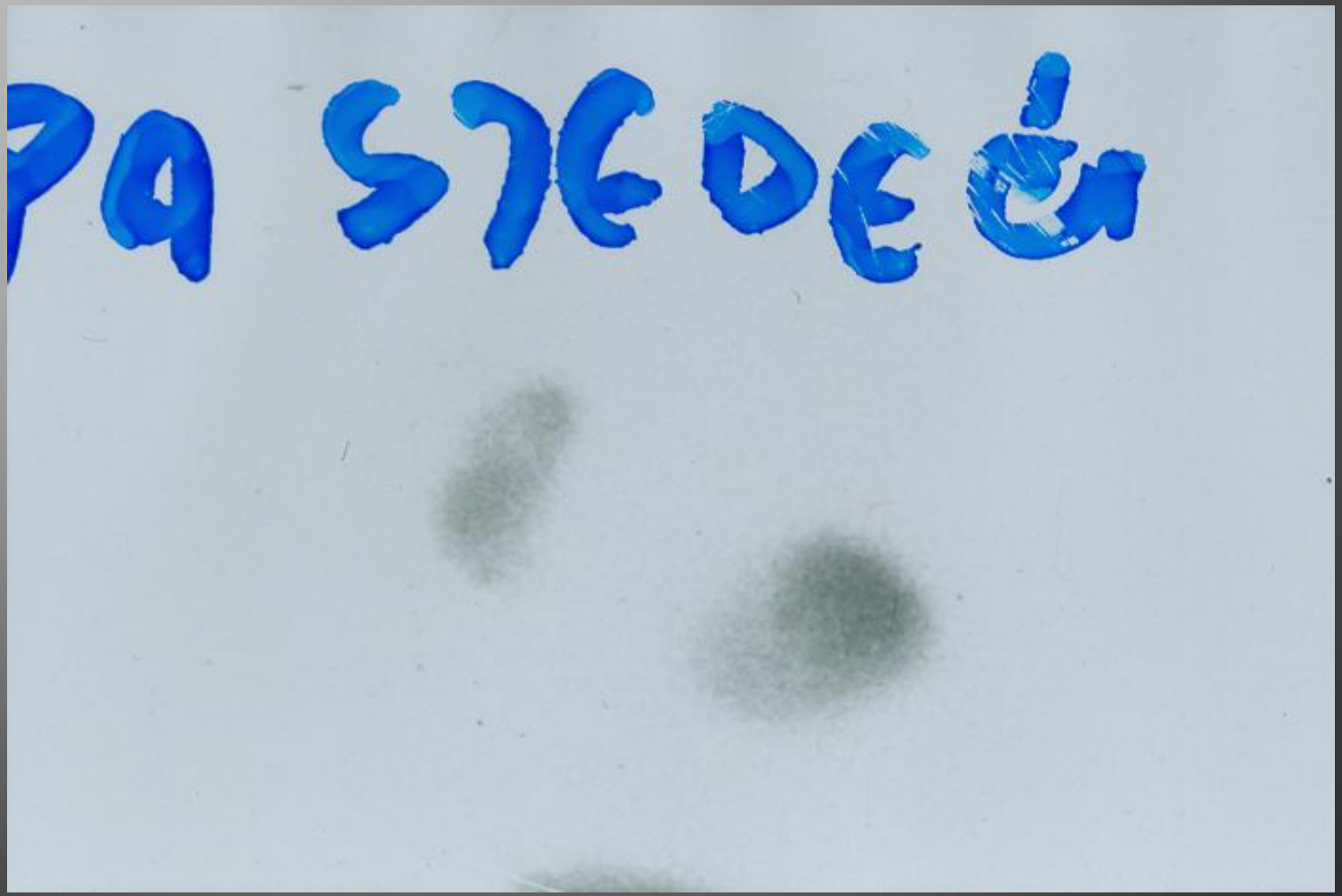


PA standing position

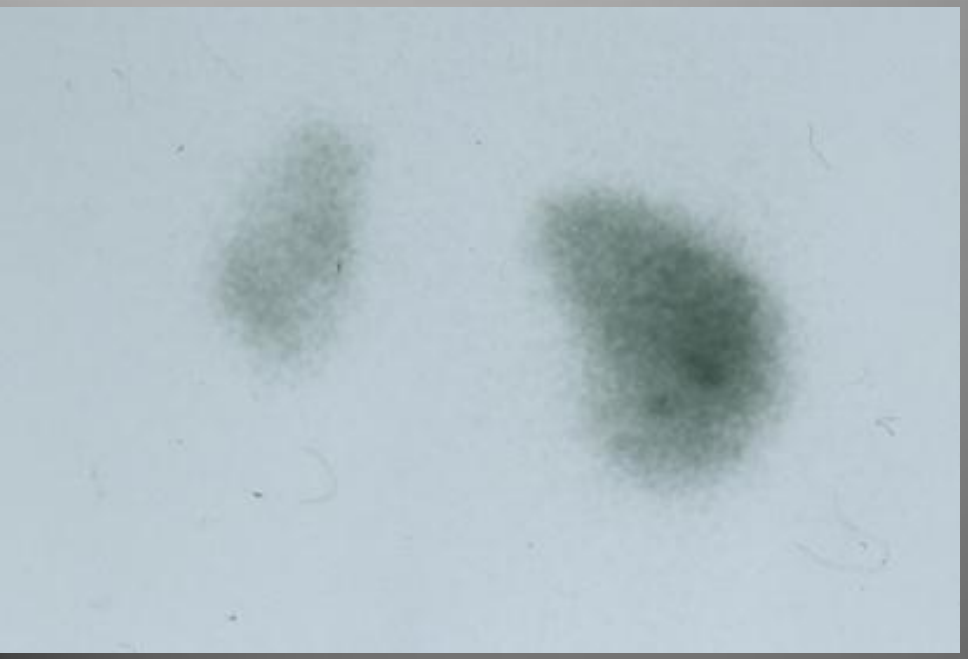
Movable, migrating kidney- lying position

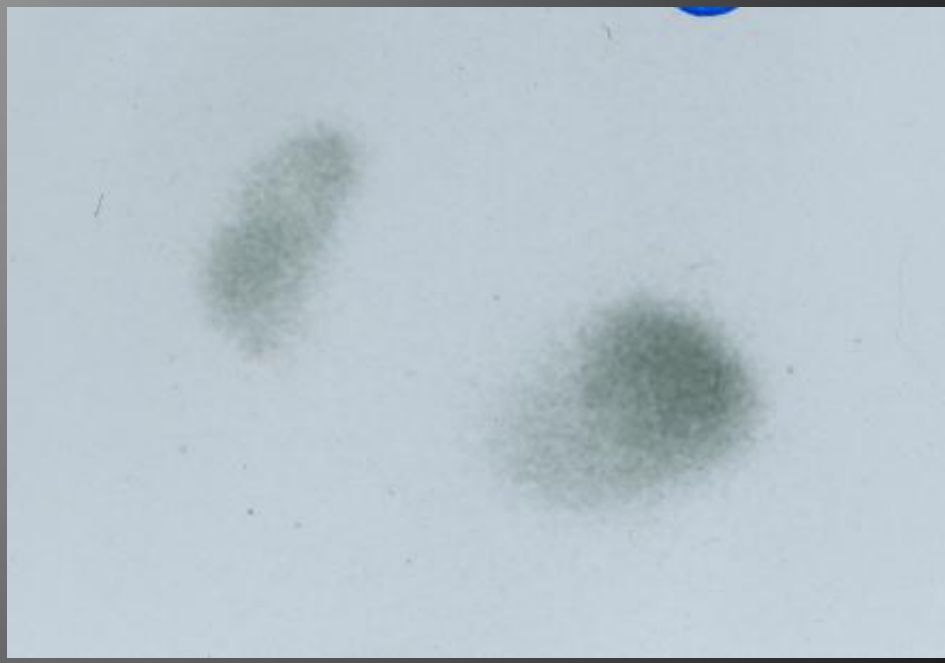


Movable, migrating kidney- sitting position



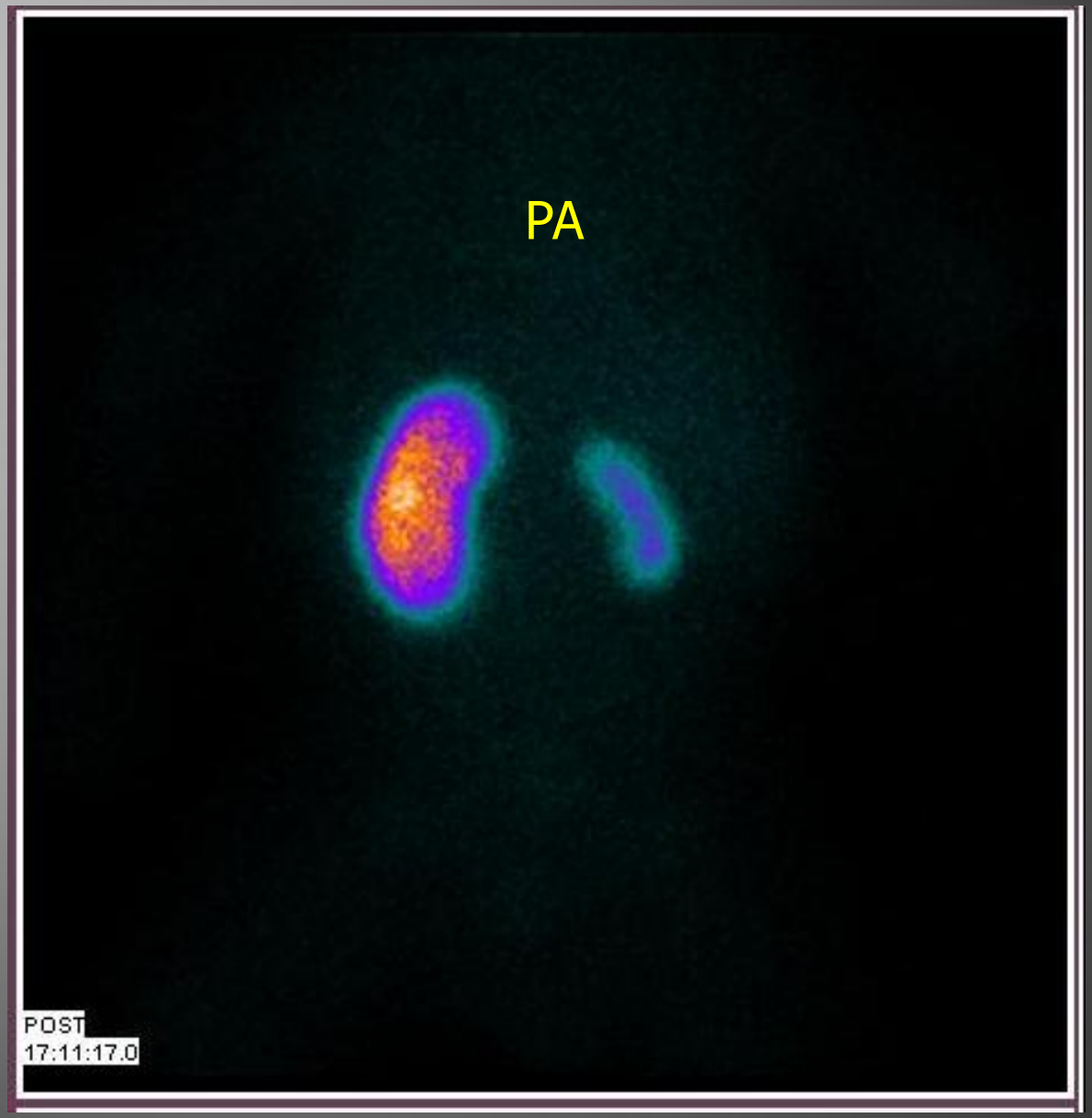
Movable, migrating kidney



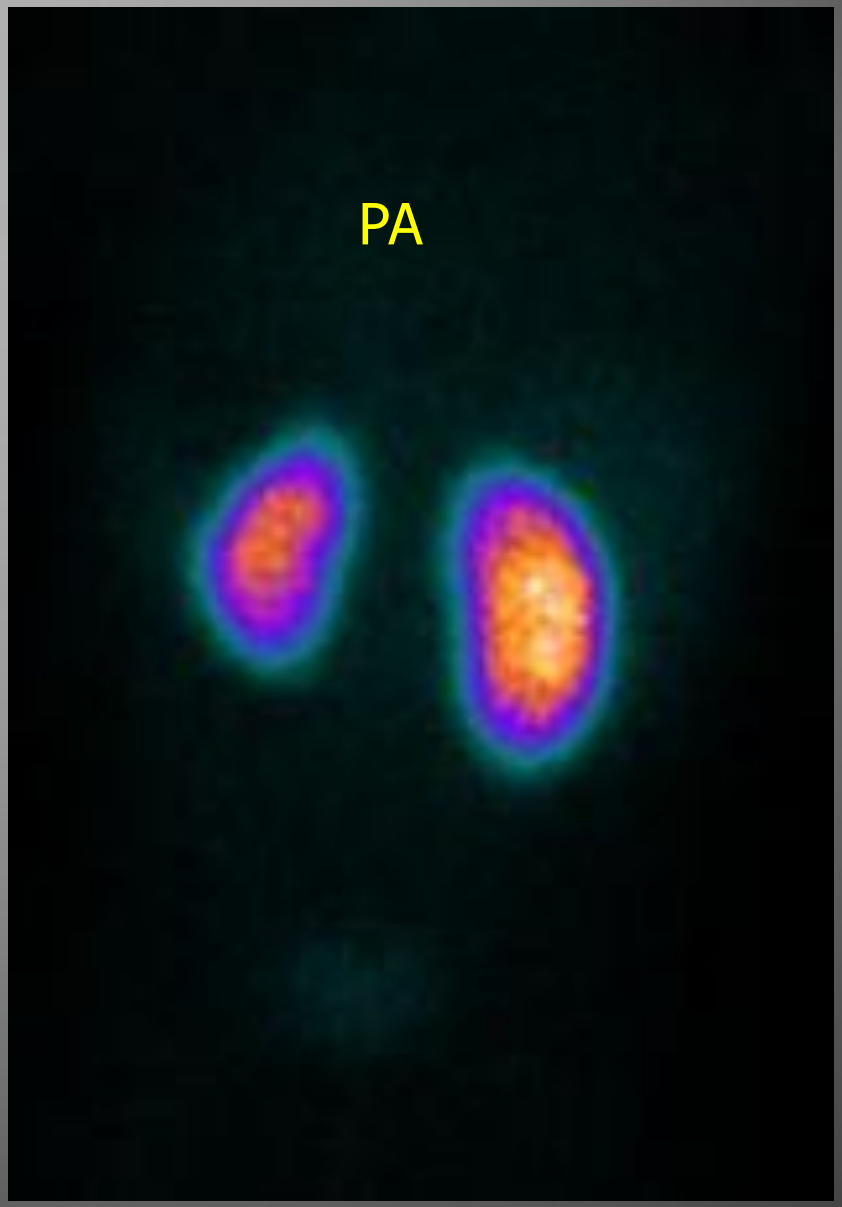


PA lying position

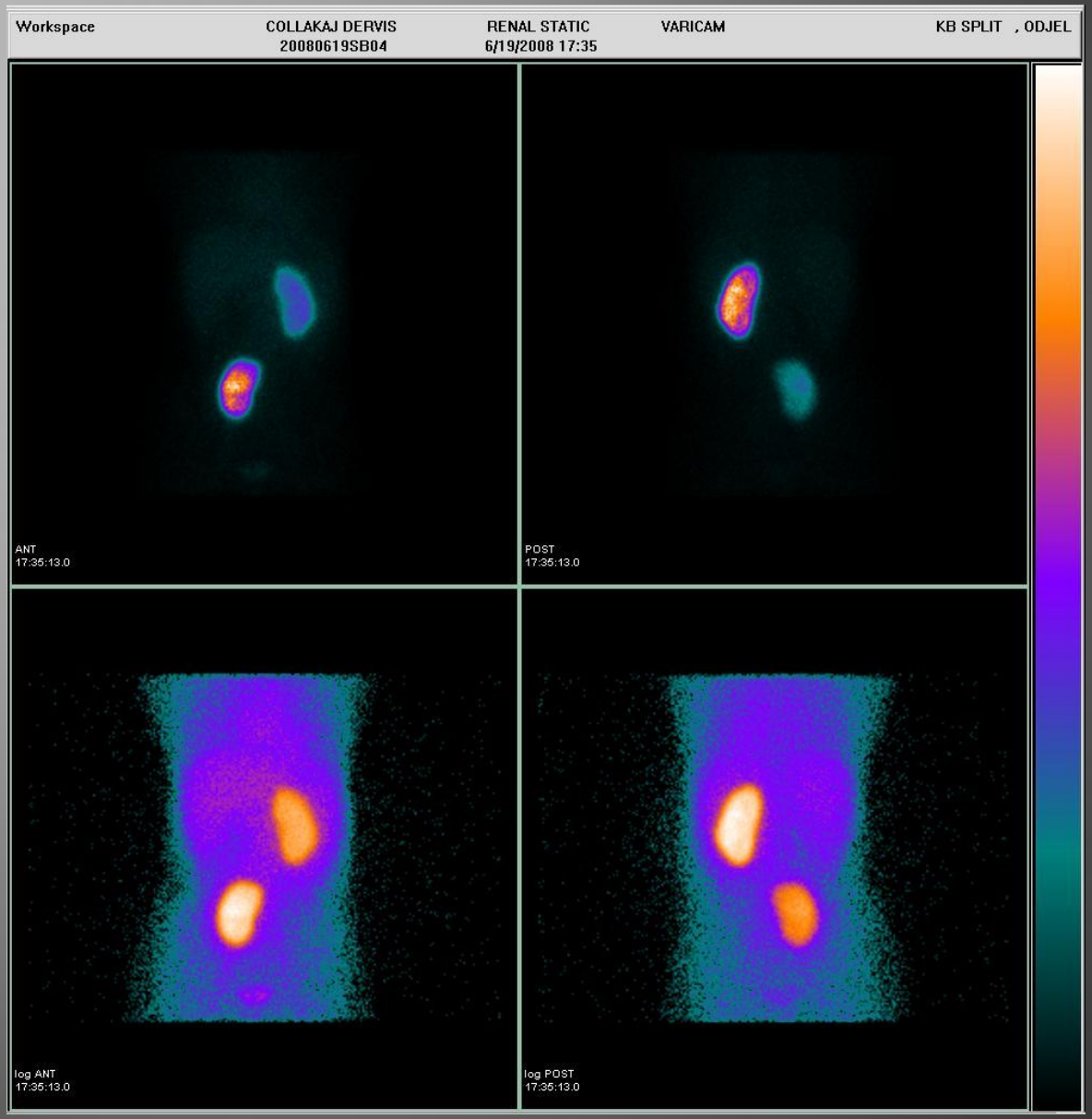
PA sitting position



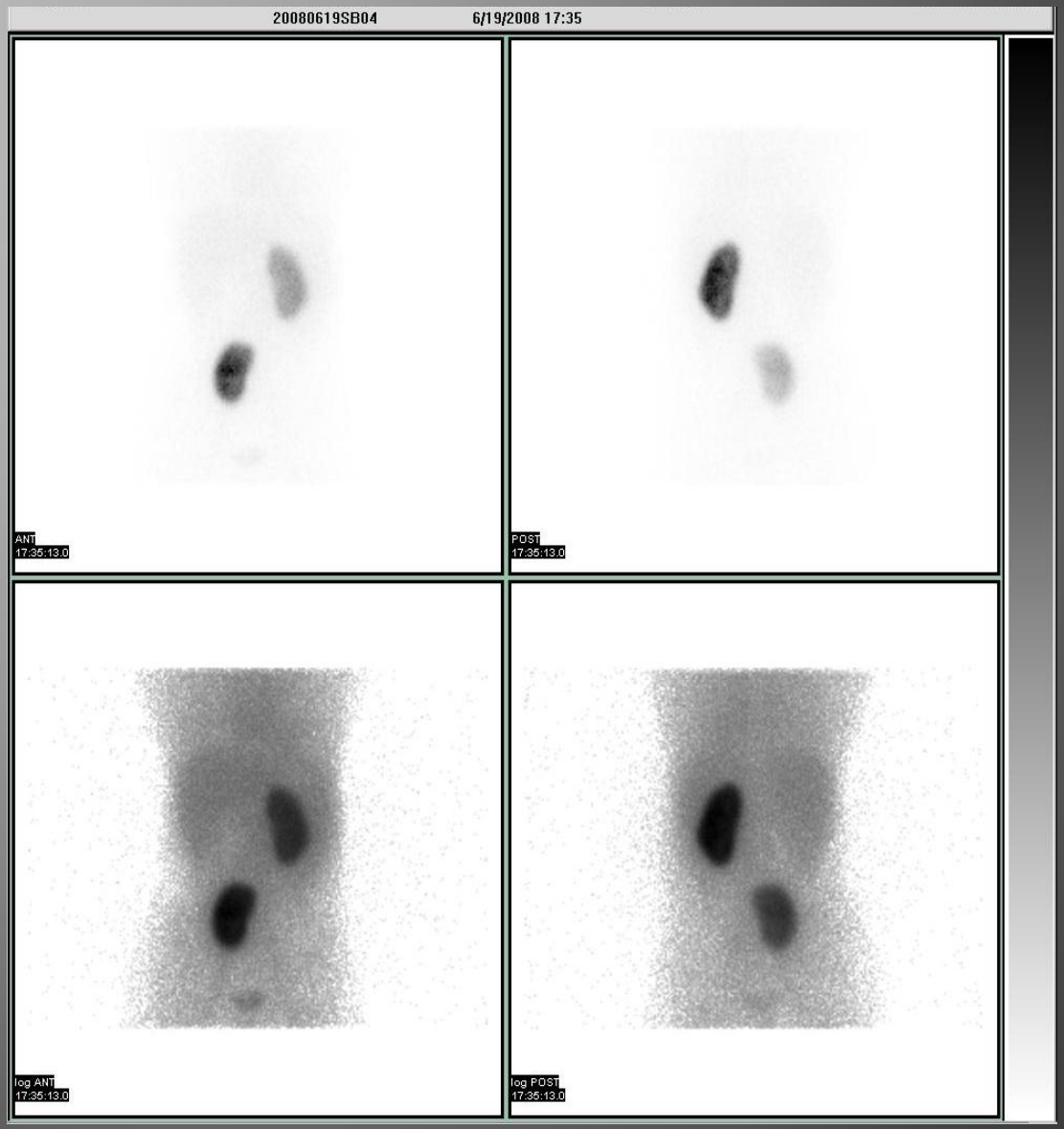
Small right kidney



Smaller left kidney

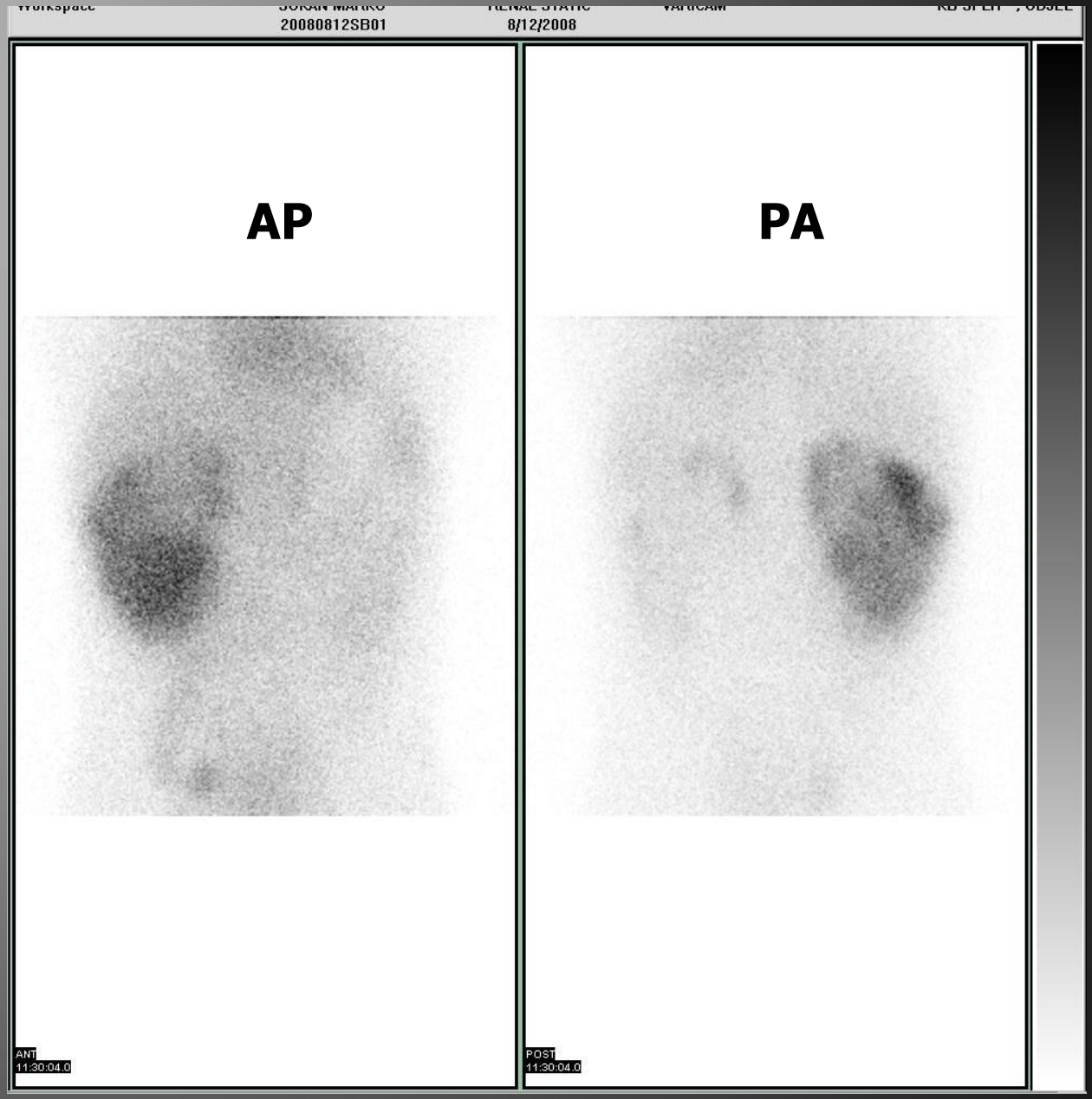


Right kidney ptosis

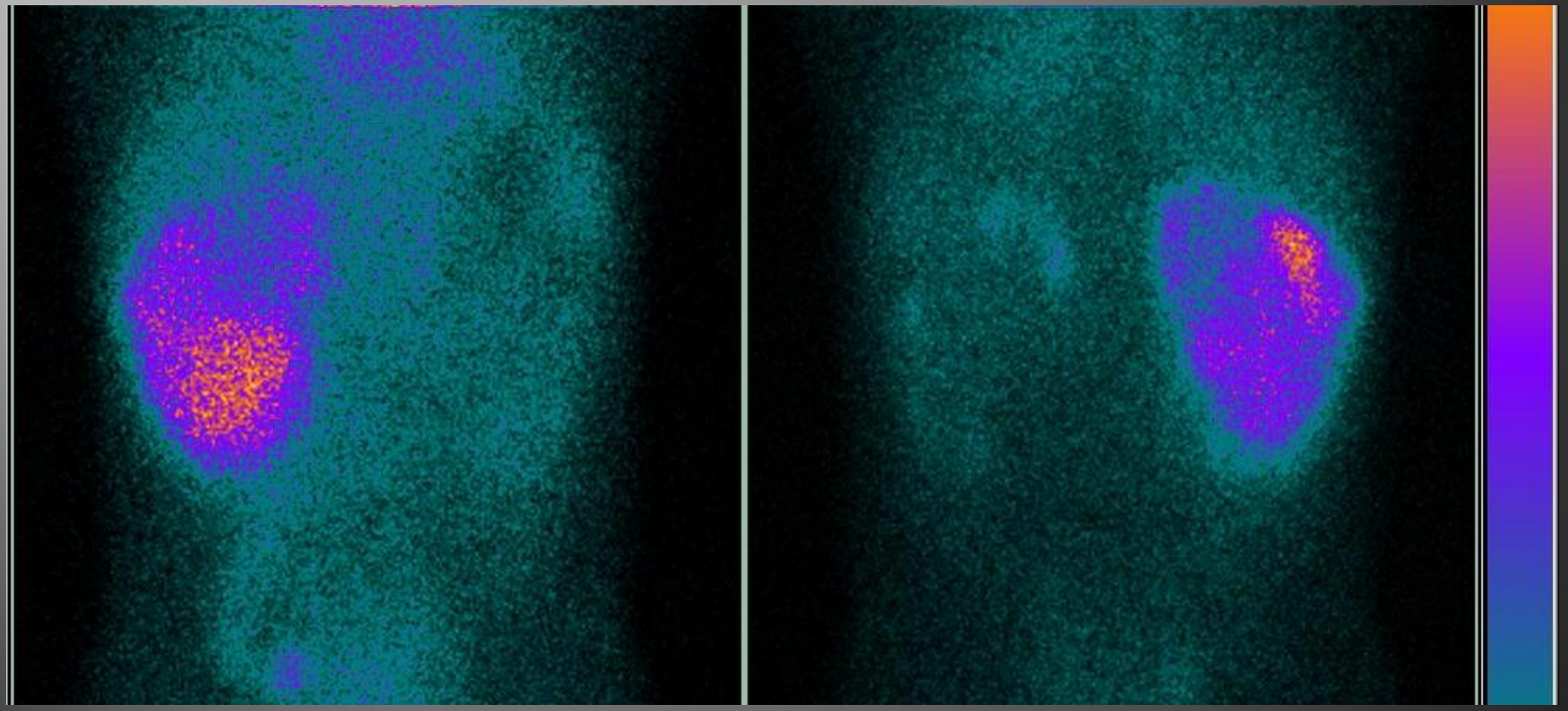


Right kidney ptosis

Hydronephrosis



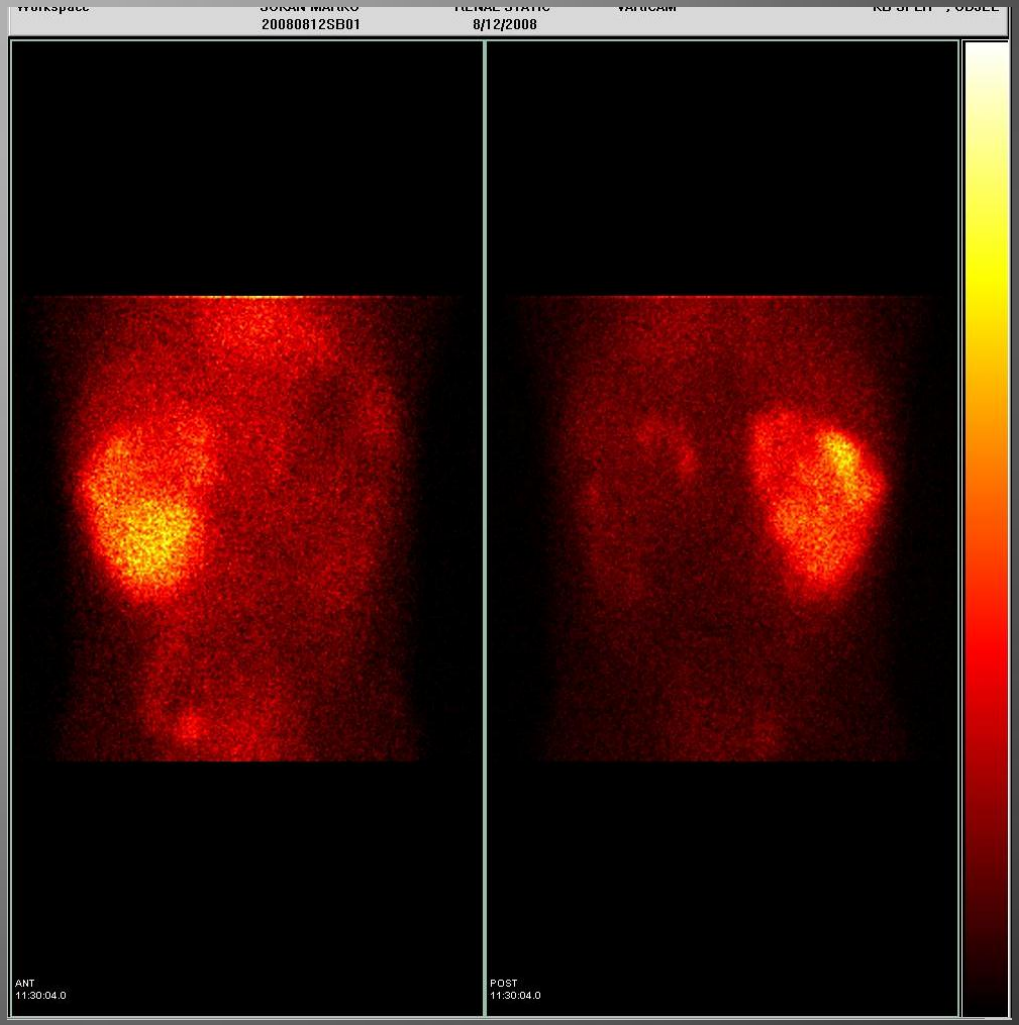
Hydronephrosis



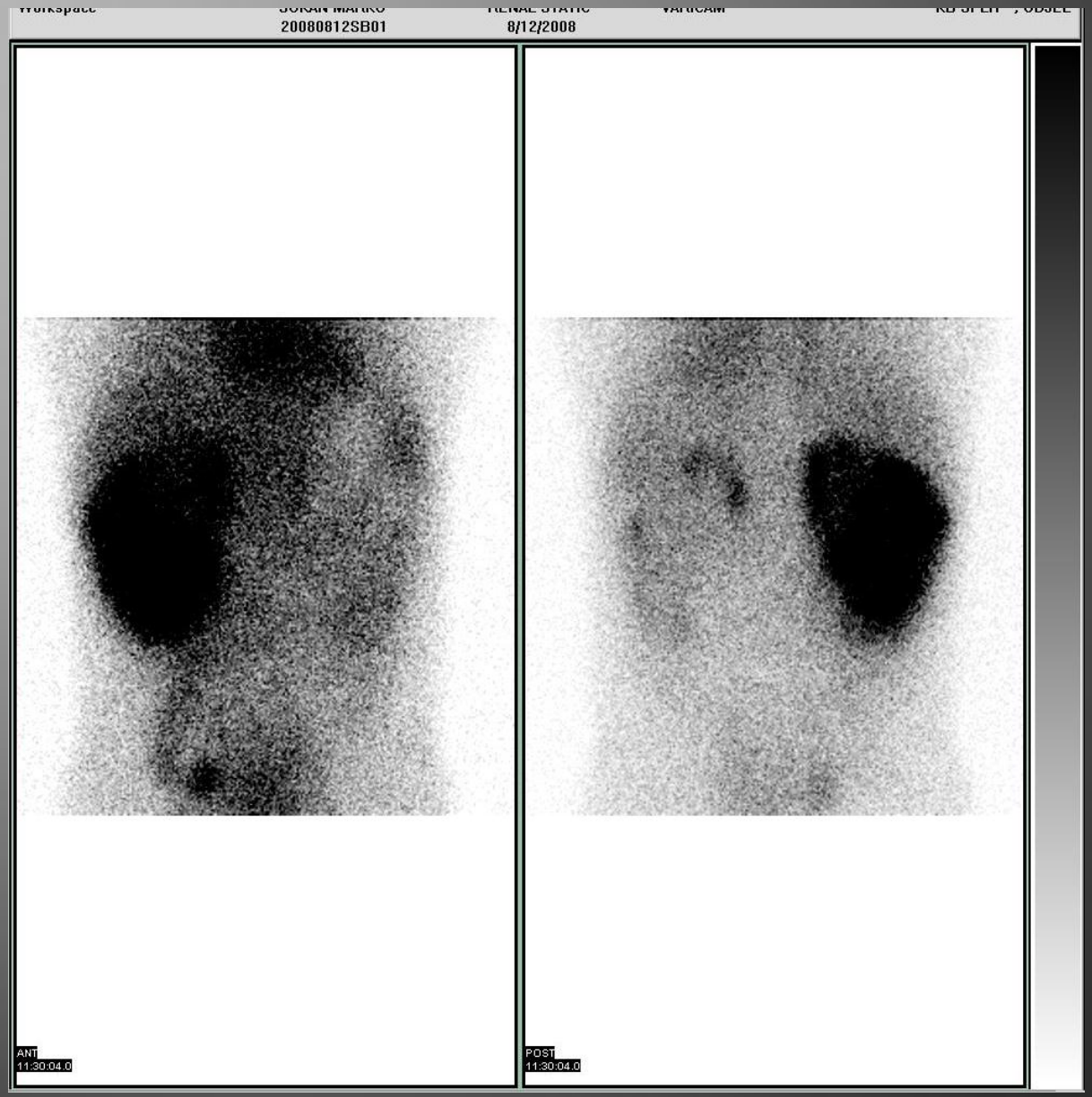
AP

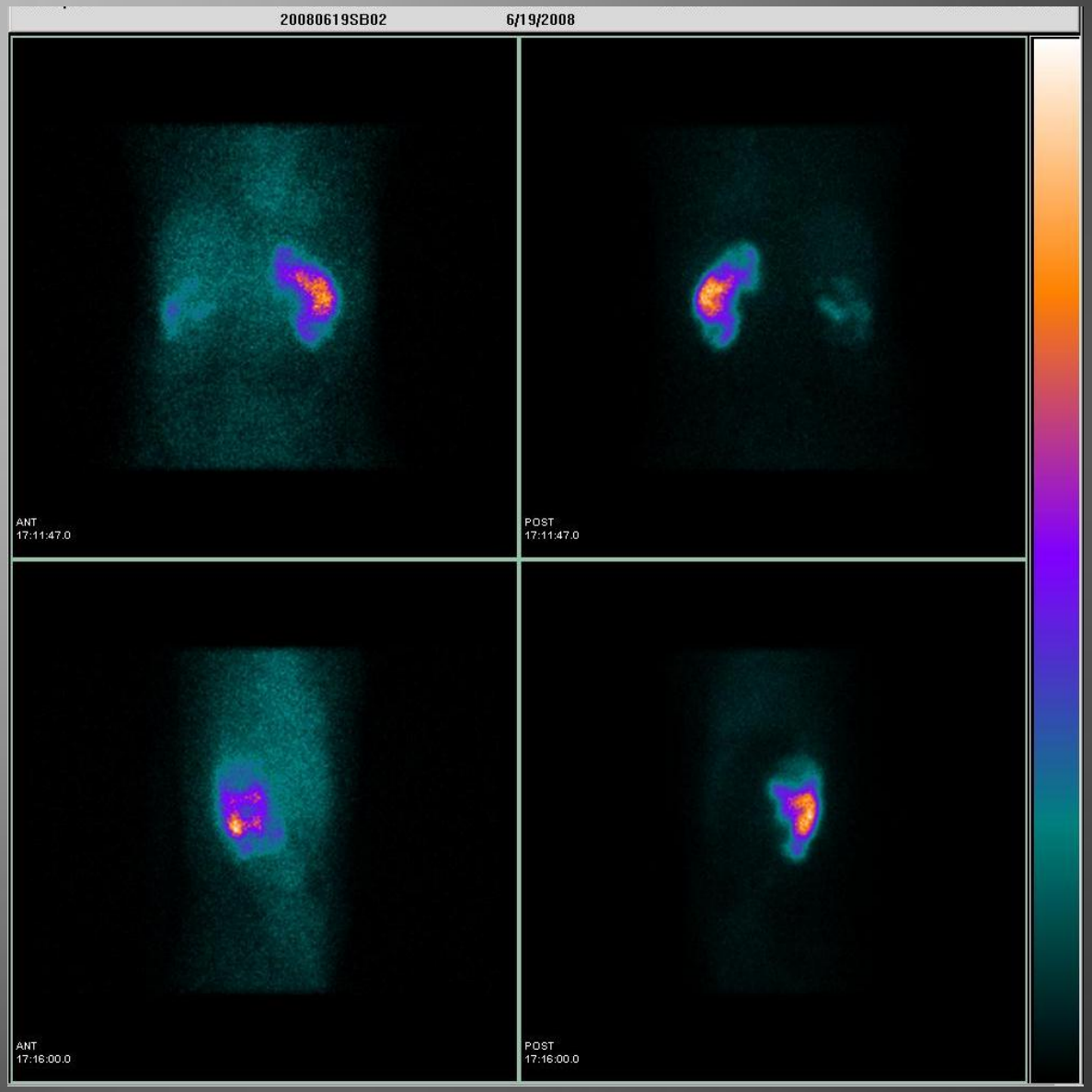
PA

Hydronephrosis



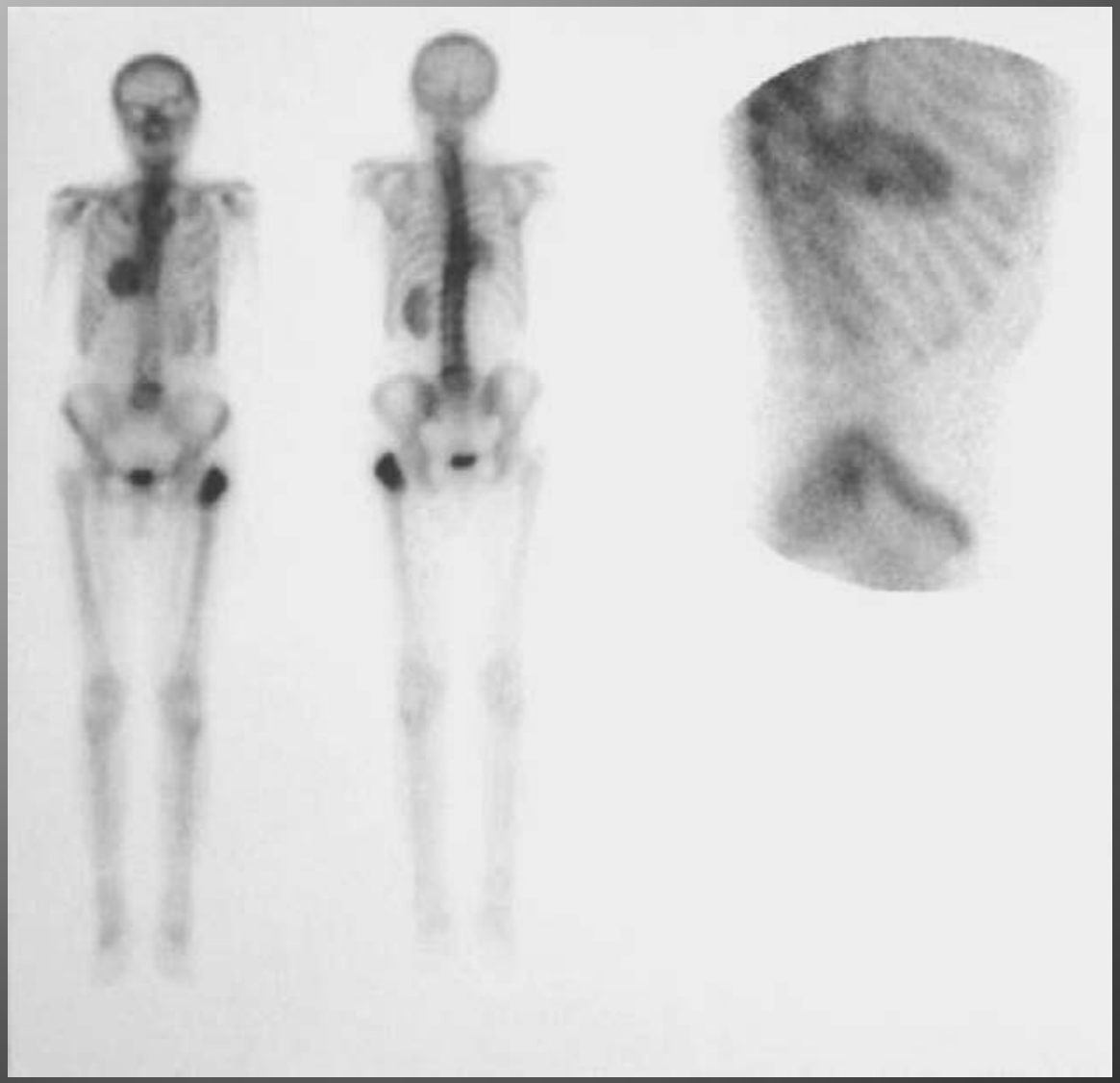
Hydronephrosis



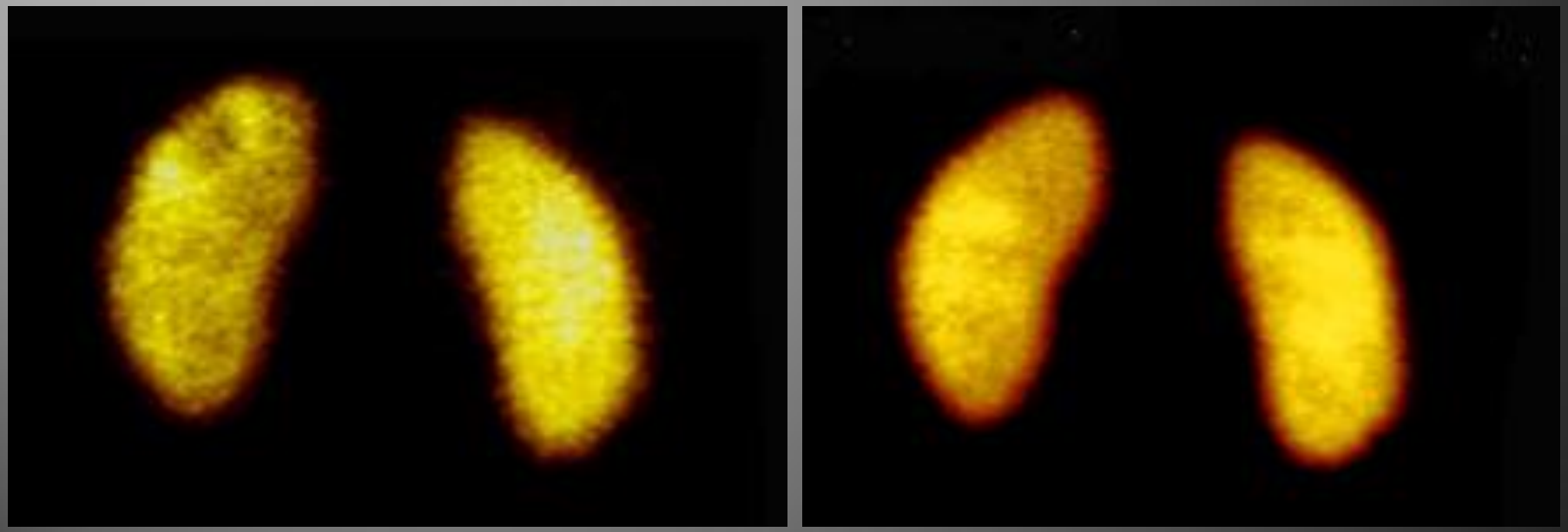


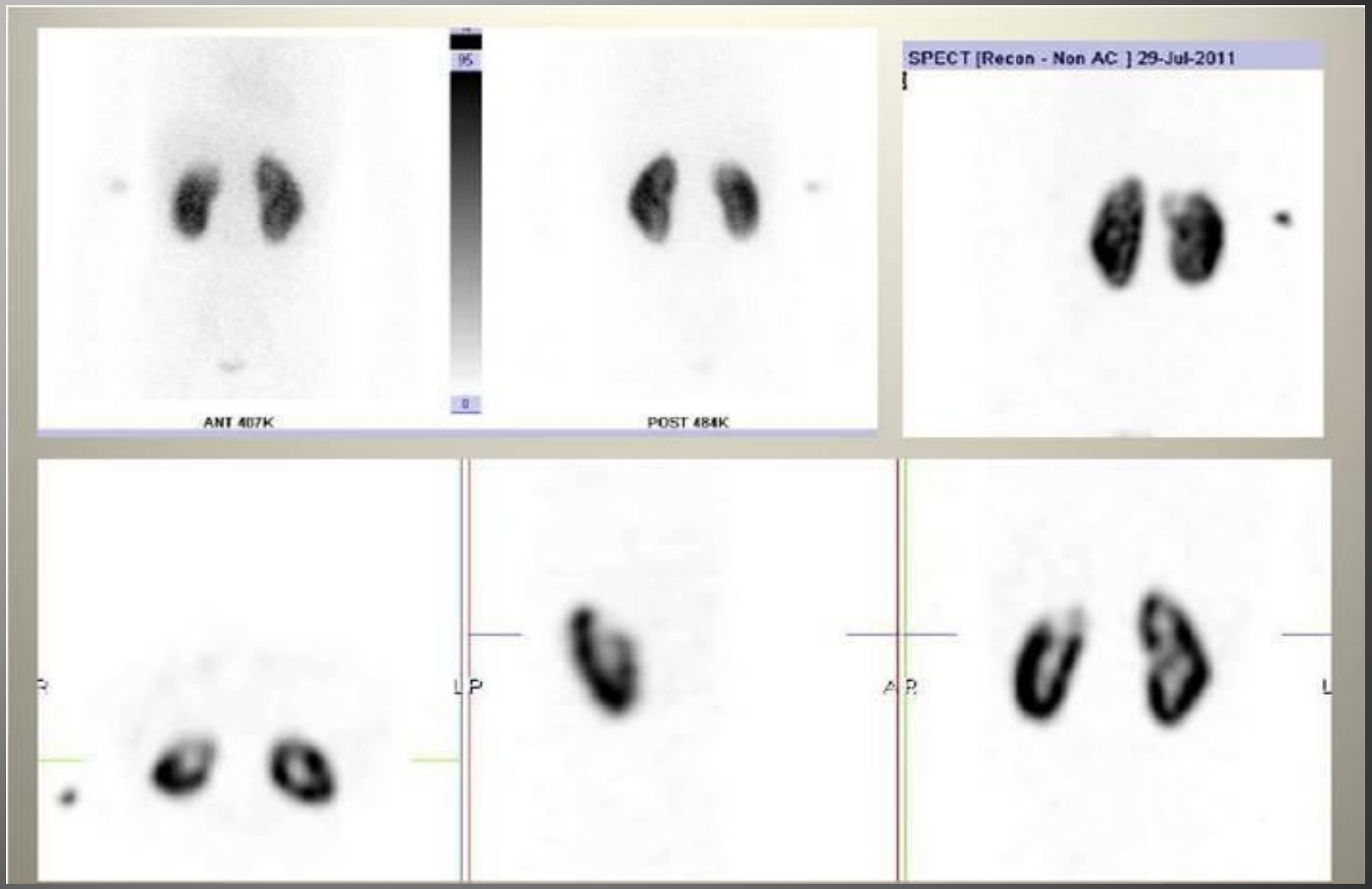
Hydronephrosis due to calculi

Where is the right kidney?

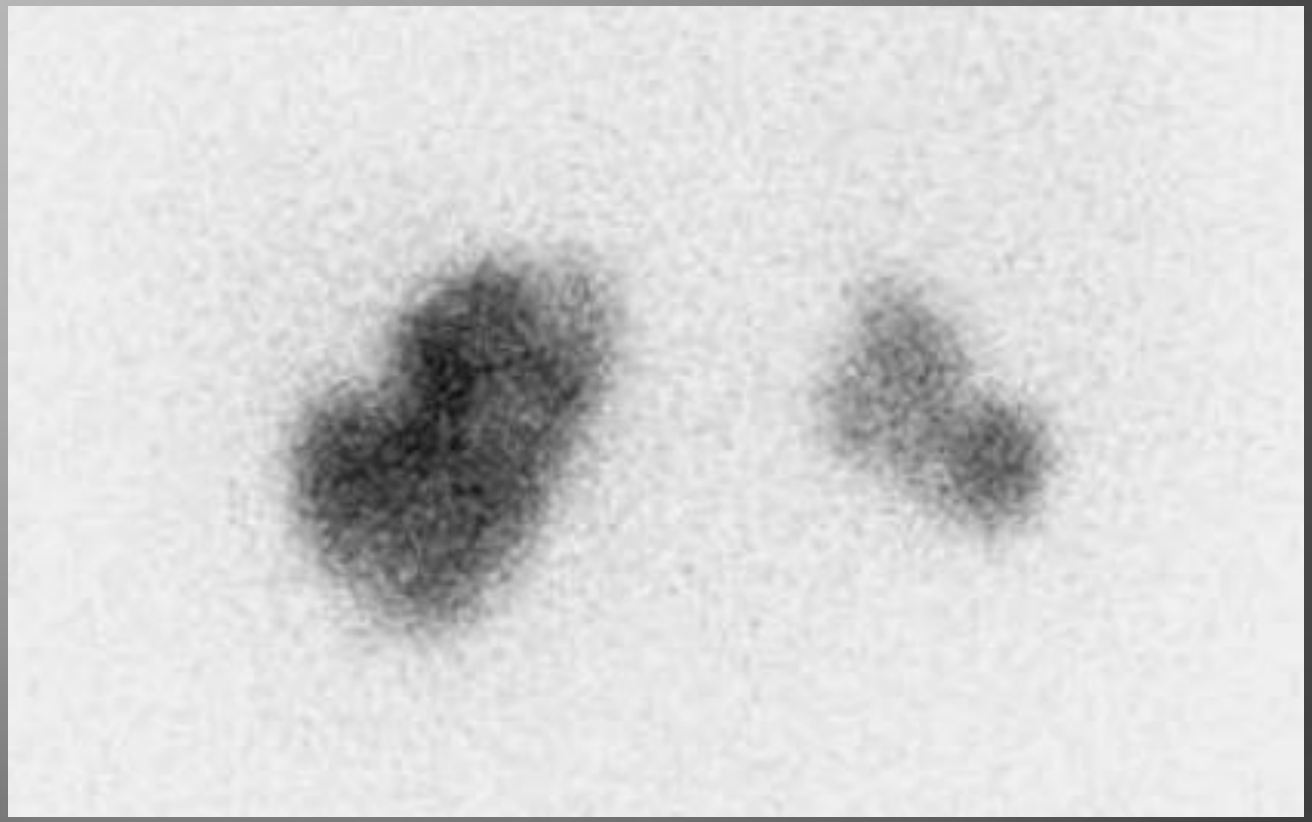


Parenchymal lesion of the upper pole of the left kidney in acute pyelonephritis and complete recovery a few months later

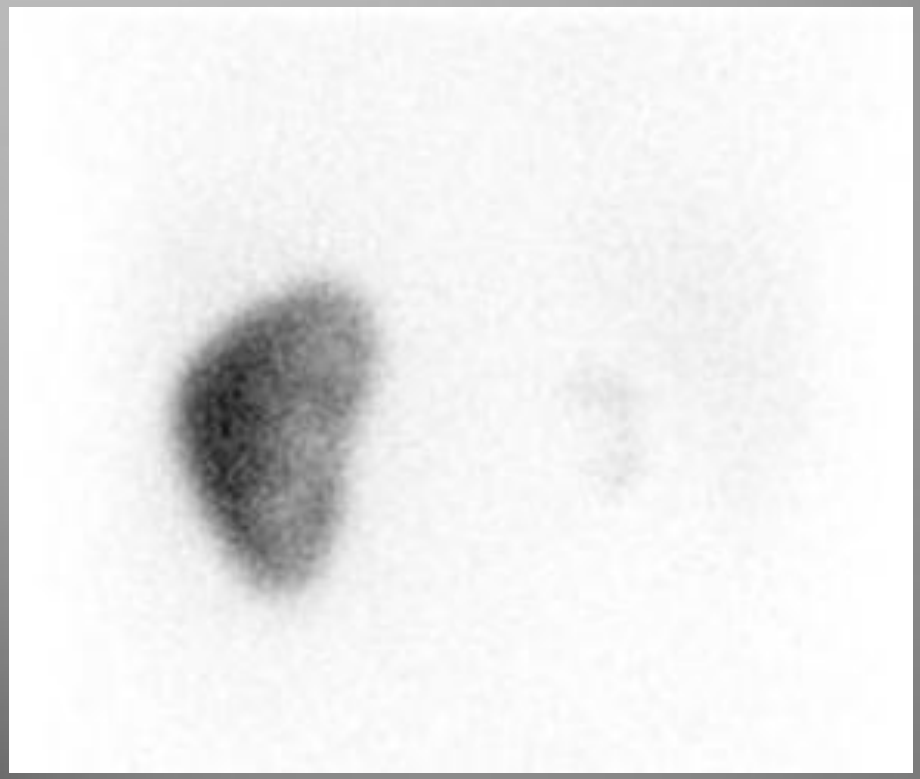


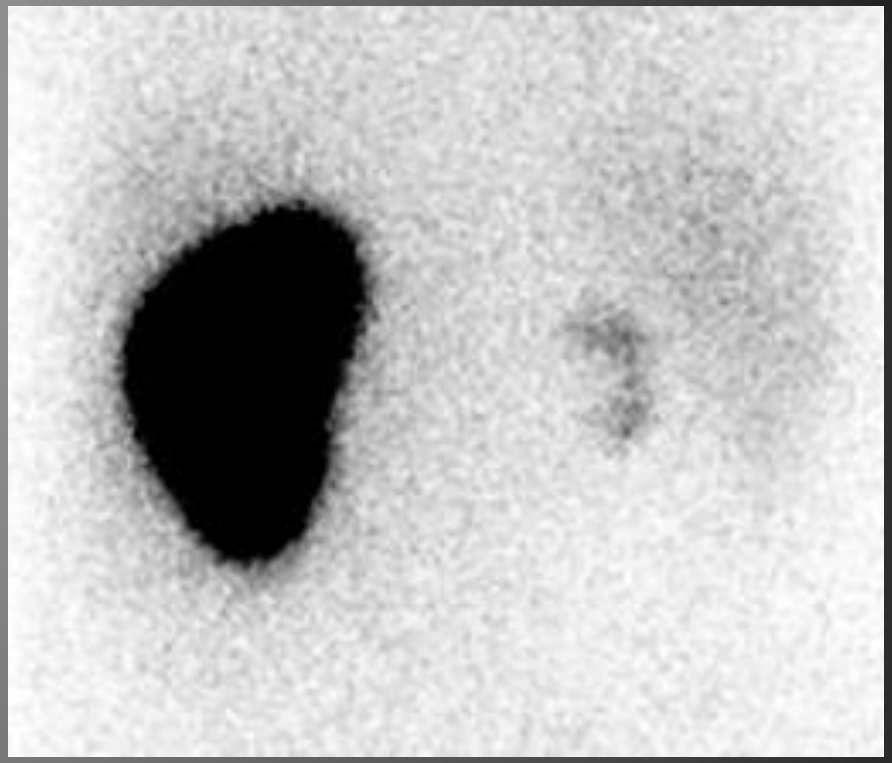


Reflux nephropathy: planar scintigrams and SPECT: parenchymal defect of upper pole of the right kidney



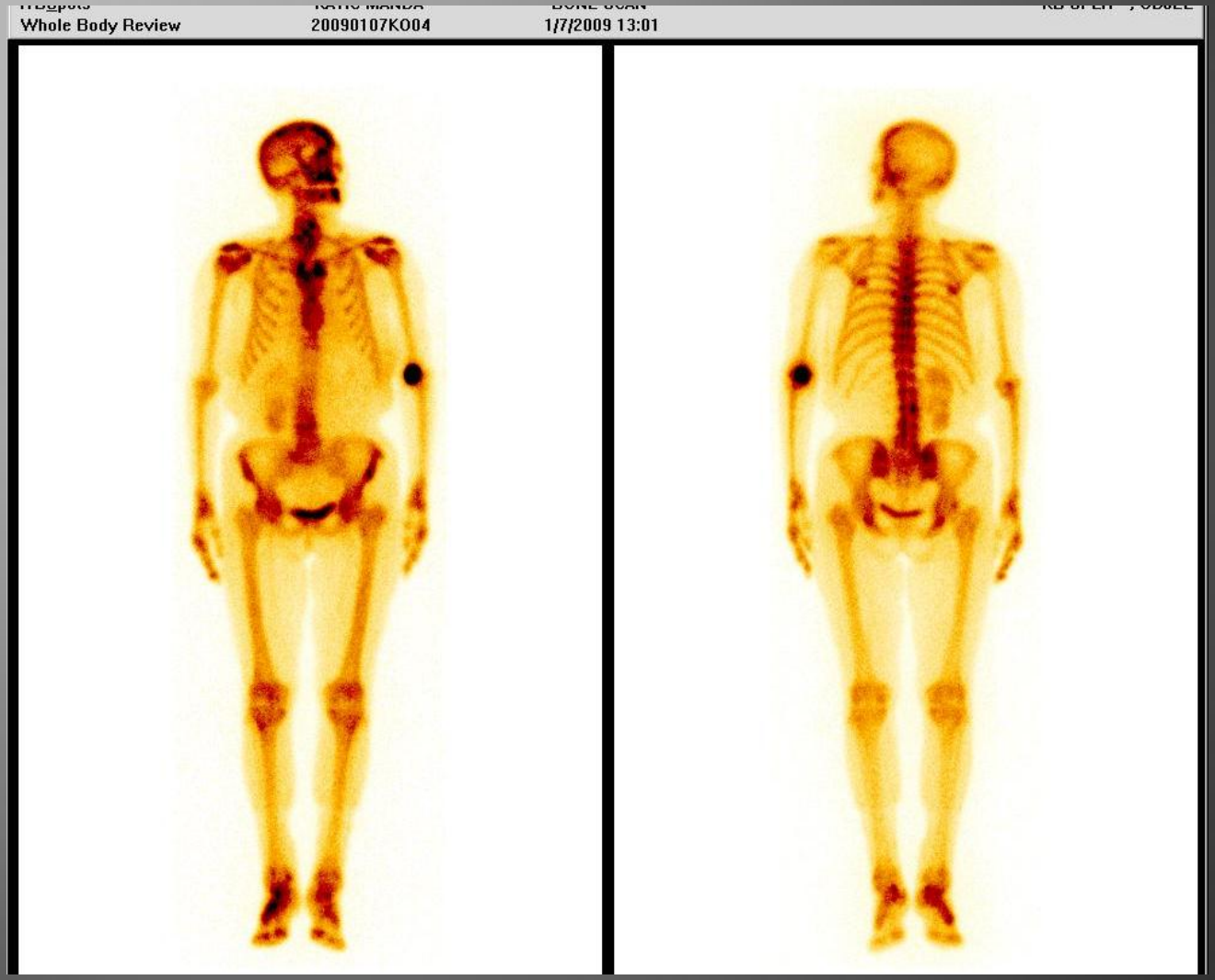
The scar of the left kidney, smaller and scars- changed right kidney





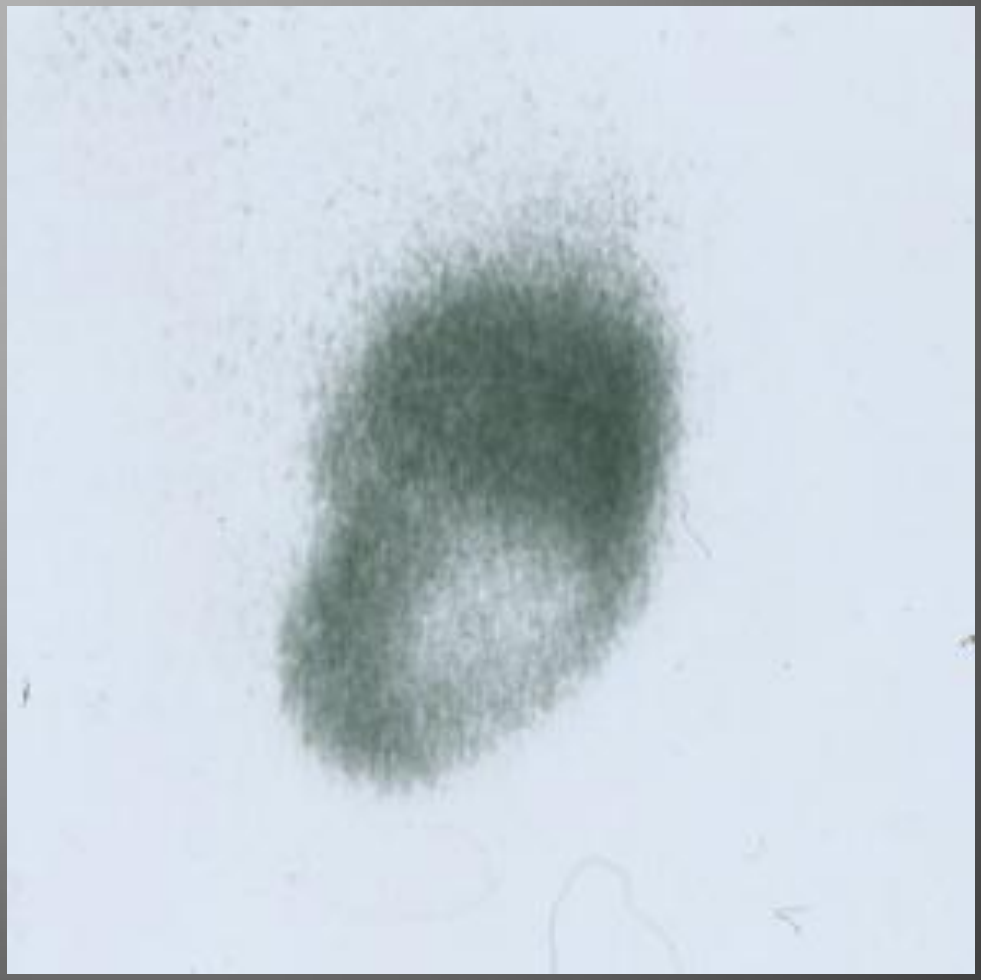
Shrunken right kidney, mildly hydronephrotic left kidney

Where is the left kidney?



Crossed ectopia

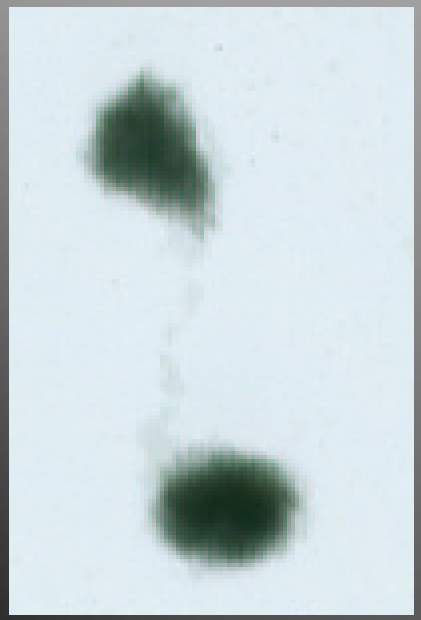
Simple kidney cyst

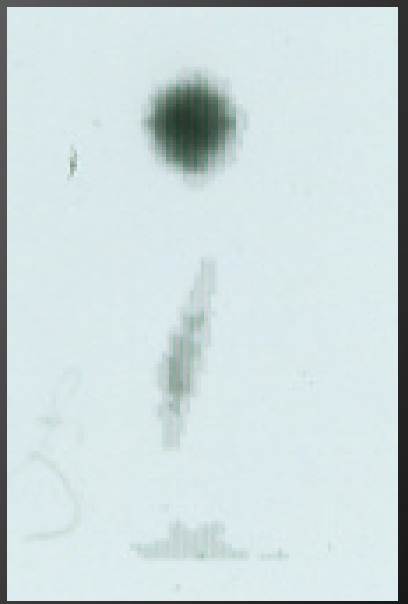


DIRECT AND INDIRECT RADIONUCLIDE VOIDING CYSTOGRAPHY

Vesicoureteral reflux

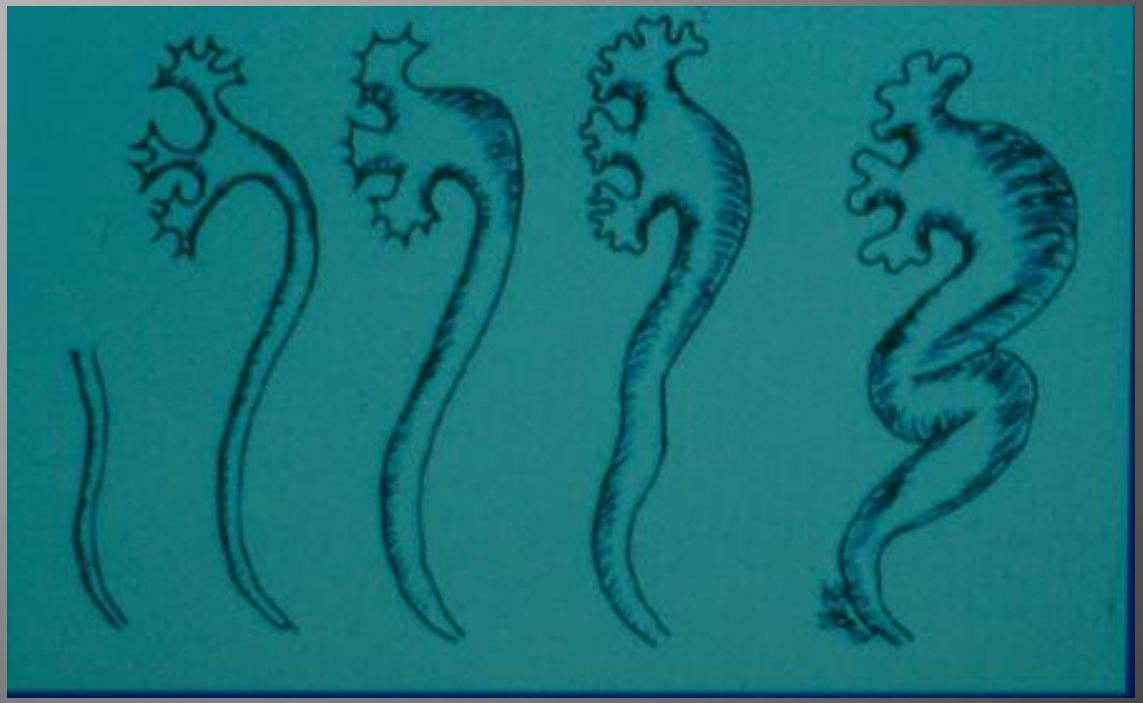
Vesicoureteral reflux (VUR) represents the return of urine (flow) through incompetent vesicoureteral orifice (junction) into the ureter, pelvis and kidney.



VUR

- Classical method for VUR detection and description is radiological method - voiding cystouretrography (VCUG).



Five degrees of VUR according to the IRSC (International Reflux Study Committee)

Non-dilated: I and II degree
Dilated: III, IV and V degree

Types of VUR

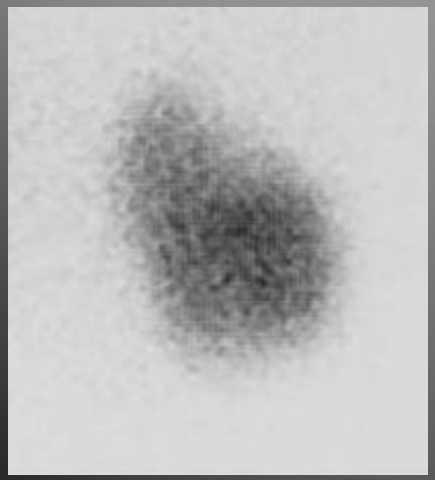
- Primary: a consequence of congenital anomalies of development vesicoureteral orifice; appearance and position of the orifice is determined by cystoscopy; occurs at normal pressures in the bladder; the most common.

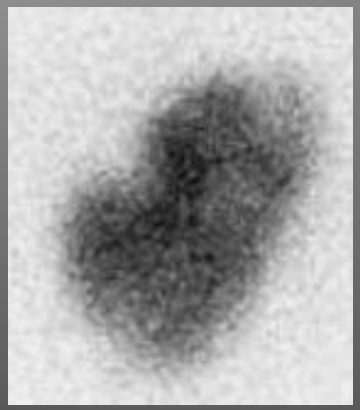
- Secondary: occurs as a result of obstruction of the urinary outlet section of the bladder or posterior urethra (congenital valve of the posterior urethra, neurogenic bladder), and in infections of the urinary bladder (inflammatory reflux). It is characterized by permanently increased intravesical pressure.

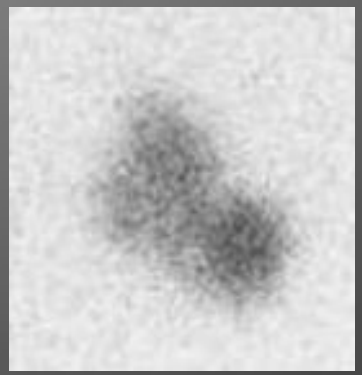
- Iatrogenic VUR: occurs due to surgical procedures to vesicoureteral
- junction.

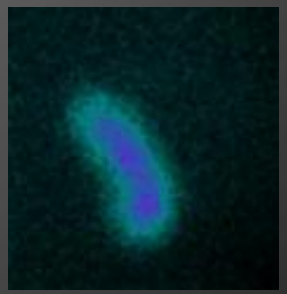
Pathological effects of VUR

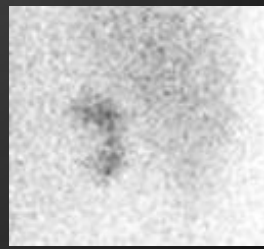
The backwards transfer of urine, bacteria and pressure, depending on their intensity and frequency, leading to a spectrum of pathological changes in the kidney (functional and morphologic) known as reflux nephropathy.



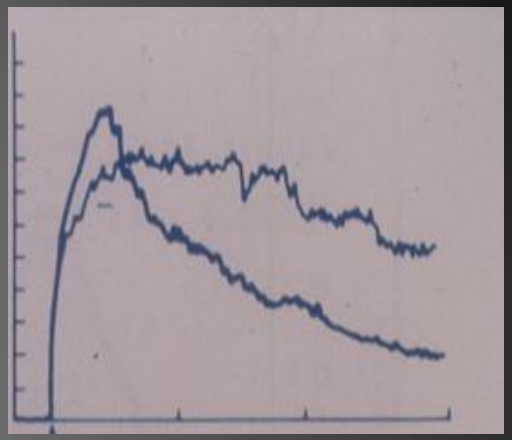




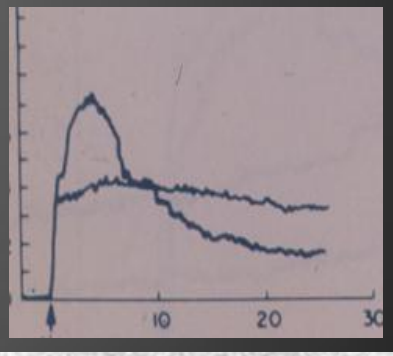


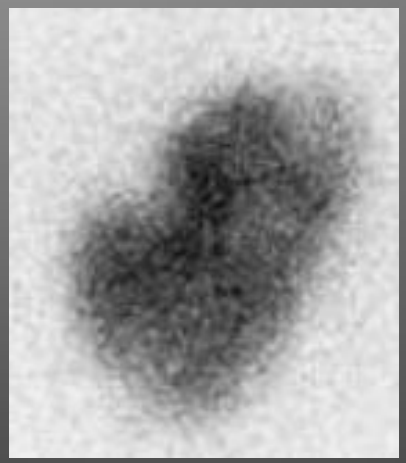


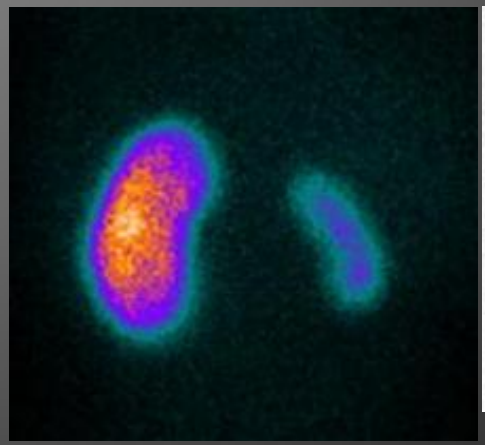
Reflux nephropathy:

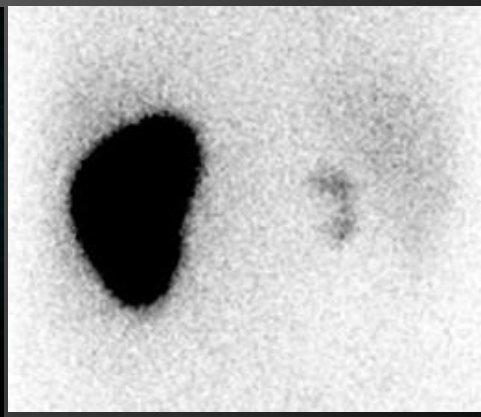


- scarring of the renal parenchyma
- impairment of renal function
- changes in shape, size and structure of the kidney
- retardation of kidney growth, its scarring and shrinking contraction
- arterial hypertension
- renal failure

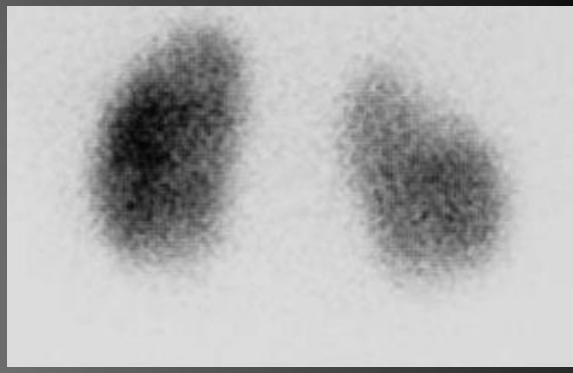




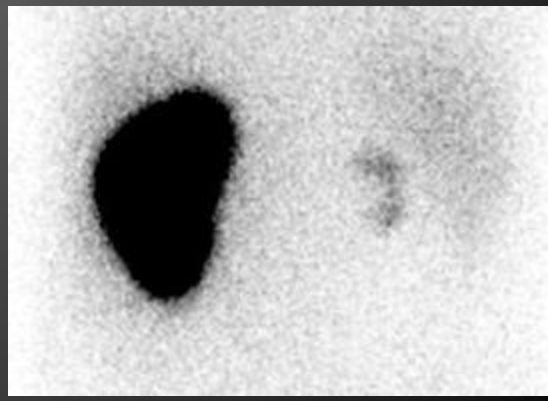




Reflux nephropathy



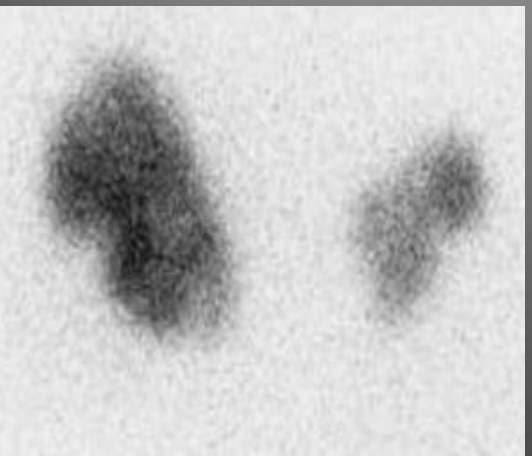
Reflux nephropathy is found in 10-18% of non-dilated VUR (grade I and II); and in about 65% of dilated of VUR (III, IV and V degree), of which 50% have a scar changes, and 15% thinning of the renal parenchyma. In about 5% of patients with dilated VUR kidney atrophia result.



Reflux nephropathy

The sensitivity of the renal parenchyma on the pathological effects of VUR is greatest in the first months and years of life. The likelihood of renal scarring after urinary tract infections is:

- 19.8% in the first year of life
- 9.8% beetwen 2-4 years of life
- 4.6% after 4 years of life



Arterial hypertension develops in 10-20 % cases of reflux nephropathy.

Frequency and heredity of VUR

- In 1: 200 in female children and 1: 1000 male children.
- In 29-50% of children with recurrent urinary tract infections.
- In 85-100% of children with chronic pyelonephritis.
- VUR is more common in younger children with urinary tract infections:
  - 70% of children up to 1 y.,
  - 25% of children up to 4 y.,
  - 15% of children up to 12 y.,
  - 5% of adults.
- The probability that a brother or sister of a child with VUR will also have VUR is 27-33%, and in children whose parents had VUR is higher.

The natural course of VUR

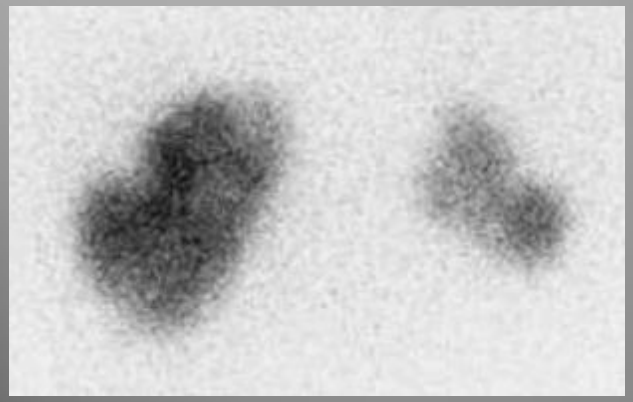
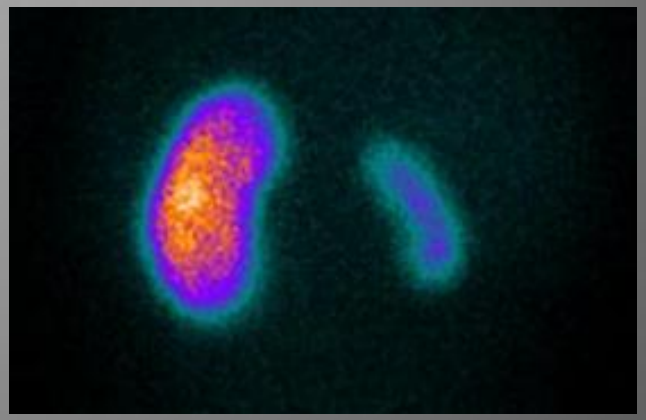
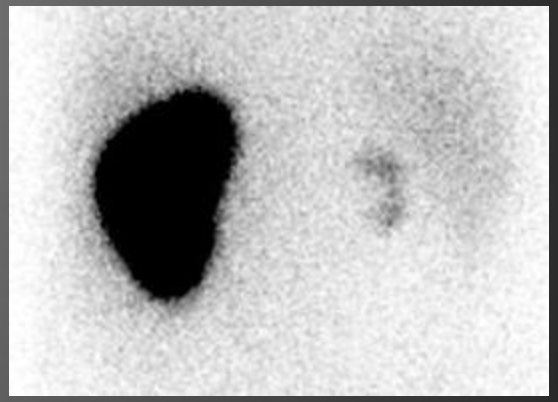
1. Spontaneous healing

Non - dilated refluxes (I and II degree according to IRSC division) are regresed spontaneously in 80% of cases over time.

Dilated refluxes (III, IV, and V degree at IRSC division) are regresed spontaneously after five years of follow-up in 28% of cases.

The natural course of VUR

2. The development of reflux nephropathy:

The scars, reduction of the renal parenchyma, the impairment of renal function, shrunken kidney, hypertension, chronic renal failure.

Treatment of VUR

Conservative: non-dilated VUR.

Surgical or endoscopic correction of vesicoureteral junction: dilated VUR.

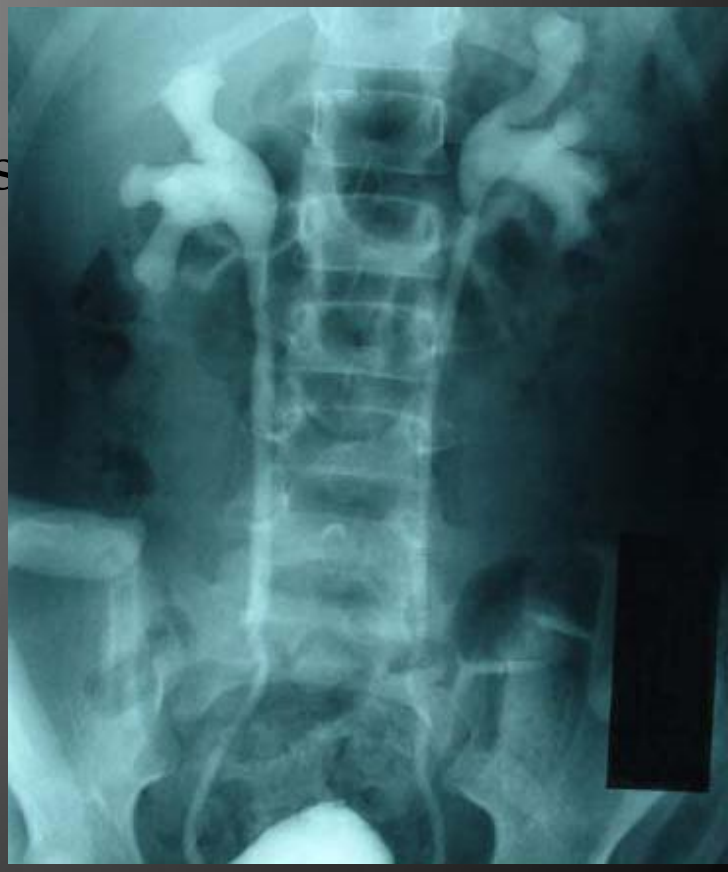
Diagnostic methods and classification of VUR

- Voiding cystouretrography (VCUG)
- Direct radionuclide voiding cystography (DRVC)
- Indirect radionuclide voiding cystography (IRVC)
- Voiding ultrasonography (VUS)

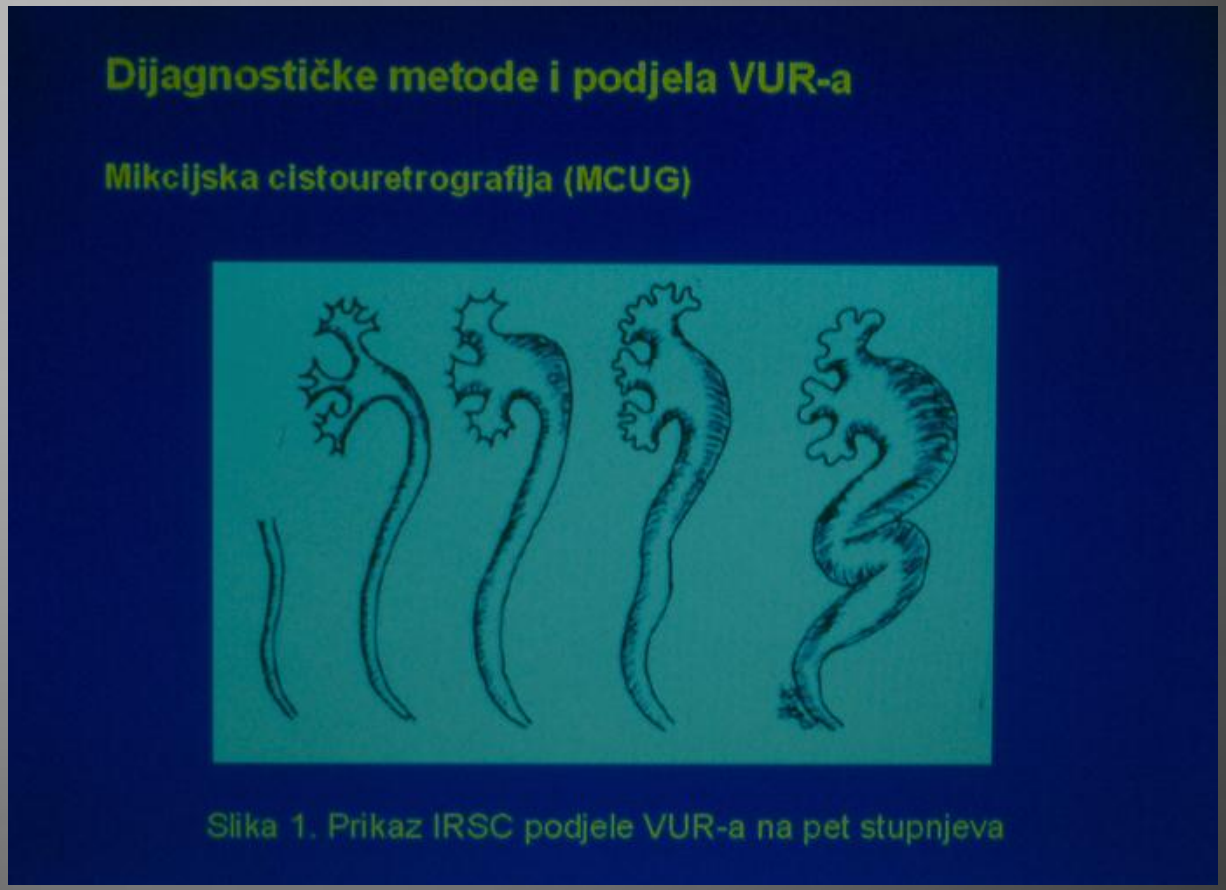
Voiding cystouretrography

- Classical method of VUR detection is radiological contrast voiding cystouretrography (VCUG).

- Provides good morphological details of the bladder and urethra, and at the presence of of VUR provides good morphological changes of ureter and pyelon.



● In addition to establishing the existence of reflux, it provides a good view at morphological changes of ureter and pyelon.

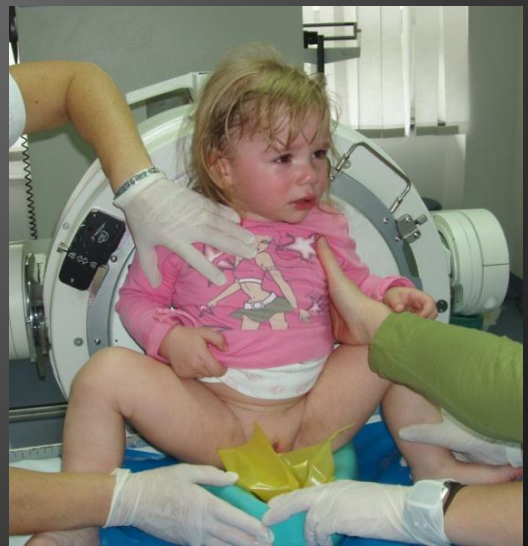


• Its main disadvantage is a significant radiation burden

of patients which disables continuously monitoring of patients during the examination.

Direct radionuclide voiding cystography

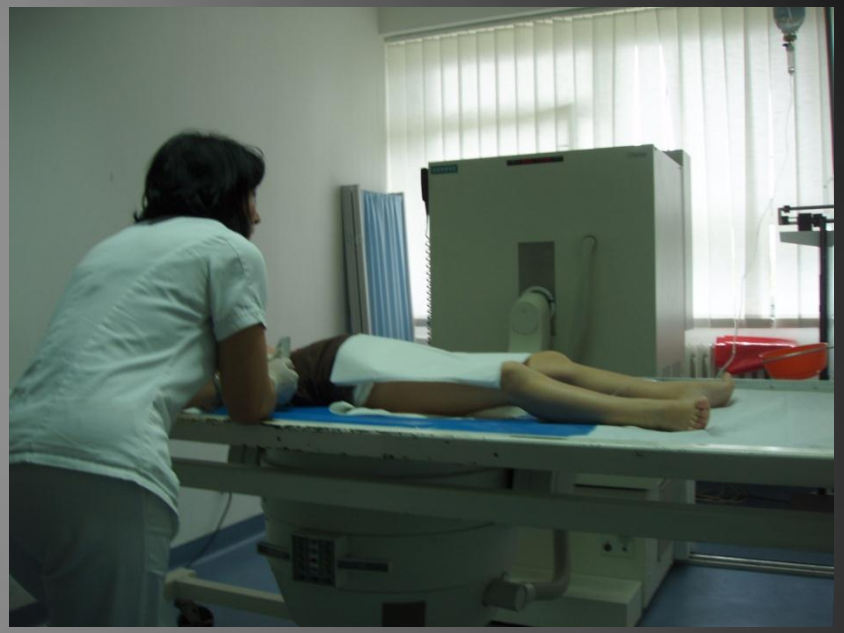
- Methodologicaly it is similar to VCUG.

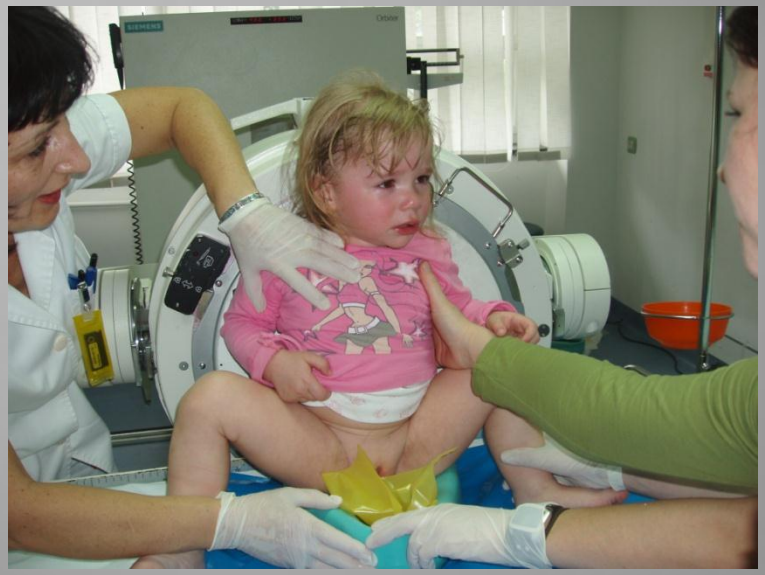


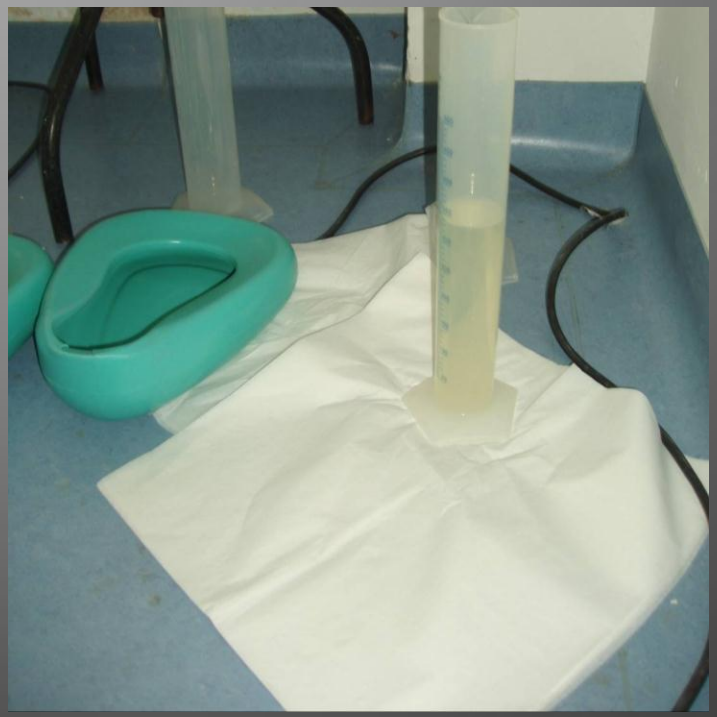
Direct radionuclide voiding cystography

Radiopharmaceuticals:

- Tc-99m-pertehnetat
- Tc-99m-DTPA
- Tc-99m-colloid
- Dose (activity): 0,5 mCi (18,5 MBq) in 500 ml saline solution warmed to 37^0 C



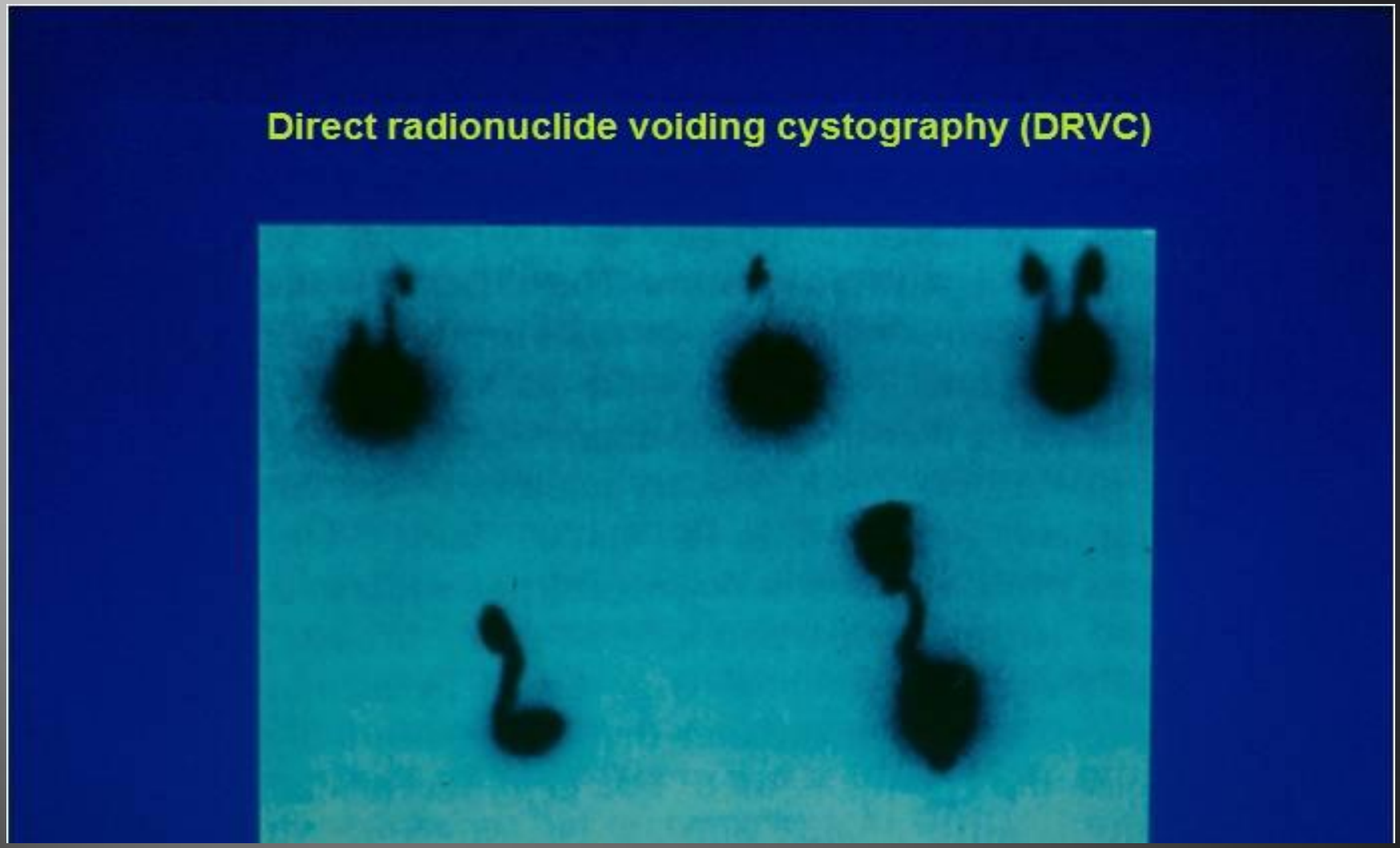




Direct radionuclide voiding cystography

- With 20-100 x less radiation it allows continuous monitoring of the filling and emptying of the bladder.

- In addition to higher sensitivity in the detection of VUR (93 vs. 74% for nedilated reflux) it allows the quantification of a variety of functional parameters ie. bladder volume and urine volume of refluxing at any stage time.

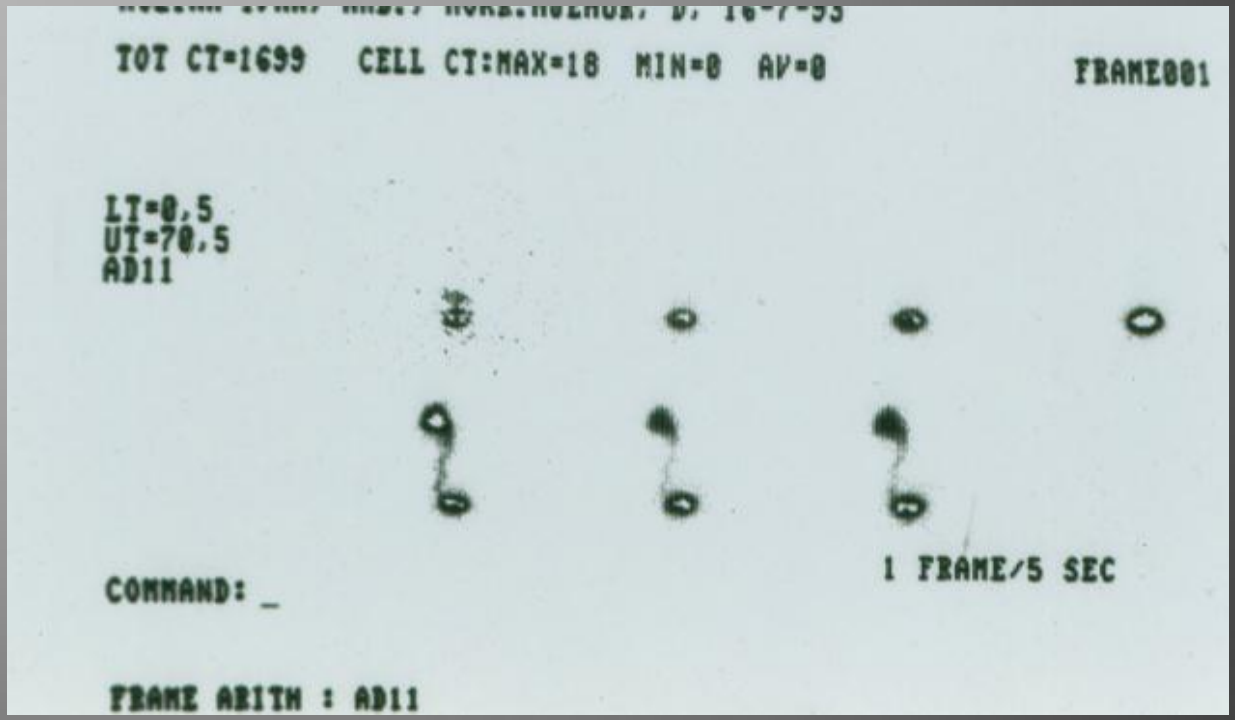


Five degrees of VUR acording to DRVC

Radiation burden of DRVC for the activity of 18.5 MBq (0.5 mCi) Tc-99m and examination duration of 30 min.

- Effective dose: 0,048 mSv
- Bladder: 0,09-0,14 mGy
- Ovary: 0,005-0,01 mGy
- Testicle less

- Unlike VCUG, DRVC provides continuous monitoring of all phases of examinations without increasing the radiation dose.

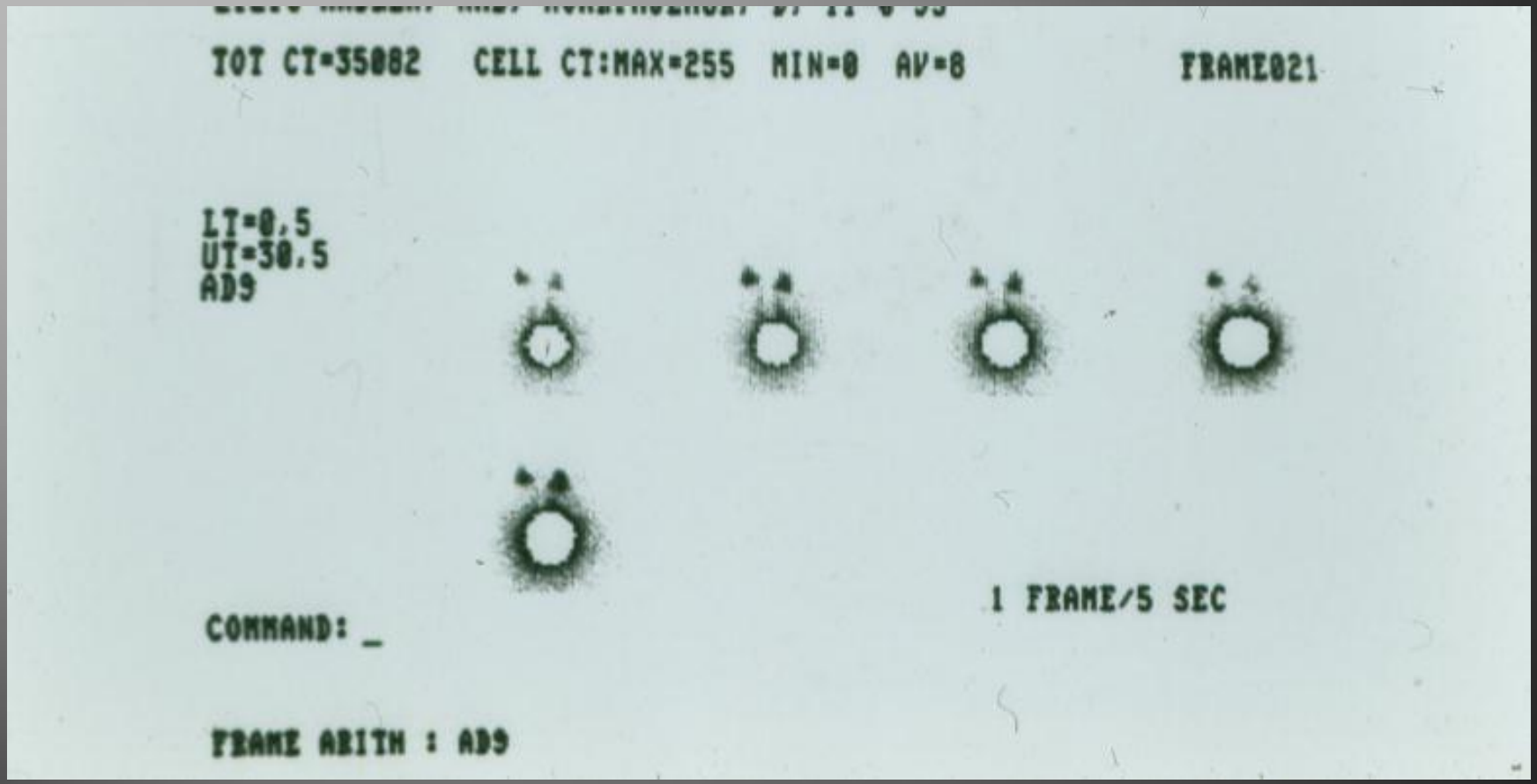


- For the same radiation dose that a patient receives for one VCUG it is possible to make tens to hundreds DRVC.

- The most determined parameters are:

  - the volume of the bladder when VUR occurs
  - the capacity of bladder
  - RU (Residual Urine)
  - **occupancy ((%) of bladder fullness) on the occurrence of VUR**
  - maximum refluxing volume of urine
  - % refluxing volume of urine in relation to the volume of the bladder
  - residual refluxing volume of urine
  - % refluxing residual volume urine compared to the capacity of the bladder
  - average and maximum speed of urination

Enjoy the next several scintigrams



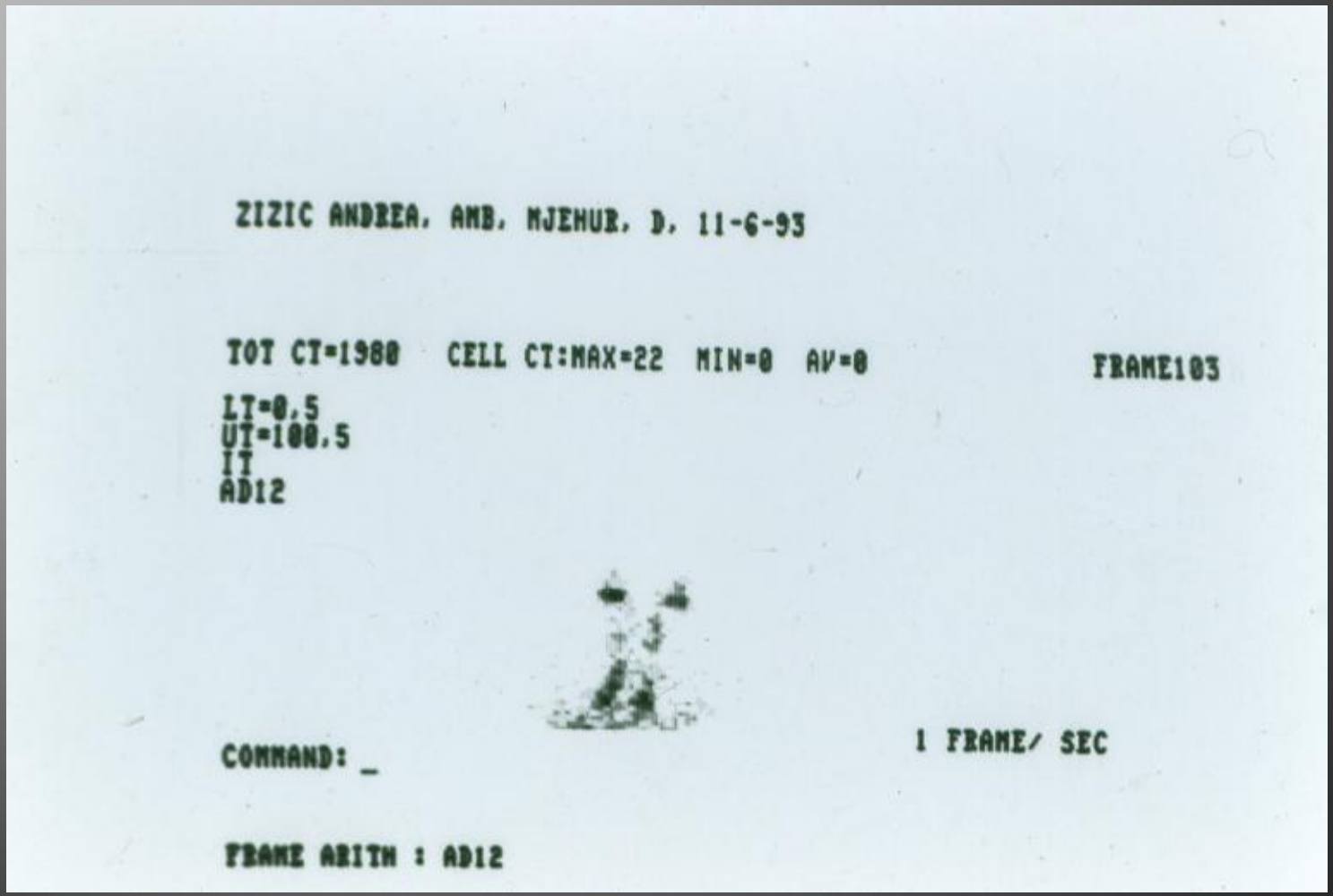
TOT CT=43268 CELL CT:MAX=255 MIN=0 AV=10 FRAME031

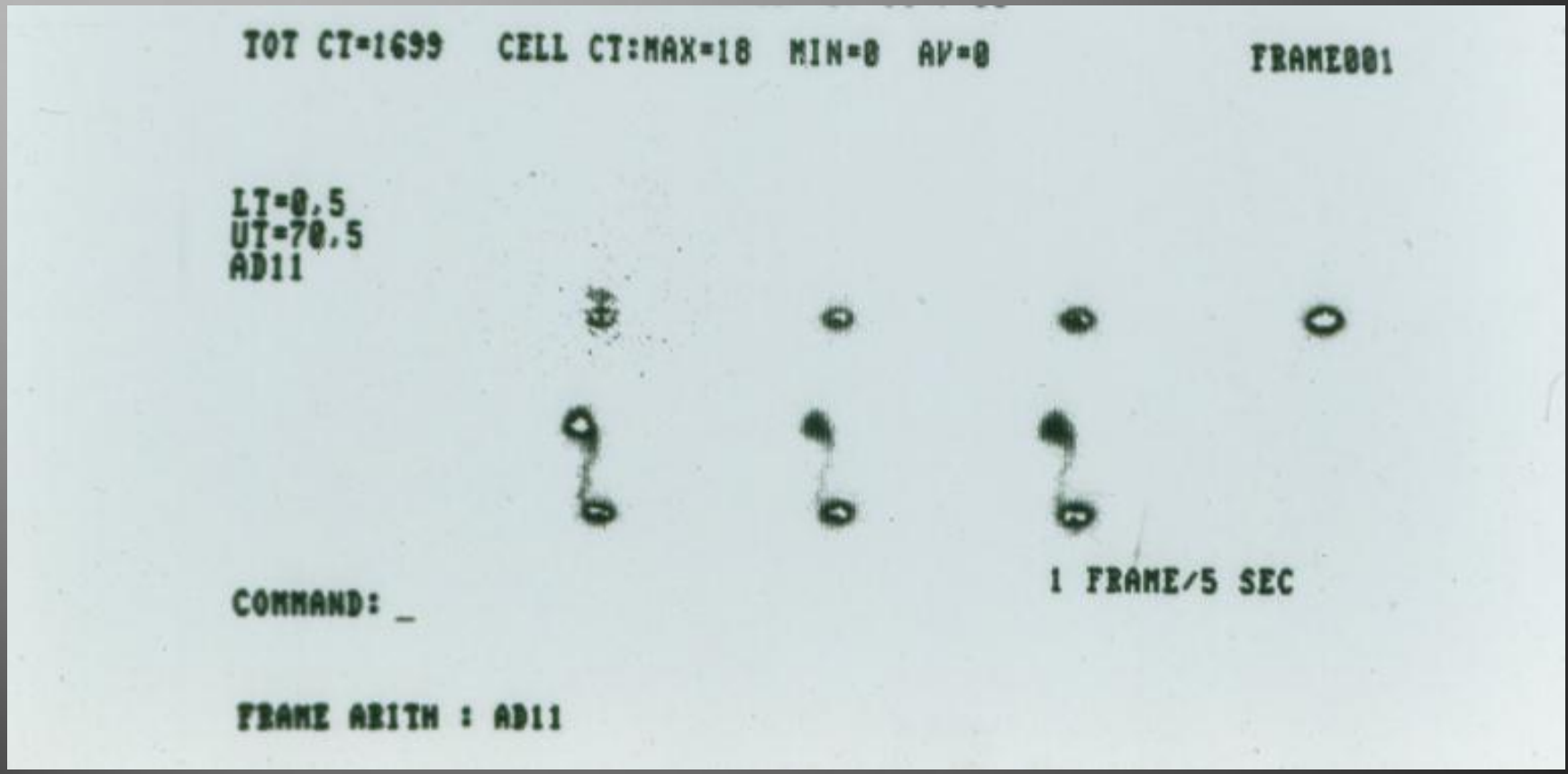
LT=0.5
UT=30.5
AD9

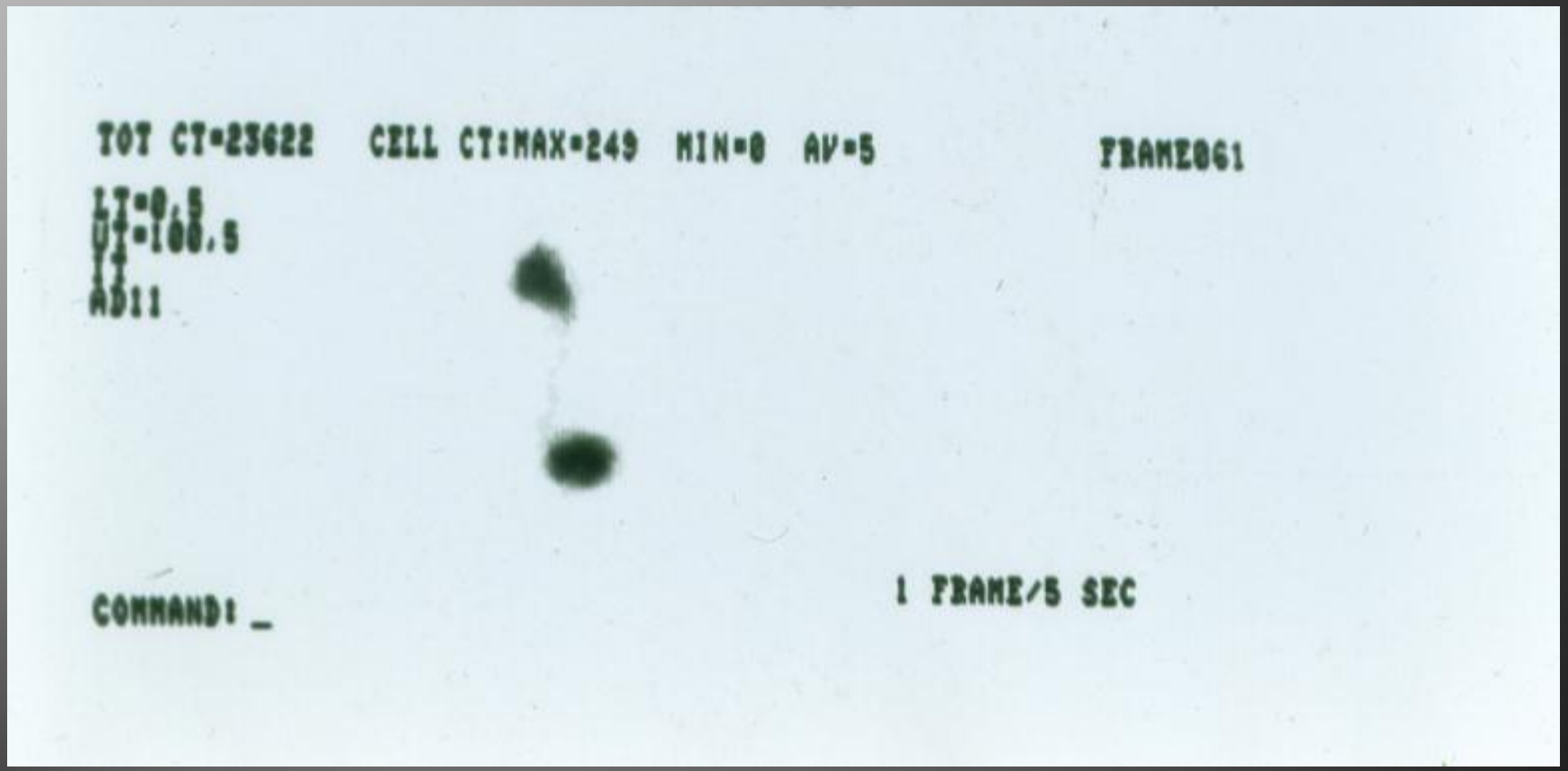
COMMAND: _

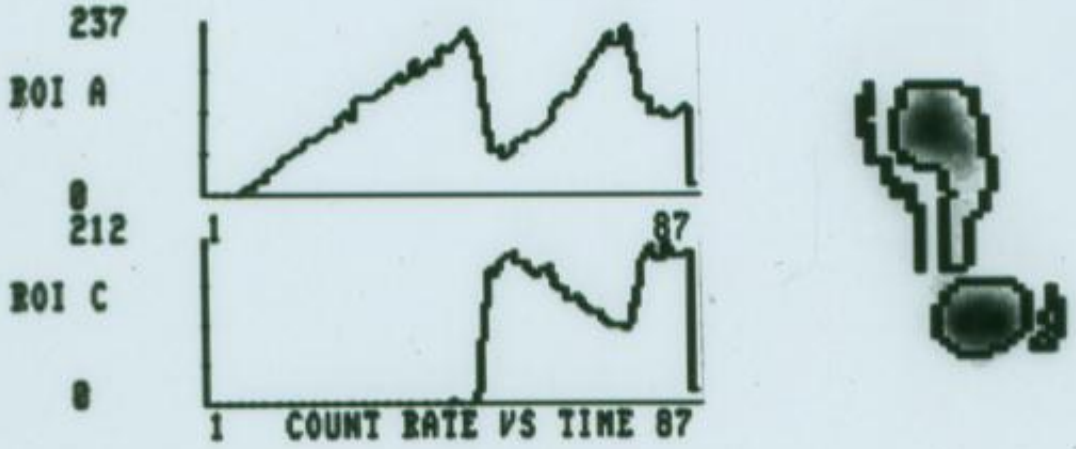
1 FRAME/5 SEC

Residual refluxing urine



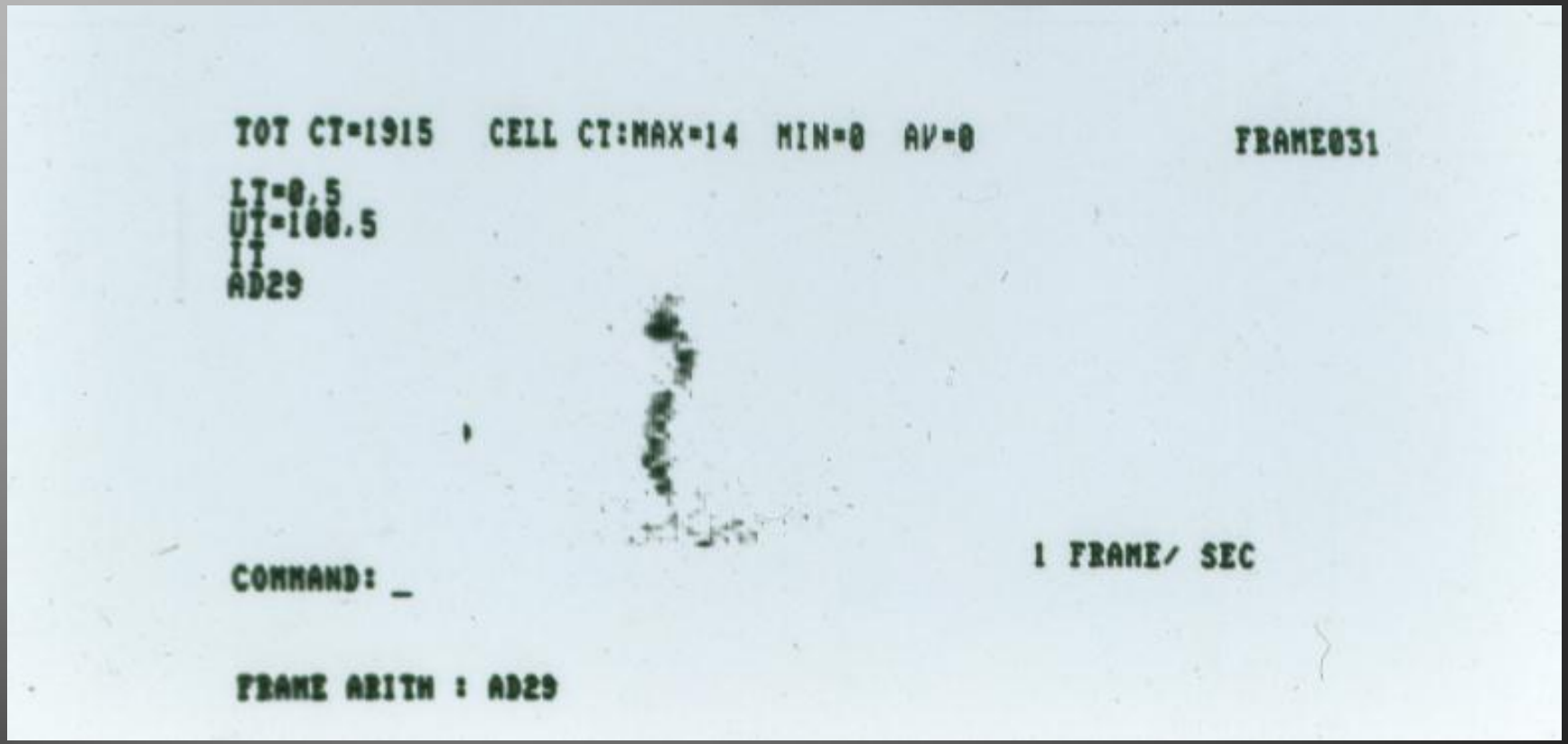

TOT CT=1699 CELL CT:MAX=18 MIN=0 AV=0 FRAME001
LT=0.5
UT=70.5
AD11
1 FRAME/5 SEC
COMMAND: _
FRAME ARITH : AD11


TOT CT=23622 CELL CT:MAX=249 MIN=0 AV=5 FRAME061
LT=0.5
UT=100.5
AD11
COMMAND: _
1 FRAME/5 SEC

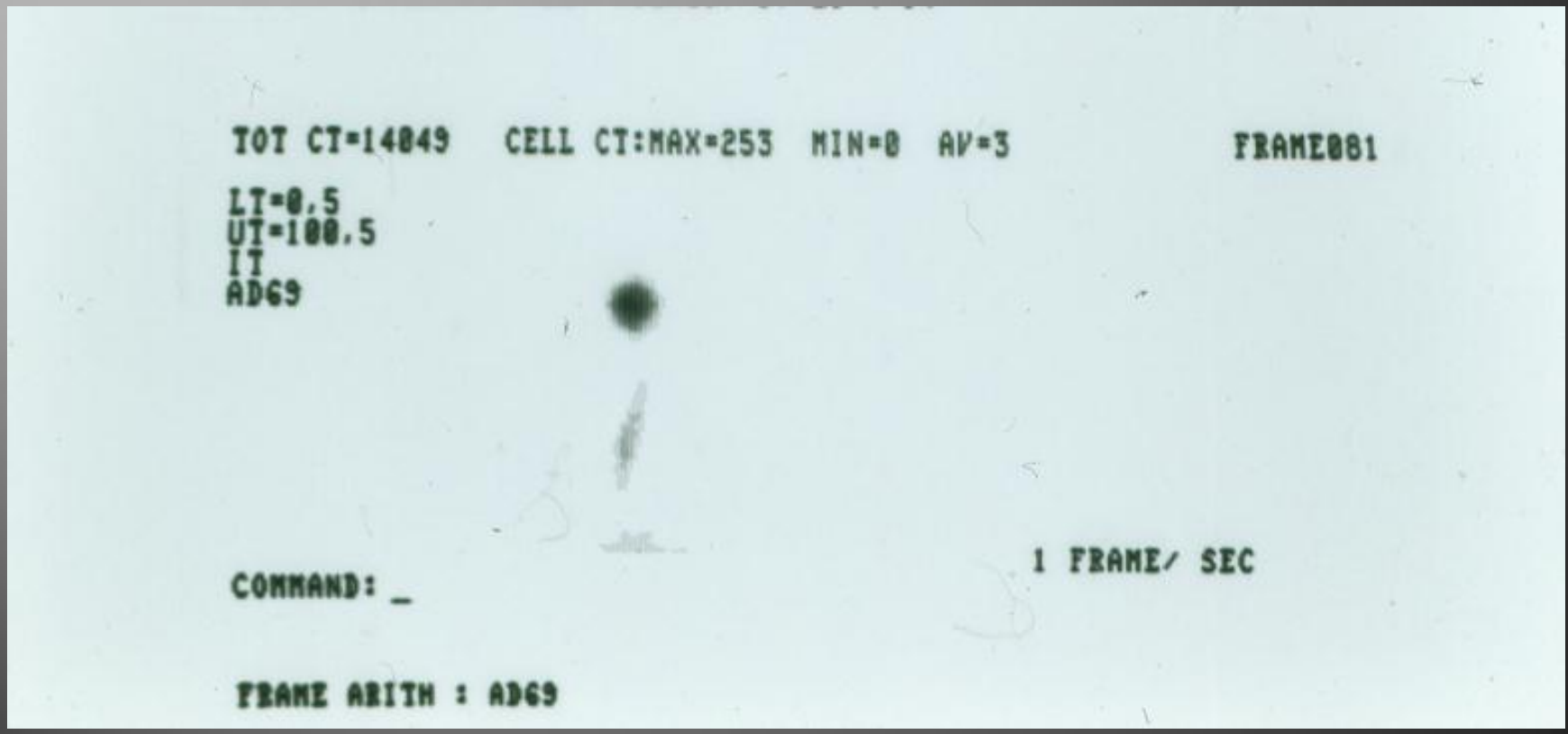

237
ROI A
0
212
ROI C
0
1
87
1
COUNT RATE VS TIME 87

COUNT RATE VS TIME

Residual refluxing urine



Residual refluxing urine



DRVC vs. VCUG

- DRVC has greater sensitivity

- Conway JJ. Radionuclide cystography. U: Tauxe WN, Dubowski EV, ur. Nuclear Medicine in Clinical Urology and Nephrology, Appleton-Century Crofts, Norwalks, Connecticut,1985:305-320.
- Smellie JM. Commentary: Management of children with severe vesicoureteral reflux. J Urol 1992;148:1676-1682.
- Dikshit MP, Acharya VN, Shihara S, Merchant S, Pardanani DS. Comparison of direct radionuclide cystography with micturating cystourethrography for the diagnosis of vesicoureteric reflux, and its correlation with cystoscopic appearance of the ureteric orificies. Nephrol Dial Transplant 1993;8:600-602.
- Kogan SJ, Sigler L, Levitt SB, Reda EF, Weiss R, Graifer J.Elussive vesicoureteral reflux in children with normal contrast cystograms. J Urol 1986;136:325-328.
- Jaya G, Bal CS, Padhy AK, et al. Radionuclide studies in the evaluation of urinary tract infections. Indian Pediatr 1996;33:635-640.
- Saraga M, Stanicic A, Markovic V. The role of direct radionuclide cystography in evaluation of vesicoureteral reflux. Scan J Urol Nephrol 1996;30:367-371.
- Marković V. Valjanost Kvantitativne direktne radionuklidne mikcijske cistografije i Mikcijske cistouretrografije u detekciji nedilatirajućih vezikoureteralnih refluksa u djece. [magisterij]. Zagreb:Medicinski Fakultet;2002.

Quantitative parameters

- In addition to higher sensitivity in the detection of VUR and 20-100 times less radiation, DRVC provides

- quantification of the whole range of operating parameters, ie. the volume of the bladder and refluxing urine volume at any stage time.

By quantitative analysis the following parameters can be obtained :

BC – bladder capacity (ml)

VB –volume of the bladder when VUR (ml) occurs

MRV –maximal refluxing urine volume (mL)

RU – residual urine (ml)

RRV –residual refluxing urine volume (mL)

VB/BC (%)- the occupancy of bladder when VUR occurs (bladder vol. (%) when VUR occurs)

MRV/BC (%)- percentage of maximum refluxing urine volume according to the capacity of the bladder

RRV/BC (%)- percentage of residual refluxing urine volume according to the capacity of the bladder

Quantitative parameters

Prognostic use:

- Reflux that occurs on the consecutive cystographys during increasing occupancy of the bladder, ie. later during the bladder filling, indicates on possible disappearance of the same *
- Reducing the volume of refluxing urine on consecutive cystographys also points to the disappearance of VUR *

*Nasrallah PF, Conway JJ, King LR, et al. Quantitative nuclear cystogram: An aid in determining spontaneous resolution of vesicoureteral reflux. Urology. 1978;12:654-658.

*Maizels M, Weiss S, Conway JJ, et al.The cystometric nuclear cystogram. J Urol. 1979;121:203-205.

Quantitative parameters

Prognostic use:

The patients in whom VUR appeared after 60% occupancy of the bladder at first DRVC had a lower risk at a later stage to be treated surgically *

It is also less likely that the patients, whose maximum refluxing urine volume is less than 2% of the bladder capacity are gonna be surgically treated

*Mozley PD et al. Direct vesicoureteral scintigraphy: Quantifying early outcome predictors in children with primary reflux. J Nucl Med. 1994; 35:1062-1067.

Quantitative parameters

* A higher degree VUR, characterized by quantitative parameters of the DRVC, has the following characteristics:

a) occurs earlier during bladder filling, ie. at lower-occupancy of bladder and lasts longer

b) yields a larger amount of refluxing urine

c) gives a greater amount of residual refluxing urine

*Marković V. Valjanost Kvantitativne direktne radionuklidne mikcijske cistografije i Mikcijske cistouretrografije u detekciji nedilatirajućih vezikoureteralnih refluksa u djece. [magisterij]. Zagreb:Medicinski Fakultet;2002.

DRVC vs. VCUG

- DRVC has a higher sensitivity
- DRVC provides continuous monitoring of the whole examination, ie. phase of filling and emptying of the bladder
- DRVC allows quantification of several functional parameters, some of which have prognostic value
- DRVC provides 20-100x lower dose of radiation, ie. for one VCUG 20-100 DRVC can be made
- VCUG has a better resolution image, ie. better morphological display of ureter, renal pelvis and calyx

Contraindications

- There are not.
- Implies that the child is not catheterised during the active phase of inflammation.

Indirect radionuclide voiding cystography

- Recorded in the continuation of dynamic renal study
- It does not require catheterization
- Seeking cooperation of the child (not urinate 1- 2 hours) - can not be recorded in young children up to 3 years, in which VUR is frequent and most important to diagnose
- Good renal function is needed
- No passive phase - only study of urination
- Significantly lower sensitivity than DRVC (41% false negatives examinations) *

*De Sadeleer C, De Boe V, Keuppens F, Desprechins B, Verboven M, Piepsz A. How good is technetium-99m mercaptoacetyltriglycine indirect cystography? Eur J Nucl Med. 1994 Mar; 21(3): 223-7.

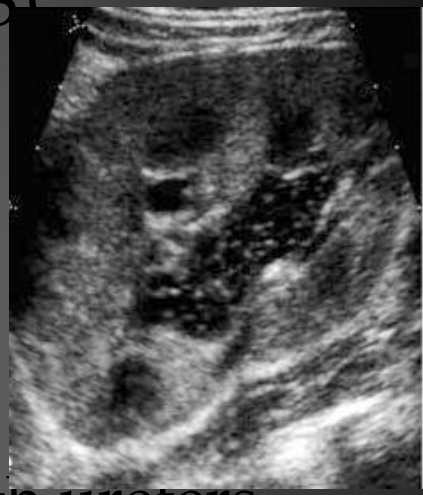
* Majd M, Kass EJ, Belman AB. Radionuclide cystography in children: comparison of direct (retrograde) and indirect (intravenous) techniques. Ann Radiol Paris. 1985; 28(3-4): 322-8.

*Cremin B J. Observations on vesico-ureteric reflux and intrarenal reflux. A review and survey of material. Clin Radiol 1979, 30; 607-621.

*Majd M, Belman AB. Nuclear cystography in infants and children. Urol Clin North Am. 1979 Jun; 6(2): 395-407.

*Merrick MV, Uttley WS, Wild R. A comparison of two techniques of detecting vesico-ureteric reflux. Br J Radiol. 1979 Oct; 52(622): 792-5.

Voiding ultrasonography (VUS)



- No radiation
- Catheterization is needed
- It is not possible to continuously monitor both ureters and kidneys during the emptying of the bladder
- There is no possibility of quantifying
- The image resolution is better than the DRVC
- Sensitivity: VCUG> VUS <DRVC

Due to the high sensitivity in the detection of VUR, the minimum radiation dose and prognostic value of some quantitative parameters; DRVC is used as the method of choice:

1. in the detection of VUR in girls of all ages

2. in the detection of VUR in boys older than one year

3. in monitoring patients on conservative treatment VUR

4. to assess the effectiveness of corrective procedures in patients with VUR

- 5. in brothers and sisters of patients with VUR or
- children whose parents had reflux or reflux nephropathy

6. in the detection of VUR in patients with transplanted kidney and detecting VUR in dysfunctional bladder diseases, such as neurogenic bladder

7. quantitative parameters, primarily the occupancy of the bladder when VUR occurs, are used in prognostic purposes, ie, in the decision between conservative and surgical treatment of VUR.

Scrotal scintigraphy

- Scrotal scintigraphy includes scrotal angioscintigraphy and static scrotal scintigraphy (sc. of the vascular space of scrotum).

- Dose: iv. 740 MBq (20 mCi) Tc-99m- pertechnetate as a bolus injection.

- Indications:

-**Testicular torsion**: reduced perfusion, and oval sc. cold zones on static sc.

- **Missed torsion:** reduced perfusion in the testicular artery and increased in pudendal artery; and the hot ring of the activity on the static sc. around the centrally located oval, sc. cold zone.

- **Acute epididymitis**: increased perfusion and increased uptake of crescent shape on the static sc.

- **Trauma**: increased perfusion and increased activitiy on the static scintigram.

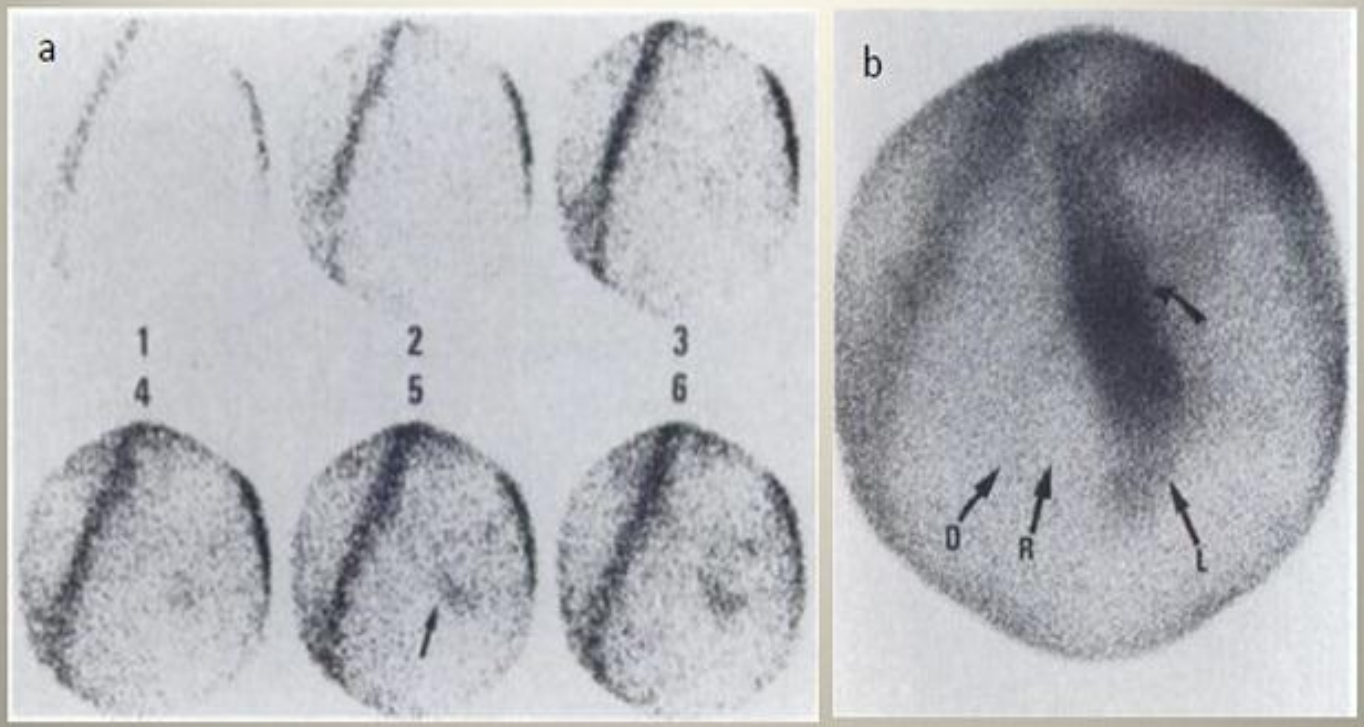
- Hematomas and hydrocele: crescent cold defect or oval sc. cold zone that expells testicle laterally.

- **Tumors**: usually increased perfusion and increased accumulation of activity on the static sc.

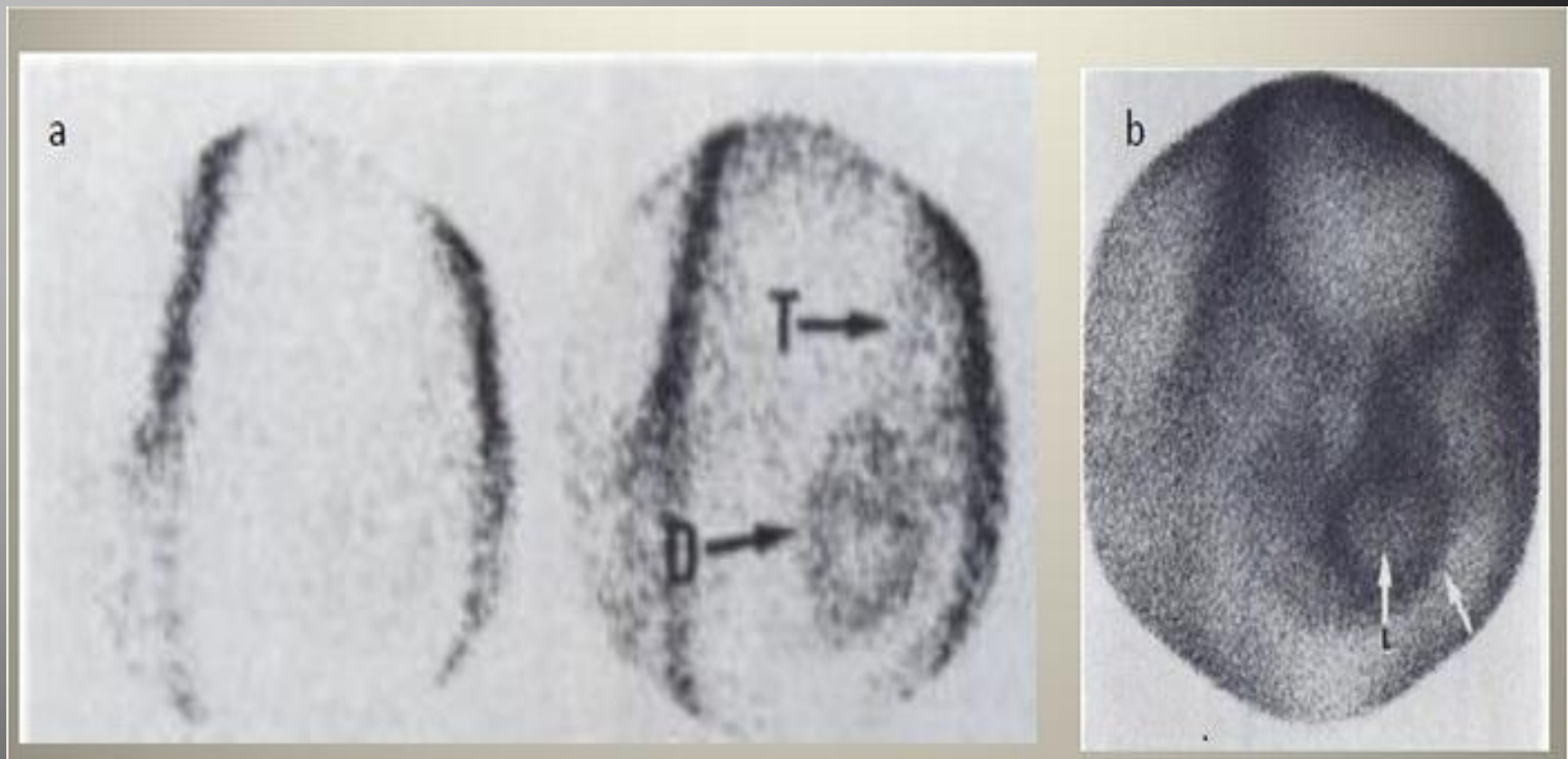
- **Varicocele:** normal arterial phase of the perfusion and intense uptake in the venous phase of the perfusion studies and on the static sc.

● as an **urgent** nuclear medicine examination, **scrotal scintigraphy** is used in **diff. diagnosis of testicular torsion** as an surgical emergency condition and **acute epididymitis** being treated conservatively because both conditions are present clinically with the same symptoms (swelling, pain and redness).

Testicular torsion

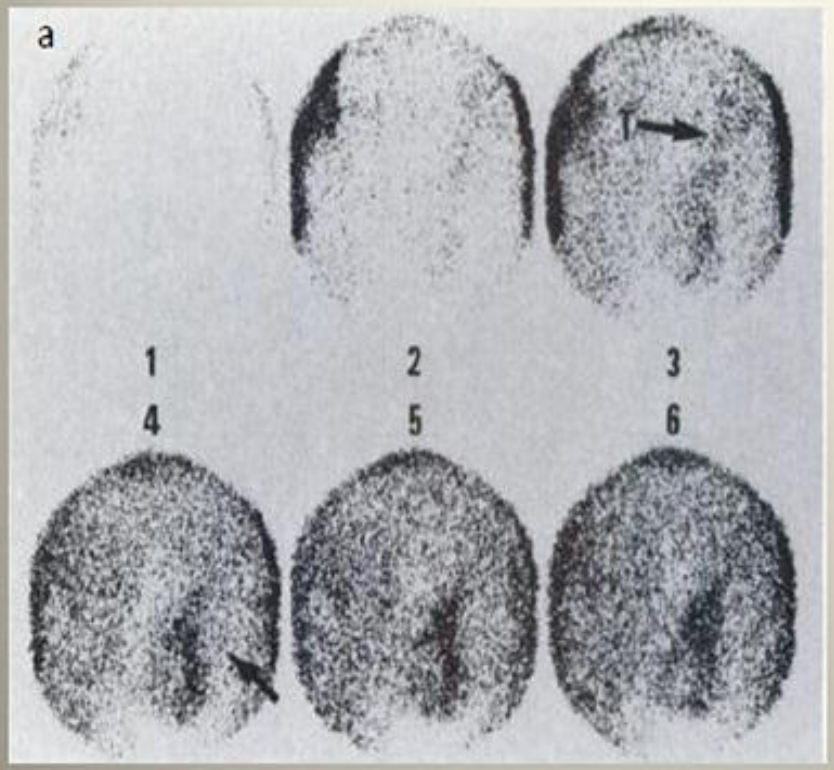


Picture 35. Testicular torsion - early phase: a) on angioscintigraphic part of study there is no perfusion in right hemiscrotum. In later phase of angioscintigraphic study the minimal scrotal perfusion can be seen in base of penis (the arrow); b) on the scrotal, static scintigram the avascular right testicle can be seen (R) without increased activity in dartos (D), with normal left testicle (L). The narrow arrow points on increasing activity in penis (if during the examination the same was not suspended cranially) that sometimescan be seen and there is no significant diagnostic importance to it.



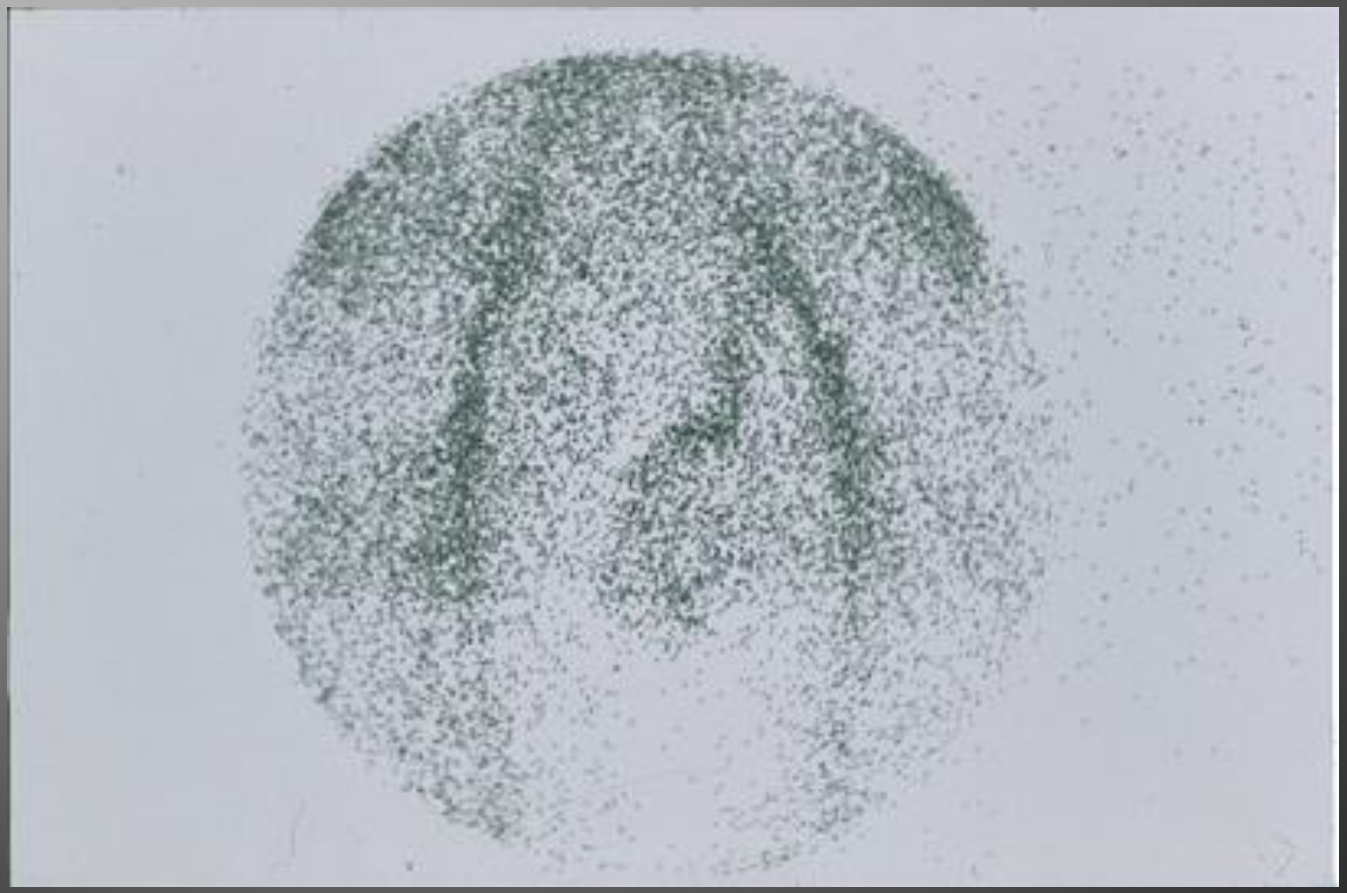
Picture 36. Testicular torsion - later phase: a) on angioscintigraphic part of study the increased perfusion, through left testicular artery (T), can not be seen, while the perfusion of dartos through pudendal artery is increased (D); b) on the static scintigram there can be seen the ring of increased activity accumulation around scintigraphic cold zone ie. the infarcted left testicle (L).

Epididymitis acuta

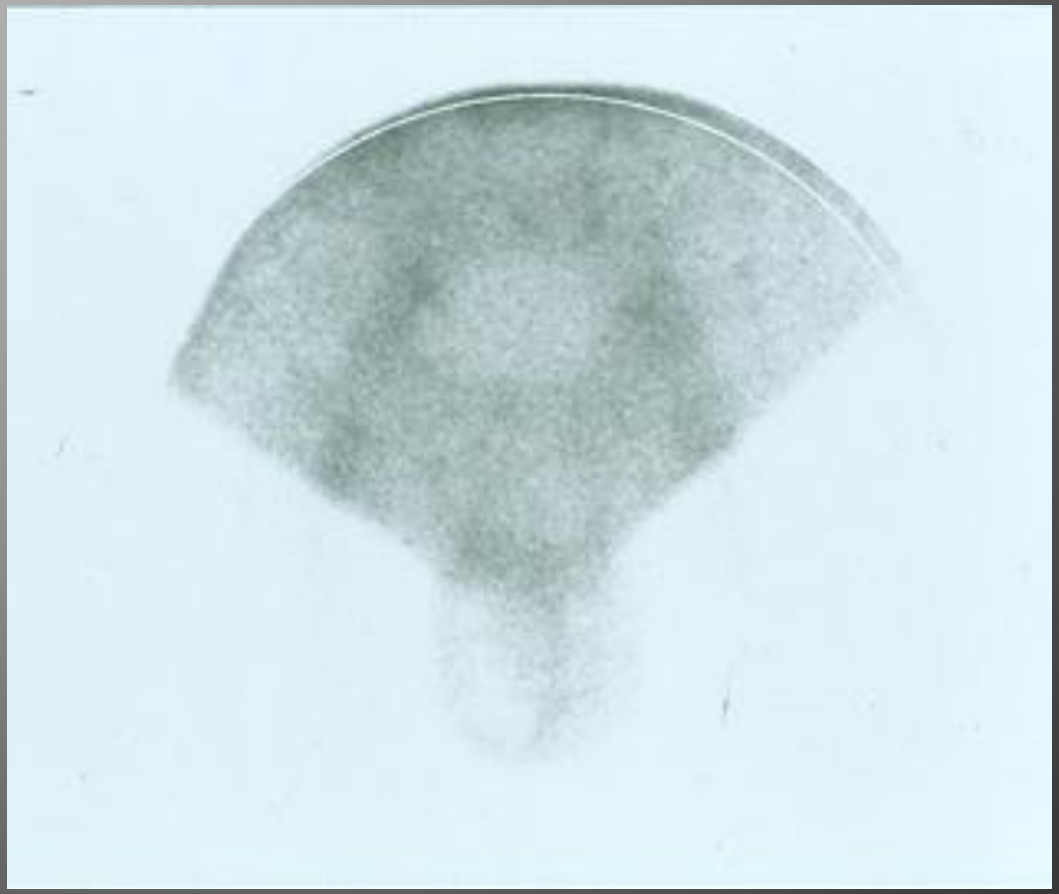


Picture 37. Acute epididymitis: a) on angioscintigraphic part of study the increased perfusion can be seen in testicular artery (T) and in part of epididymis of the left testicle (following the narrow shape of epididymis); b) on the scrotal scintigram there can be seen increased activity accumulation of semicircular shape in epididymis of the left testicle

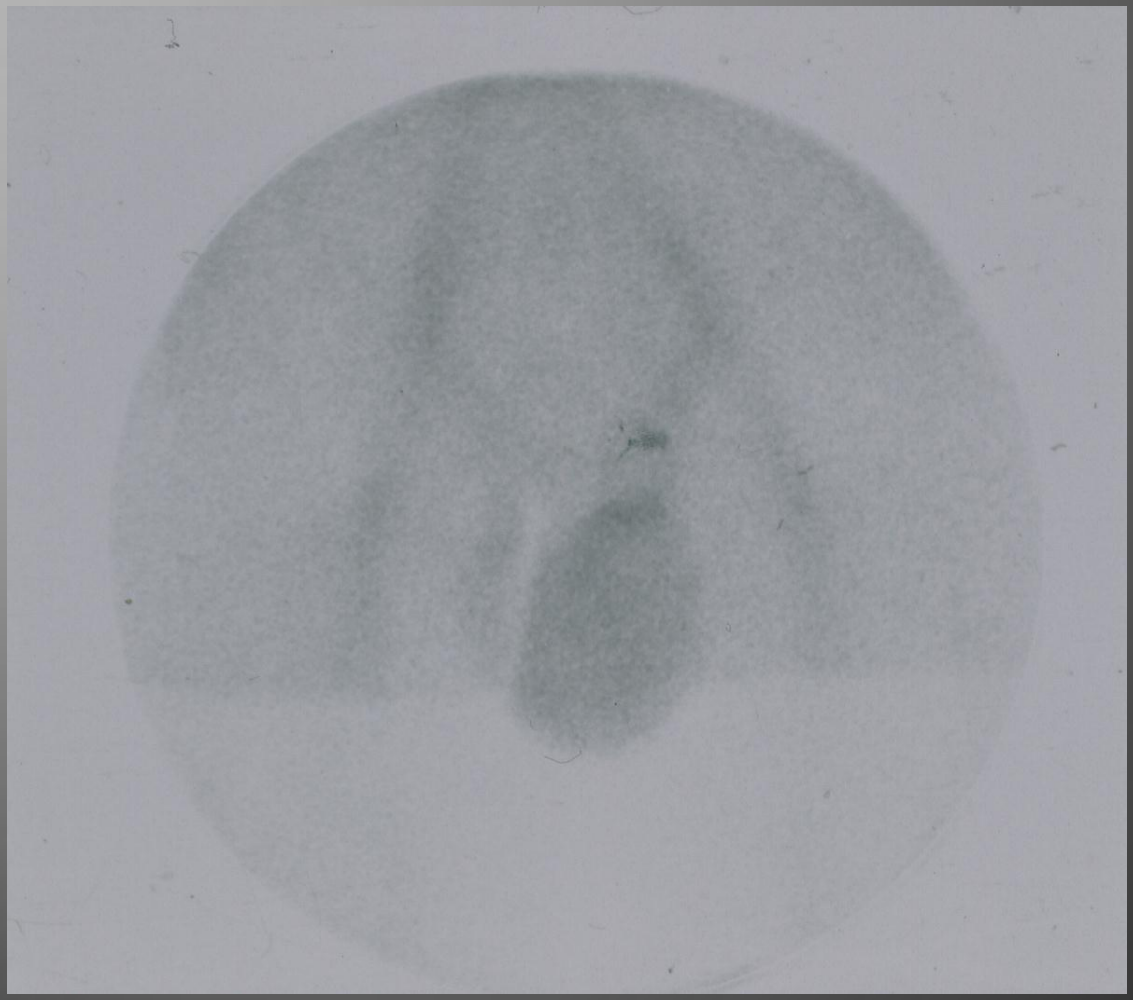
Acute epididymitis on the left side



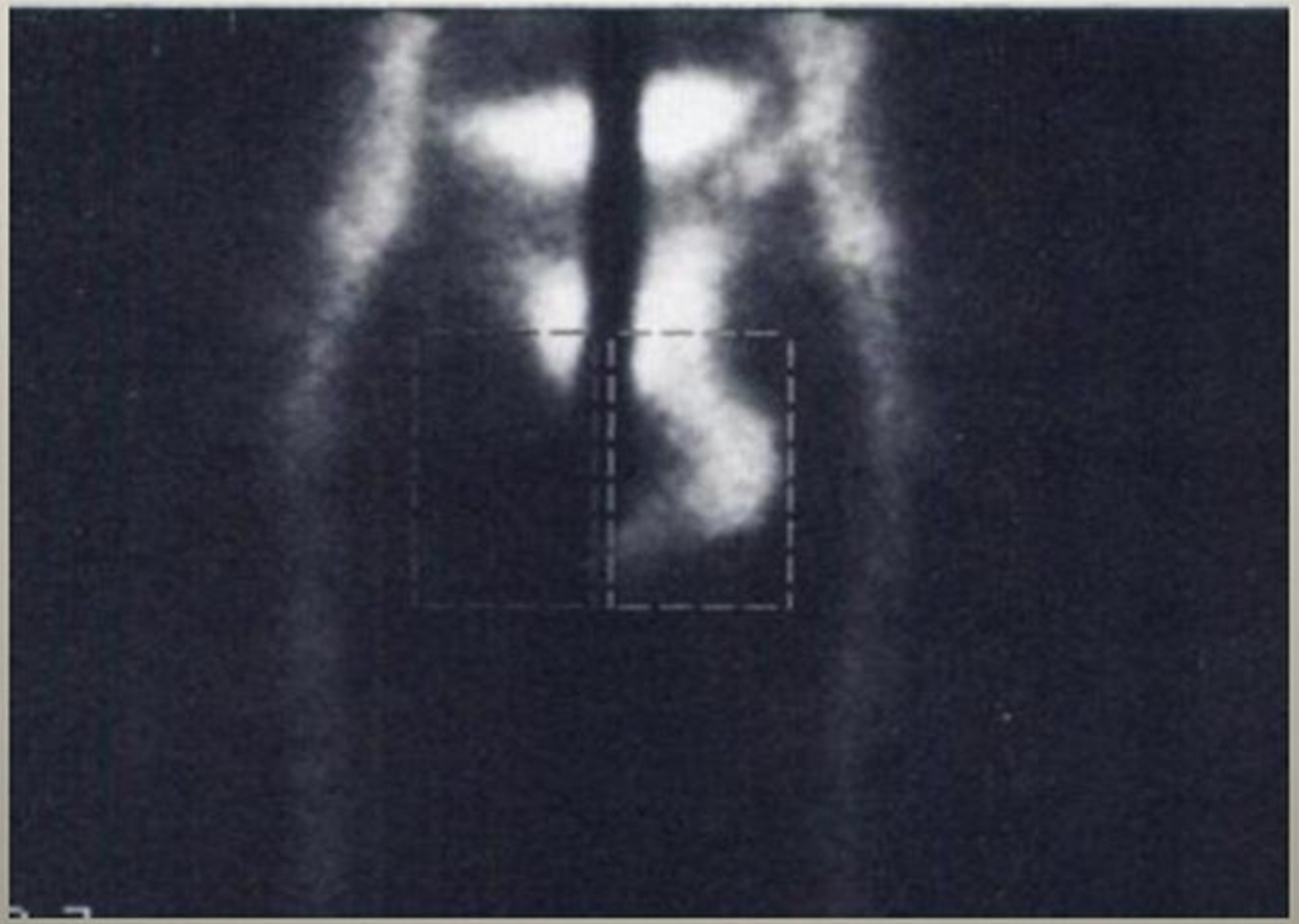
Hydrocele on the right side



Testicular tumor



Varicocele on the left side



Picture 40. Scrotal scintigram: varicocela on the left side

The end