

Kinetics of Radiopharmaceuticals in the Kidney as a Whole and in Different Regions of Interest

Karl zum Winkel, Ferdinand Marx, Horst-Michael Sonderkamp,
Heidemarie Jost, Lothar Schertel, and Günter Golde

The Universitäts-Strahleninstitut Berlin, Klinikum Westend
(Director: Prof. Dr. K. zum Winkel)

Physiology

The kidneys maintain the water and electrolyte balances of the body and eliminate numerous metabolic products. There are three different mechanisms serving these purposes

1. glomerular filtration
2. tubular secretion
3. tubular reabsorption.

Regarding the renal scanning the introduction of the "tubular fixation" as a 4th mechanism seems to be useful.

The glomerular filtration as well as the tubular secretion take place in the renal cortex. As an average the filtration rate is 19 per cent; that means 19 per cent of the renal plasma flow becomes glomerular filtrate. The glomerular filtrate entering the tubules of the nephron flows through the proximal tubule, through the loop of Henle into the distal tubule and through the collecting duct into the renal pelvis. Along this course, substances are additionally secreted or selectively reabsorbed by the tubular epithelium. The proximal and distal tubules are situated in the renal cortex, the other parts of the nephron are located in the renal medulla.

Radiopharmacology

The basic mechanisms of the renal function can be studied using radioactive labelled compounds; some by measurements on samples in vitro, others by external measurements in vivo.

Glomerular filtrated substances are ^{131}I -Inulin or Chelates labelled with $^{113\text{m}}\text{In}$ or ^{51}Cr . Tubular reabsorbed radiopharmaceuticals are Iodide or Per-technetate. Hippuric acid is eliminated by tubular secretion, whereas considerable parts of Diodrast due to their hepatic excretion can be measured in the biliary tract, too. Mercury compounds as well as Technetium-Iron-Complexes are eliminated by tubular fixation within the cells of the proximal tubule or the distal tubule, respectively.

Methodical and technical bases

Since 1964 we performed some experimental and clinical studies in Heidelberg and since 1969 in Berlin with the scintillation camera. Usually, a sequence of scintiphotos was performed after the intravenous injection of a radiopharmaceuticals excreted either by tubular secretion or by glomerular filtration only.

We used this method for 4 reasons

1. we had learned that renograms performed with displaced detectors are misinterpreted
2. using scanning the state of the radioactivity distributed in the renal parenchyma can be estimated, Kinetic changes are not registered
3. because most of the patients with renal diseases suffer from inflammatory and vascular diseases or from a disturbed evacuation of the upper urinary tract we took a special interest in Kinetic changes

4. an exploration of the functional and the morphologic proceedings within the renal perenchyma seemed to be important because by X-ray methods informations are obtainable only about the renal vascularization and the morphology of the upper urinary tract.

Using the sequential scintigraphy we could record the tracer inflow and its parenchymatous distribution, intrarenal transport and evacuation from the pelvic region. For this reason 1 hour after 10 ml of fluids per 1 kg body weight 500 μ Ci ^{131}I -o-Iodhippuric acid or 1 to 2 mCi $^{113\text{m}}\text{In}$ -EDTA are injected. During the first minute 2 scintiphotos are performed with an exposure time of 15 sec each. Thereafter, the exposure time is 2 min; further scintiphotos are made 1, 4, 8, 14 and 24 min after the injection.

An Irtetechnique store system of a 4096 channel analyzer and an Ampex digital tape was installed in 1970. This system is computer compatible and allows the functional evaluation of the kidneys by minimizing the radioactivity of the pararenal tissues. During the examination of the patient an integral is made on the store oscilloscope of the Inter-technique system. Then the digital magnetic tape is replayed, 4 regions of interest are determined by means of a light pen, and the curves of the 4 selected areas are draw simultaneously. Each point of these curves corresponds with the integral of the radioactivity in the area. Using diverse periods of 3, 6, 12, 24 and 48 sec, respectively, we prefer a period of 3 or 6 sec for each registration. In this way the radiopharmacokinetics in distinct parts inside or outside of the kidney or of the whole organ are revealed. As a routine this operation does not require more than 8 min.

Aside from numerous crinical examinations mostly performed as a routine method a lot of experimental studies improved our knowledge of the pathophysiological conditions, which leads to the optimal interpretation of the obtained results.

Experimental basis

With the aid of deep frozen microautoradiography the movement of ^{131}I -o-Iodhippuric acid in the

renal cortex was disclosed. For this reason rats in mannit diuresis were examined. An exact localization could be made because of the small microscopic sections of 5 μ thickness and because of the alternative use of the sections for autoradiography and microscopy. 5 sec after the intravenous injection the radioactivity was located preponderantly in the glomerula, small parts were seen in the proximal tubule. 10 sec after the iniecton the radioactivity was situated in the proximal tubules. After 60 sec some further cortical deposits of radioactivity were found.

Using radiopharmaceuticals labelled with soft gamma-ray emitters such as ^{125}I , we have differentiated their kinetics in the renal cortex from that in the organ as a whole (zum Winkel et al., 1968). In anaesthetized dogs a single-hole collimator with a cylindrical aperture of 1 cm was placed first over one decapsulated kidney in such a way that the cortex as well as the medulla and the pelvis were registered globally. After the intra-aortic injection of Radiohippuric acid or Radioinulin, both labelled with ^{125}I , curves are registered which correspond with the conventional renograms performed after the intravenous injection of compounds eliminated either by tubular secretion or glomerular filtration only. Note that the peak is not reached before 2 min. Due to the rapid tubular reabsorption, when radioiodine was applied after an initial rise led the radioactivity fall continuously.

In positioning the collimator exclusively over the upper pole for the predominant registration of the renal cortex only we obtained different renograms. After Radioinulin the highest radioacactivity was registered immediately. Thereafter, a plateau was observed during nearly 20 seconds, which was followed by a decreased radioactivity. The radioactivity increased again 40 sec after the injection; after nearly 1 min a definite decline ocured. These curves corresponded well with the passage of the simultaneonsly applied Lissamingreen through the cortical vessels, the proximal and the distal tubules observed by in-vivo incident light microscopy. Both, Inulin as well as Lissamingreen are excreted by glomerular filtration

only. Passing the loops of Henle the radioactivity dropped, while the dye could not be seen on the surface of the kidney. Because of the extraction rate of Inulin is only 20 per cent, the initial peak of the renogram is the highest. In contrast, because of the additional tubular secretion the radioactivity is much more concentrated following Radiohippuran. The passage times through the loops of Henle and through the distal tubules, however, are the same as after Inulin. As these findings suggest equal passage times for Hippuric acid and Inulin, we suppose the transit time for the transfer of Hippuric acid from the peritubular capillaries through the tubular cells to the lumen of the proximal nephron does not exceed several seconds.

Further experimental studies in dogs were performed as series scintigraphies. On the whole the movement of the radioactivity toward the renal medulla and pelvis was revealed. Moreover, the pelvic evacuation could be found out by the decreased radioactivity. Injecting the same amounts of ^{131}I more radioactivity was seen after Hippuric acid because of the tubular secretion. Nearly the same radioactivity could be observed after Inulin as after Hippuric acid, when in consequence of a previous infusion of 4 g para-amino-hippuric acid (PAH) the tubular secretion was inhibited by overloading and the glomerular filtration H_2S resulted only.

Scintiphotos taken with the scintillation camera and with an exposure time of 10 sec each showed 5 to 15 sec after the intraarterial application of ^{131}I -o-Iodhippuric acid a bigger area of radioactivity than those made from 23 to 33 sec. Thereafter, the area was larger again, but diminished afterwards. The smaller area corresponded with the passage time of Lissamingreen through the loops of Henle. Although the concentration was somewhat lower similar results were noticeable after Inulin. The changes in size could be revealed by planimetry of the areas, too. After the injection of Sodium-Iodide, which is reabsorbed in the proximal tubules, an initial concentration was seen followed by a continuous decrease. Radioactivity was found in the dogs stomach after 15 min.

In dogs unilateral renal artery stenosis performed by clamping led to a reduced initial uptake of Hippuric acid or Inulin and a delayed transport of the radioactivity within the affected kidney. The evacuation occurred delayed due to the reduced urine flow. However, the reabsorption of Iodine was less affected after clamping the renal artery even to a pressure of 40 mm of Mercury. If the blood pressure of the examined kidney was kept down to an average of 30 mm Mercury no uptake of Inulin took place. However, the affected kidneys still showed some accumulation of Hippuric acid.

Simulating an ureter obstruction by increasing the ureteral pressure to 60 cm of water we observed in dogs nearly the same accumulation of Hippuric acid and Inulin in both kidneys; this means the inflow nearly was untouched. The renal pelvis of the affected side did not empty. The passage time of Lissamingreen were considerably prolonged.

Clinical results

Renograms performed by Motzkus and Bachmann after the injection of Radiohippuric acid into the renal artery showed an initial rise followed by a slight decrease because of the incomplete extraction of the radioactivity. The recirculation of that passed compound caused sometimes a slight increasing after 2 min. Thereafter, the decreasing curve demonstrated the evacuation of the renal pelvis.

Serial scintigraphies of the kidneys we performed in more than 4000 patients. Since a long time this method is used as a routine. Thus, within one year (March 1970 till March 1971) 657 patients were examined. In August 1969 a scintillation camera was installed in the Universitäts-Strahleninstitut Berlin. Since this time entirely 1247 patients were examined, the Intertechnique storage system was used to make functional curves in 856 of these patients.

We proved 28 patients after both radiopharmaceuticals, Radiohippuric acid and Indiumchelate (Hauhold et al.). As well known in normal function the peak is somewhat lower after compounds glomerular filtrated and the evacuation somewhat smaller than

after Radiohippuran which is tubular secreted. Thus, 20 min after EDTA nearly 40 per cent of the peak radioactivity are registered. 20 min after Hippuric acid only 20 to 25 per cent of the amount of the peak are measured. The reason for this difference is the rarely recorded background.

Comparing curves of the kidney as a whole with such of the renal cortex preferentially the peak time occurred earlier. In that connection it must be mentioned, that most of the patients were examined in sitting upright.

74 per cent out of 43 patients with reduced blood flow due to renal artery stenosis had pathologic signs in serial scintigraphy as a reduced tracer appearance, a reduced concentration or a delayed evacuation (table 1). Orthostatic disturbances of the renal blood circulation due to a nephroptosis could be recognised if the examination was carried out in prone position and in sitting upright. In some cases with renal artery stenosis the serial scintigraphy showed normal results, whereas a different amount of radioactivity was observed by plotting curves with the aid of a computer during 2 or 3 min.

pathological signs in the sequential scintigraphy of 43 patients with renal artery stenosis proved by angiography or operation: 38 unilateral including 4 segmental and 5 bilateral stenoses

(Feine and zum Winkel)

reduced inflow during the initial phase (15 to 30 sec)	29 (67 per cent)
reduced concentration during the parenchymal phase (1 to 3 min)	23 (54 per cent)
shrunk area of uptake	15 (35 per cent)
delayed evacuation out of the pelvis (reduced urine volume)	12 (28 per cent)
false results (negative 5, false side 6)	11 (26 per cent)

Table 1.

In several patients with hypernephroma we observed an inverse effect. Within 40 sec an increased radioactivity was seen in a region thereafter missing any uptake (Rosenthal). The inverse effect was to reveal by means of functional curves made with the storage system, too, especially by plotting the curves during 1 min after the application of Pertechenetate

(fig. 1). In cysts a permanent lack of radioactivity was found. Although we did not find remarkable differences between Radiohippuric acid and Chelates we prefer for the examination of the renal vascularization the application of pertechenetate or Chelates.

A remark should be given upon the functional changes in diffuse vascular diseases as nephrosclerosis (fig. 2). We learned a nearly constant renal distribution of Radiohippuran during half an hour and more without a visible movement toward the renal pelvis. The curves corresponded with the scintiphotos. Similar changes were seen in patients suffering from glomerulonephritis.

78 per cent out of 236 patients with inflammatory or degenerative renal diseases showed pathologic results as delayed intrarenal transport, reduced inflow and concentration, delayed evacuation or shrunk parenchyma (table 2). According to these results a hypoplastic kidney with its concentration and intrarenal kinetics on time could be distinguished from the contracted kidney due to pyelonephritis, which showed a delayed concentration and a delayed transport. In pyelonephritis the functional curves demonstrated a reduced concentration and a delayed descent. The relation of the peak radioactivity with that after 20 min was higher than normal. After therapy the curves were normalized, i. e. the concentration was higher and the radioactivity decreased more rapidly (fig. 3). Some patients with a silent kidney in pyelography without excretion of contrast medium had a slight accumulation of Radiohippuran in the affected kidney, the curves showed a slight concentration. These curves could differ from the conventional renogram because of the subtracted background. On the other side, with the aid of the integral curves a delayed peak or a delayed fall of radioactivity in the evacuation phase sometimes was more evident than in the renogram, which simulated a normal descending radioactivity due to the measured background. The integral curves were important for revealing small differences of the inflow, the peaktime and the evacuation in unilateral pyelonephritis (fig. 4). Special clinical interest had the results in circumscribed regions with functional disturbances. Although,

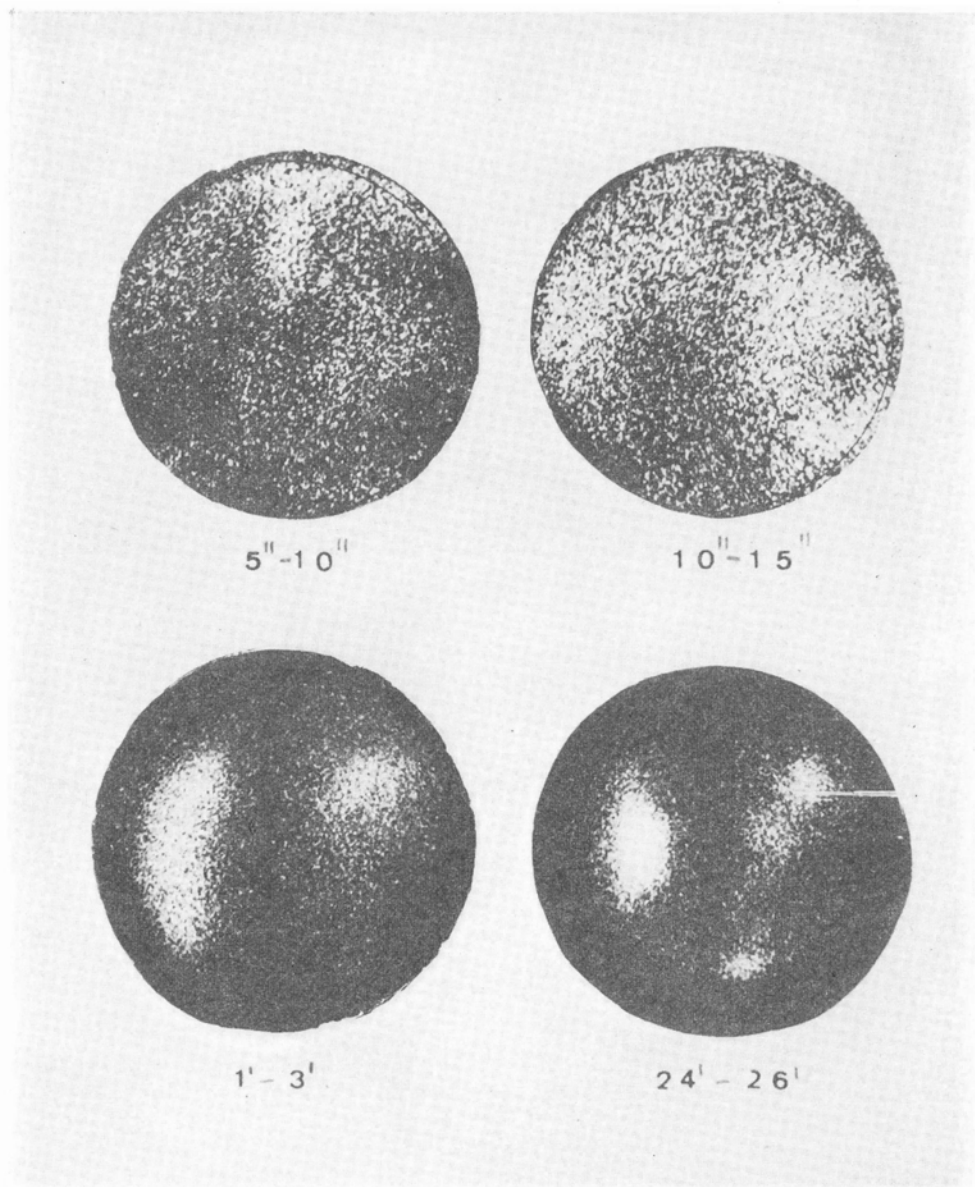


Fig. 1. a) Angioscintigraphy after $^{99m}\text{TcO}_4$ (bottom) and serial scintigraphy after ^{131}I -o-Iodohippuric acid (below) in a patient with hypernephroma of the right kidney: high vascularization in a region thereafter missing any uptake.

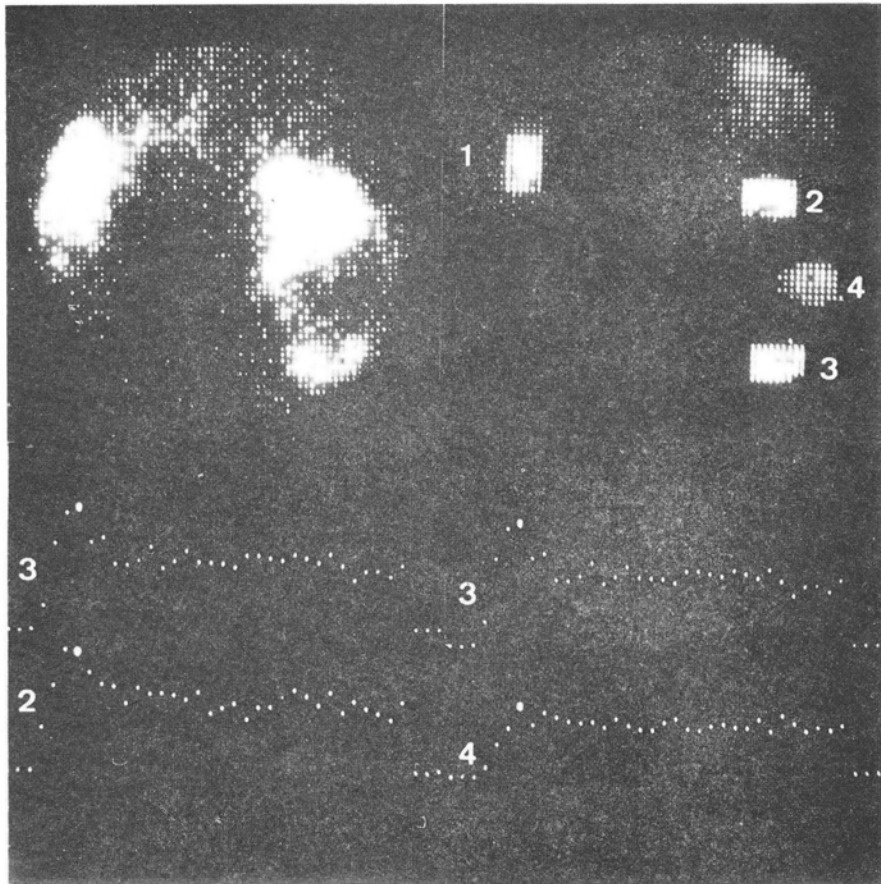


Fig. 1. b) Store scintigram, regions of interest and integral curves after Pertechnetate: initial peak followed by decreasing with the exclusion of region 4 corresponding to a central necrosis.

Pathologic signs in the sequential scintigraphy of 236 patients with inflammatory diseases (201 chronic and 8 acute pyelonephritis, 3 interstitial nephritis, 1 gouty kidney, 18 glomerulonephritis, 5 polycystic disease)
(Feine and zum Winkel)

delayed intrarenal transport	132 = 56 %
reduced concentration in the cortical phase	123 = 52 %
shrunk parenchyma	96 = 41 %
other pathologic findings	
delayed drainage of the renal pelvis	53 = 22 %
irregular contours	12
non-functioning kidney	1
negative results	66 = 28 %
53 = 22 %	

Tadle 2.

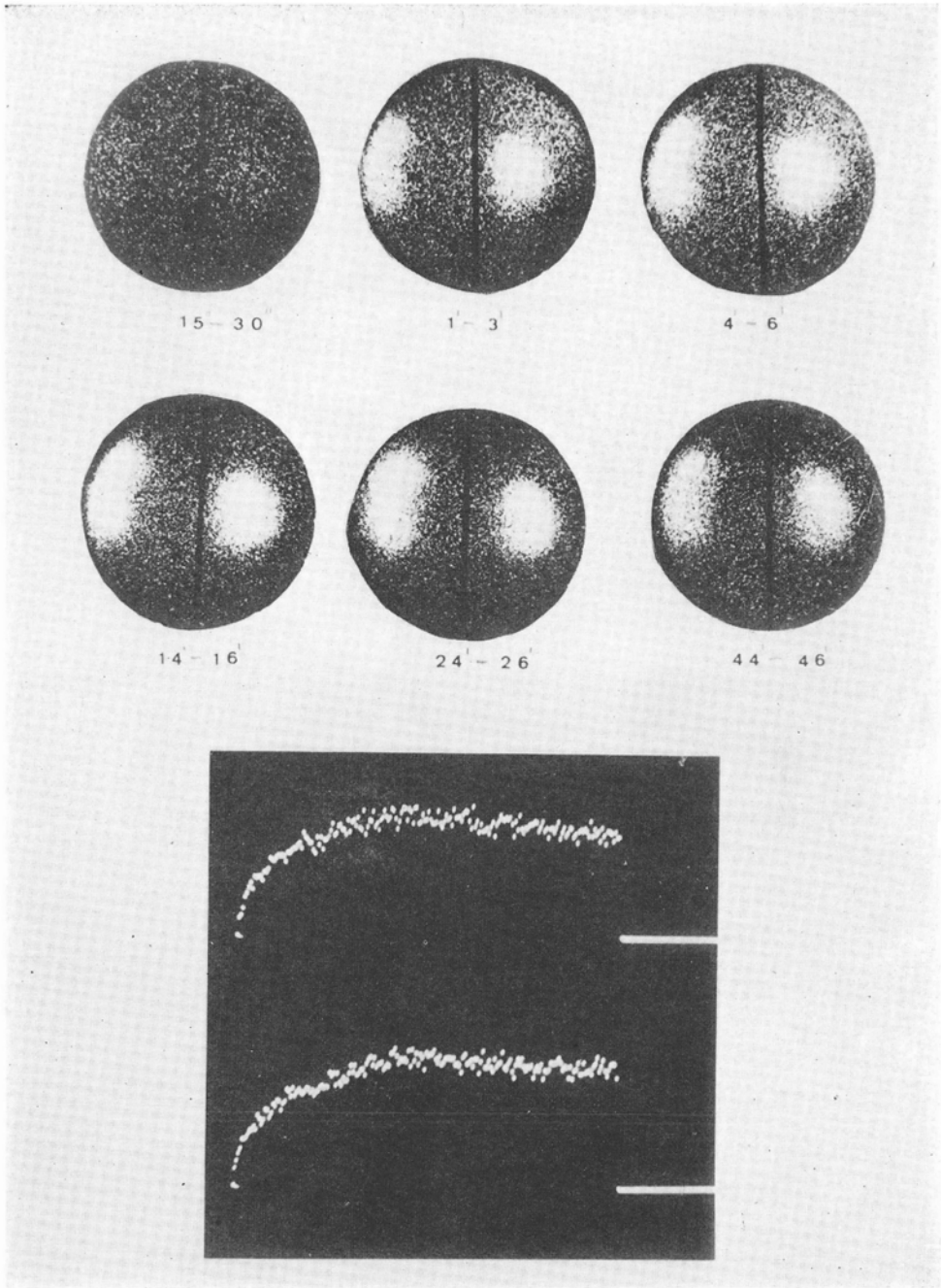
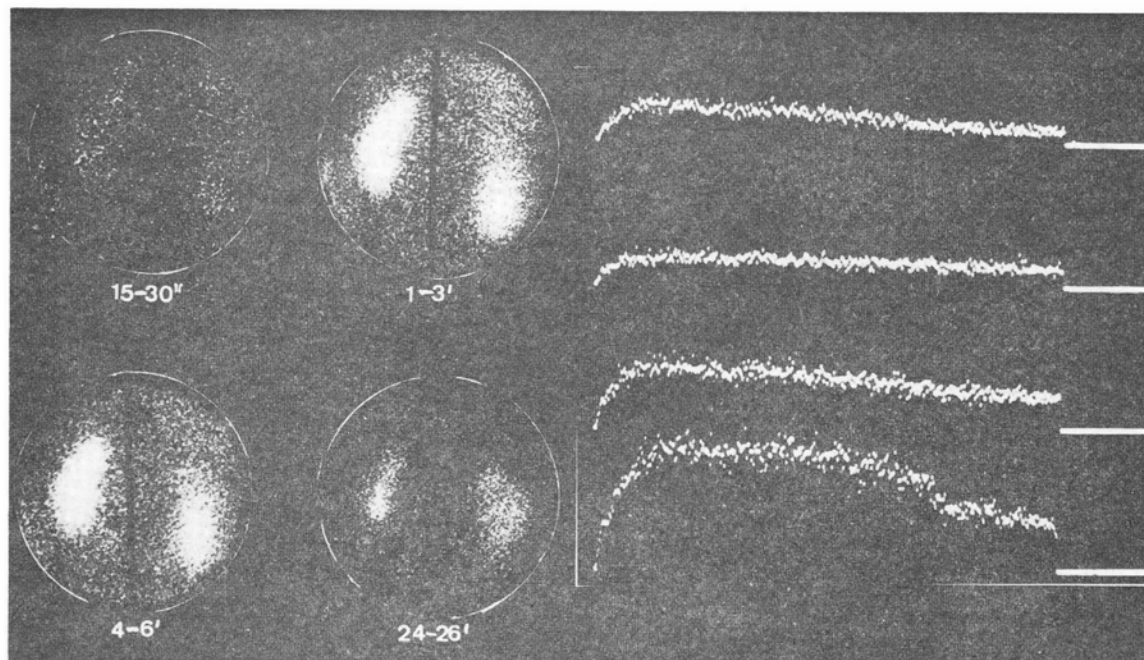
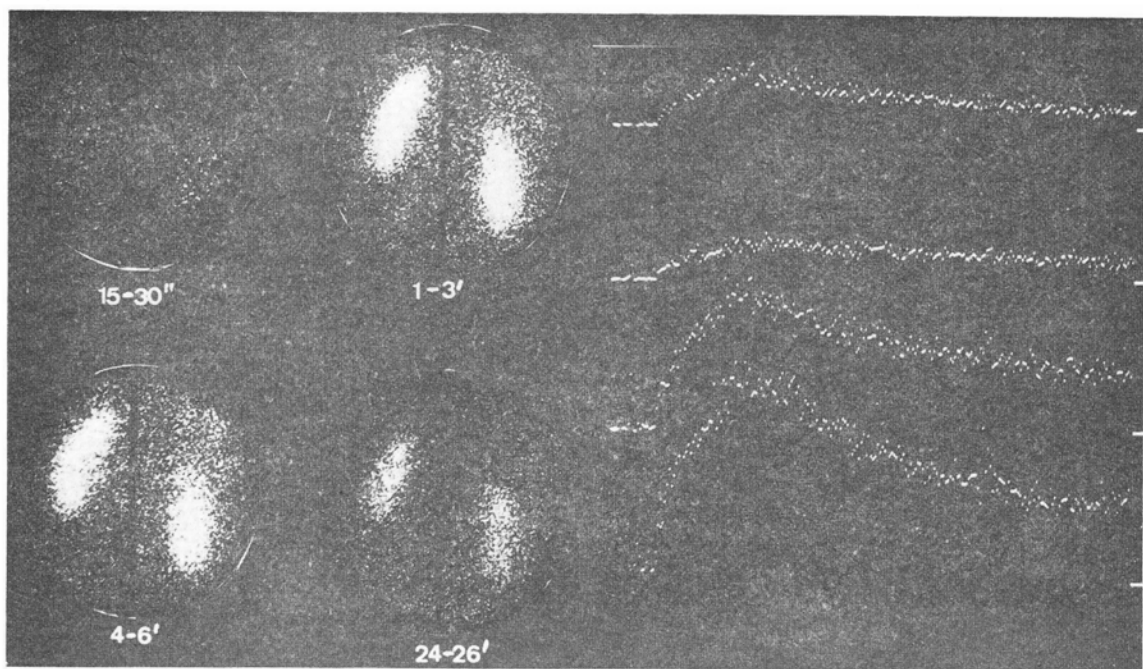


Fig. 2. Serial scintigraphy and integral curves of both kidneys in nephrosclerosis after i. v. ^{131}I -o-Iodhippuric acid ($500\ \mu\text{Ci}$): delayed inflow, distinct concentration, nearly no transport within the organs and delayed evacuation. Contracted right kidney.



(a)



(b)

Fig. 3. Serial scintigraphy and integral curves of the right lower and upper pole, right and left kidney on whole in bilateral pyelonephritis before (a) and after (b) therapy. Note the tendency to normalization.

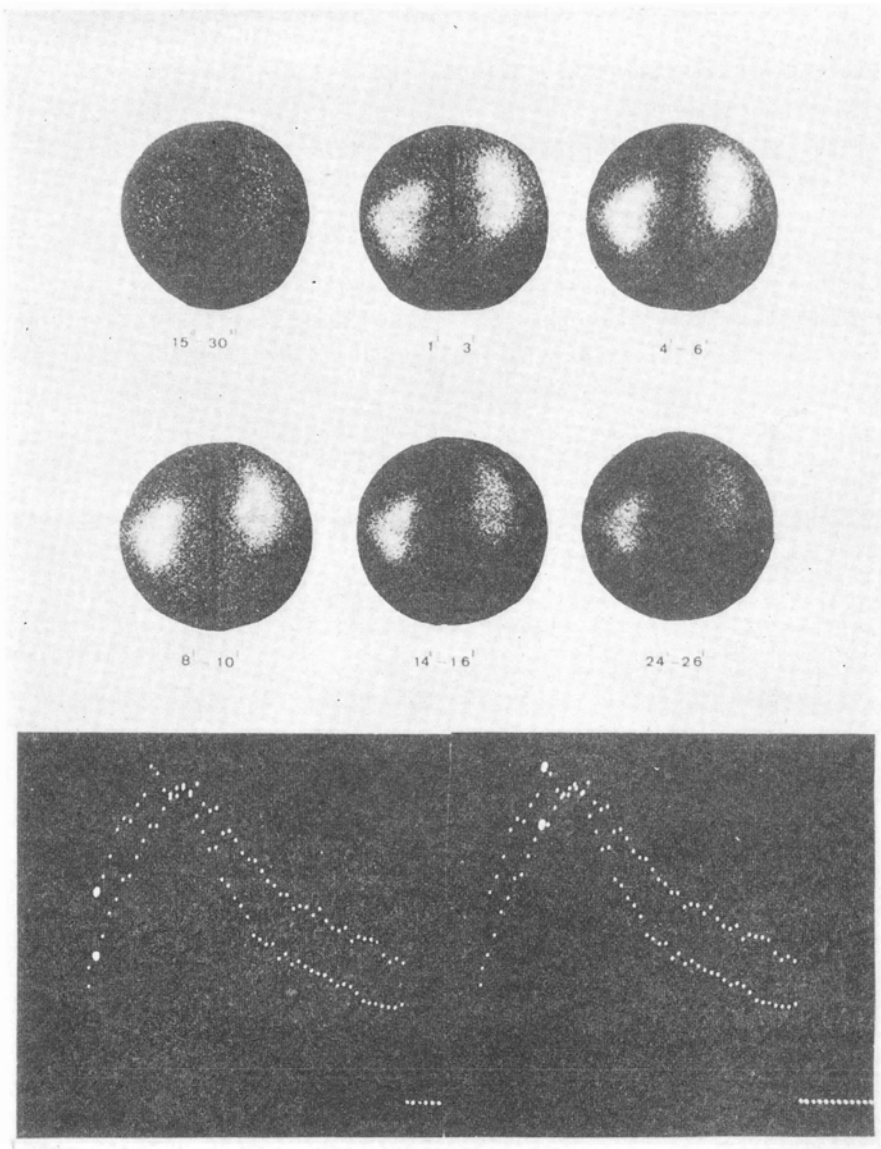


Fig. 4. Serial scintigraphy and functional analysis after 500 μ Ci ^{131}I -o-Iodohipuric acid in pyelonephritis of the left kidney: the initial peak is marked, it is reduced on the left side; the marked peak of the right side demonstrates the delayed peak and the delayed evacuation of the left kidney.

some remarks could be made regarding the results of the serial scintigraphy, the integral curves revealed more functional details as a reduced concentration and a missing evacuation. Sometimes, the curves of the whole organ were influenced particularly by the radioactivity of only one part (Fig. 5). On the other side, a partial regions could show quite a different slope of the radioactivity in comparison with the whole organ.

In several patients with urologic diseases we also obtained interesting results. Hydronephrosis due to a concrement led to a prolonged stay of radioactivity in the renal pelvis. The curves drawn from the renal parenchyma and the renal pelvis gave informations about the disturbed evacuation; sometimes

differences in time between the parenchymatous and the pelvic regions existed. Moreover, it could be ascertained, that the functional curve of the whole organ was composed by two different components corresponding the renal cortex and the renal pelvis. Thus, the cortex showed a peak within a few minutes followed by a constant decrease, whereas in the pelvic region due to an obstruction a considerable delayed peak and a horizontal slope resulted. In patients with polycystic diseases both, the serial scintigraphy as well as the curves were important to obtain the best information about the morphologic and functional status (Fig. 6).

In renal transplantation a distinct accumulation of radioactivity which should be at least three times of

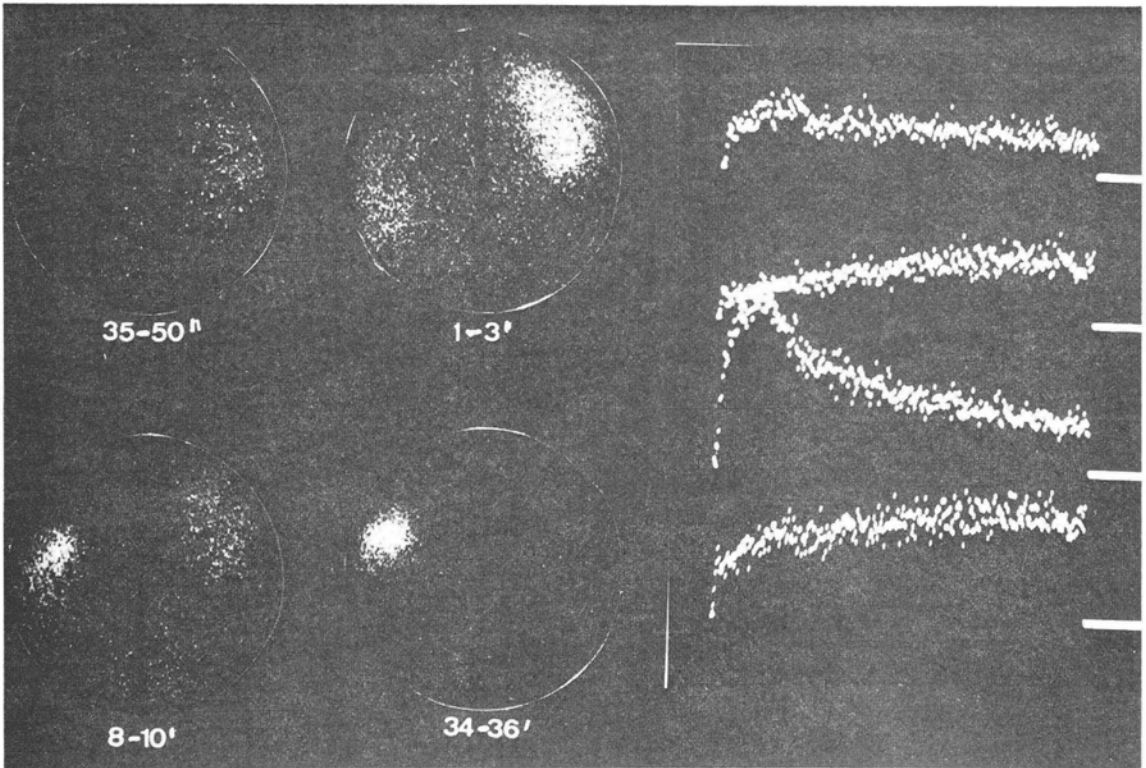


Fig. 5. Serial scintigraphy and functional analysis of the left lower and upper pole, the right and the left kidney (from bottom to top) after 500 μ Ci ^{131}I -o-Iodohippuric acid in pyelonephritis and pelvic concrement of the left kidney: reduced inflow and no evacuation on the left upper pole, the renogram of the left side is mainly influenced by the slope of the radioactivity in the left upper pole.

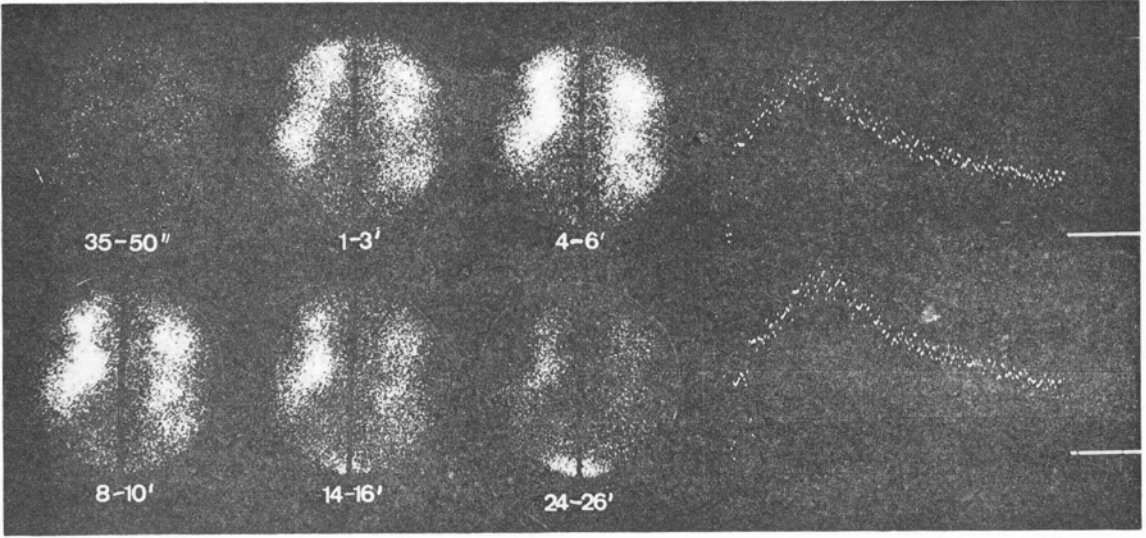


Fig. 6. Serial scintigraphy and functional analysis of the right (bottom) and the left (below) kidney in polycystic disease. Note the big defects in the enlarged kidneys, whereas the renal function is only less affected.

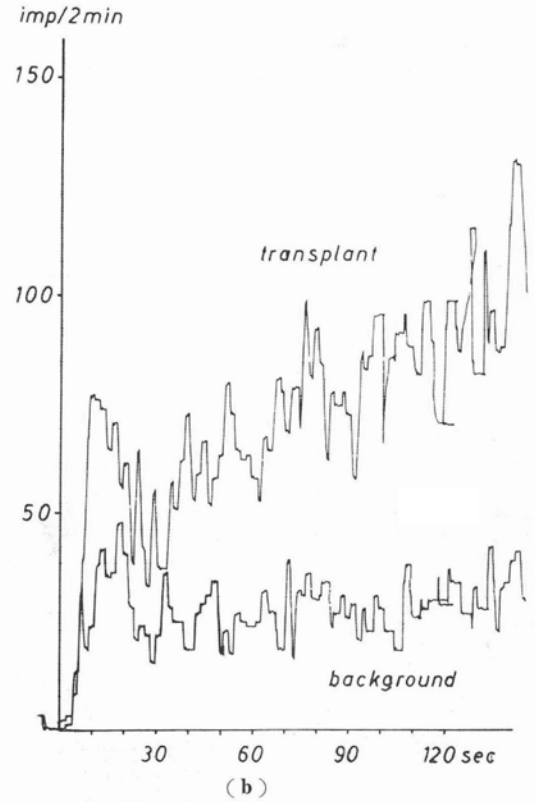
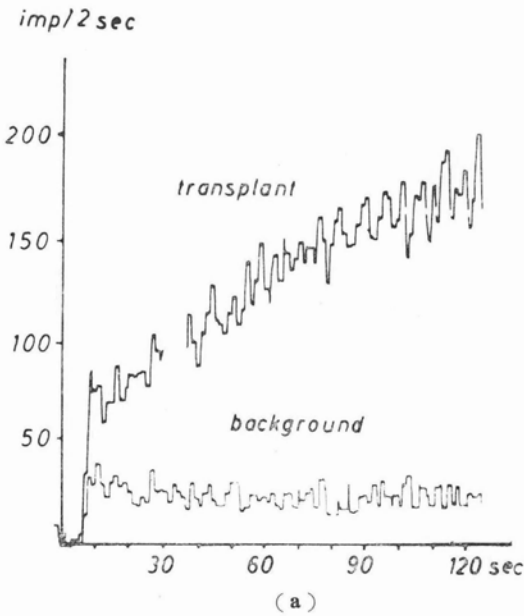


Fig. 7. Plotted curves of the whole kidney in renal transplantation and the background after 500 μCi ^{131}I -o-Iodohippuric acid in normal function (a) and in rejection (b). In rejection after the initial peak a decrease is seen in the transplant, probably caused by a reduced extraction rate.

that in the background, must be seen till 30 sec after the intravenous injection of Radiohippuran. An intrarenal transport or radioactivity in the bladder should be observed after 6 min at the latest. The transplant should contain only less radioactivity after 15 min. In renal artery thrombosis no radioactivity could be detected in the transplant (zum Winkel et al., 1968). Experimental studies in dogs revealed in rejection a reduced and delayed tracer appearance, a delayed intrarenal transport or a delayed evacuation (Müller-Beirrenhirtz). The digital evaluation of the curves demonstrated a descending radioactivity within 15 sec after the initial rise. As we obtained the same results in patients with rejection of the renal transplant we explain that sign as a reduced extraction rate of Radiohippuric acid (Fig. 7).

Regarding the results of the sequential scintigraphy and the angiography in 64 patients (Nagel et al.) the scintigraphy was superior in detecting functional disturbances and tumors of the renal pelvis. However,

the angiography was more suitable for the diagnosis of renal cysts, renal artery stenosis and in a few cases of parenchymatous tumors.

Kinetics of intra-arterially applied radiopharmaceuticals in human

Recently, in course of renal or aortic angiography according to Seldinger's technique 7 patients were applied Radiohippuric acid through the catheter, further 2 patients received ^{113m}In -EDTA in the same manner. Immediately after the intra-arterial application the catheter was drawn back.

Similar to the experimental results mentioned above (zum Winkel et al., 1968) we expected the verification of changes in size of the radioactivity area during the first minute. However, not in all cases this was to confirm. Yet, some interesting observations could be made.

Generally, considerable amount of Radiohippuran flowed out of the kidney recognizable by the high

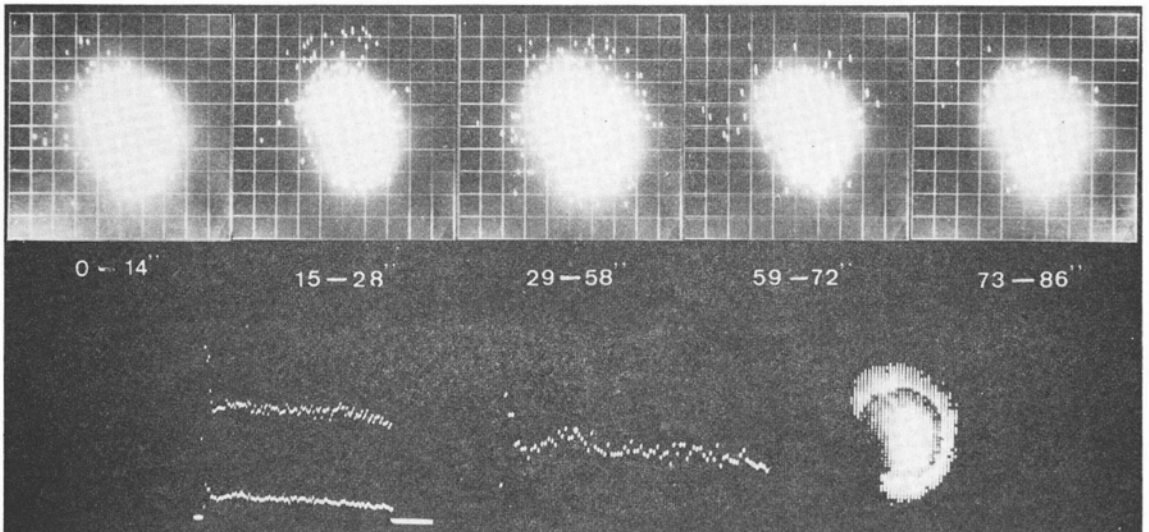


Fig. 8. Serial scintigraphy replayed from the digital tape on the oscilloscope in a patients with normal kidney function after intra-arterial applied 2 mCi ^{131}I -o-Iodhippuric acid in 3.5 ml. Functional curves of the whole kidney and the renal cortex (left part) and the renal cortex alone (middle part), each signal corresponds to 2 sec. Regions of interest. Note that the first and the third area is bigger than the second and the fourth corresponding to the transport of the radioactivity through the different parts of the nephrons.

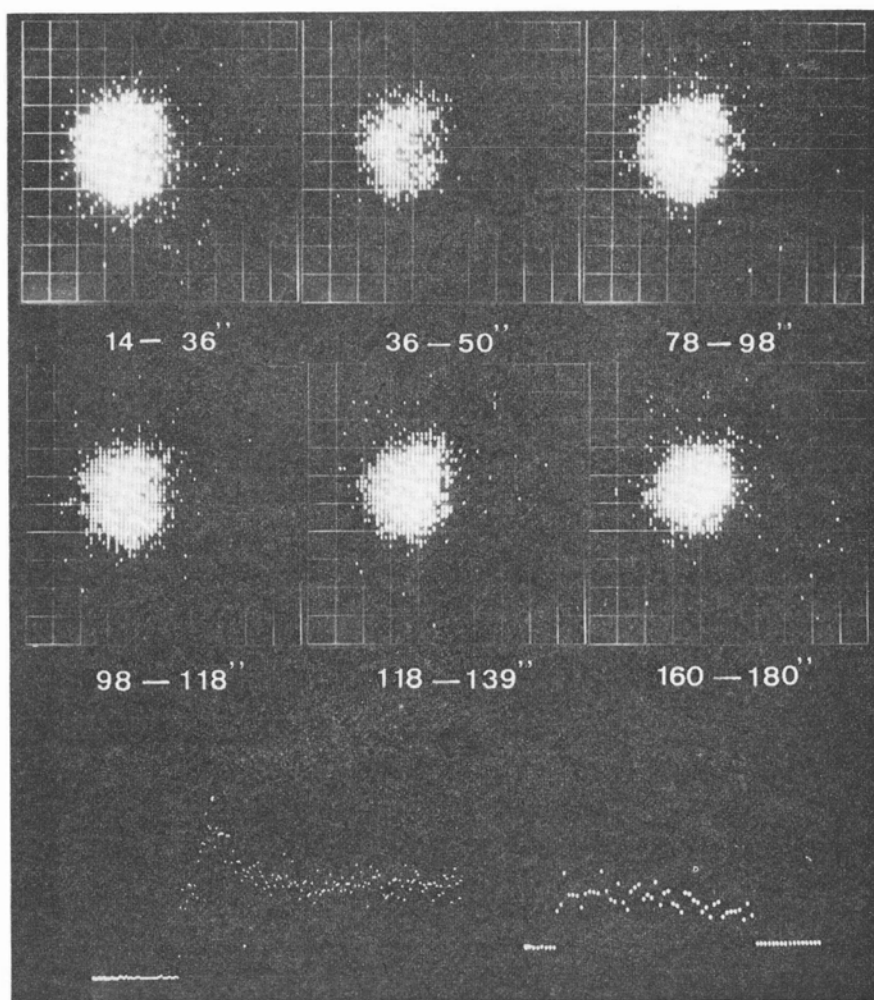


Fig. 9. Serial scintigraphy replayed on the oscilloscope and functional curves of the whole kidney and the renal cortex (each signal corresponds to 3 sec) after intra-arterial applied 1 mCi ^{131}I -o-Iodohippuric acid in a patient with slight hydronephrosis due to the compression of the renal pelvis by a small tumor. Note the reduced area in the second and sixth scintiphoto corresponding to the delayed but proved transport of the radioactivity through the nephrons.

initial peak followed by a rapid fall. Regarding the curve of the renal cortex only a second peak was seen 40 sec after a slightly decreased radioactivity. This corresponded with the changes in size of the radioactivity area, which was bigger first than after 20 sec. It was enlarged again till 60 sec and was reduced definitely thereafter (Fig. 8).

A few seconds after the injection of Hippuran radioactivity medial and cranial of the kidney was seen at the same time, which one can explain as the filling of the vena cava and perhaps of the heart. 2 min after the intra-arterial application the radioactivity decreased distinctly corresponding to the evacuation from the renal pelvis. Because of the outflowed Radiohippuran the contralateral kidney was registered, too. Corresponding to the Radiohippuran not accumulated in the catheterized kidney one could see a renograms similar that after intravenous injection.

Most of the intra-arterially injected Indium-113m-Chelate flowed out of the kidney. Regarding the renal cortex there was a second peak 15 sec after the application corresponding to the recirculation. 6 sec after the initial peak in the renal cortex a peak could be seen in the vena cava. Thus, the blood circulation from them the renal artery or the renal cortex, respectively, to the vena cava needs nearly 6 sec. Changes in size of the area of Radio chelate were influenced by the recirculated radioactivity only. We were not able to determine the cortical, the medullar and again the cortical distributed radioactivity.

It seems to be interesting, that in pathologic cases, too, the variable size of the area accumulating Radiohippuran could be found out. Thus, in a patient with disturbed evacuation due to a tumor the delayed transport of Radiohippuran through the loops of Henle was revealed clearly (Fig. 9). In a further patient 2 regions of interest were made after the intraarterial application of Radiohippuran. The parenchymatous region showed an initial peak followed by a decreasing. Few seconds later a plateau was reached, the further slope was normal. The tumor region demonstrated an initial peak, too, but there-

after the radioactivity failed to the background.

Evaluation of the curves with the computer

For the purpose of the evaluation of the curves obtained from distinct parts of the kidney we used the computer. The clinical usefulness of diverse parameters described in the literature should be re-examined. Moreover, the limit values of normal and pathological function of the kidney should be determined with extensive elimination of the background radioactivity.

The technical procedure was following, After the serial scintigraphy, i. e. 26 min after the injection the digital tape was replayed and the regions of interest were determined by the light pen. Thereafter, the curves were produced on the display and additionally

PROGRAM "KURVE" (Experimental version)

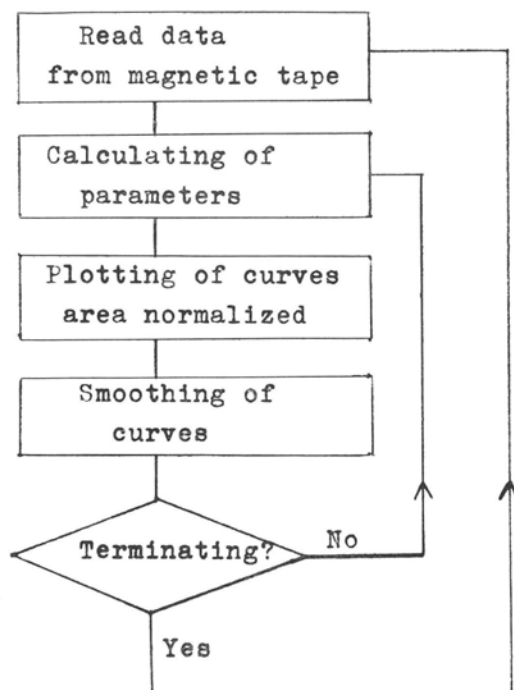


Fig. 10. Program for the evaluation of the curves with the computer.

P A R A M E T E R S

$$T_{\max}$$

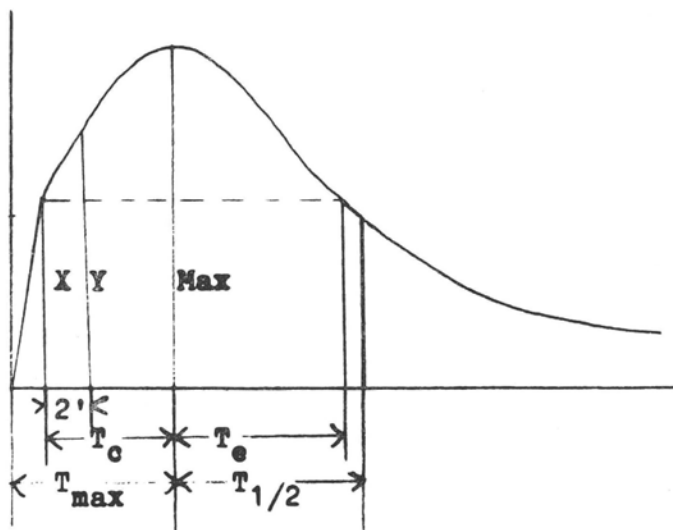
$$T_{1/2}$$

$$SW = \frac{Y}{X}$$

$$\text{Tot.Con.} = 100 \frac{\text{Max} - X}{X}$$

$$\text{Min.Con.} = \frac{\text{Tot.Con.}}{T_c}$$

$$\text{Min.Exc.} = \frac{\text{Tot.Con.}}{T_e}$$



ROI = Number of channels in the "Region of Interest"

Fig. 11. Parameters for the computer calculating of the curves.

stored on the digital tape. From that prepared digital tape the data were read in the computer Honeywell H-316. The data were evaluated with the program "KURVE" and then plotted (fig. 10). The calculated parameters concerned

1. the time of peak.
2. the SW value (Sekretonswert, zum Winkel, 1964), i. e. the relation of the radioactivity 2 min after the initial peak to the initial peak.
3. the half time during the excretion phase.
4. the total concentration, the minute concentration and the minute excretion according to Krueger et al.

The curves were plotted together with the parameters sometimes after smoothing.

Finally, the ascent of the radioactivity within 1 min after the intravenous injection was plotted, too. This technique should allow a criticism of the renal extraction rate of Radiohippuric acid, which in a normal case must be 90 per cent. We expected in cases with impaired renal function a distinct diminution after the

initial rise and before recirculation, which happens 20 sec thereafter at the latest.

Results of the computer calculating

As a continuous routine 48 patients, among them 10 with normal and 19 with pathological kidney function were evaluated. Some differences result from unilateral diseases. 19 patients had insufficient curves from a technical points of view, partly because the patient had moved, partly because of technical defects including the camera was moved for a better localization.

We set a high value on the distribution of the parameters in patients with normal or pathological renal function. In doing so it was evident, that a distinct differentiation existed in the time of the peak (T_{\max}) and the half time of the excretion phase ($T_{1/2}$ excr.) and the minute excretion, inclusively (fig. 11, 12, 13, 14).

On the contrary, the parameters for the secretion value (SW) and the minute concentration were

TMAX	= 153.6	148.4	164.0	142.8	SEK
THALB	= 198.7	182.2	193.1	197.6	SEK
SW	= 1.82	1.95	1.72	2.05	
TOT.CON.	= 90.3	93.7	70.8	107.0	%
MIN.CON.	= 38.8	41.8	29.5	46.8	%/MIN
MIN.EXC.	= 29.2	32.9	29.3	30.5	%/MIN
RØI	= 292	290	118	181	PUNKTE
1 CM ENTSPRICHT 57.8 IMP/2 SEK					

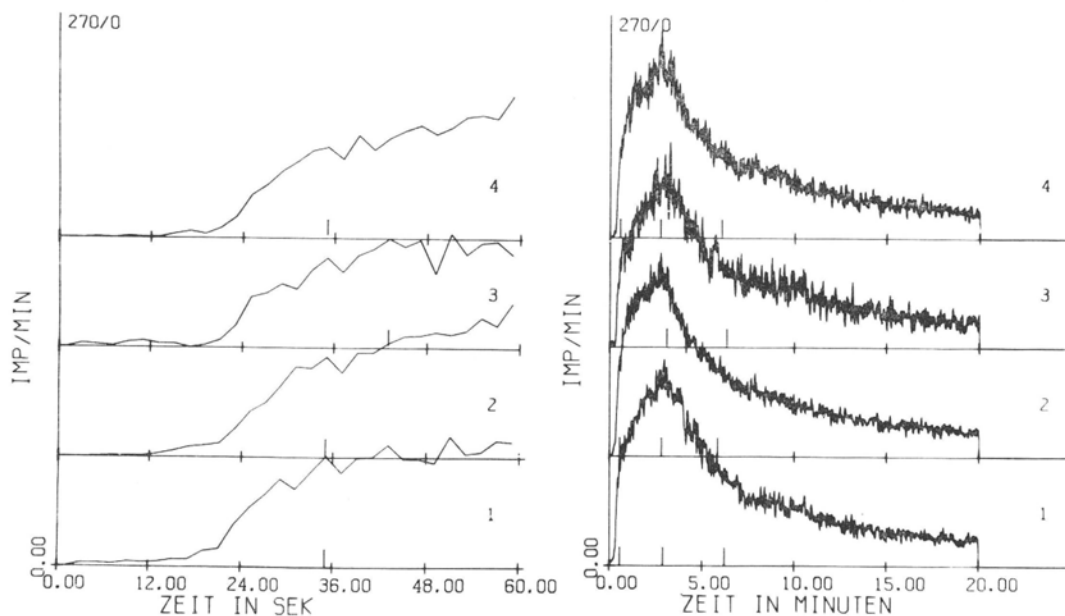


Fig. 12. Computer calculating in normal renal function of the right lower pole, left lower pole, right kidney on whole and left kidney on whole (from bottom to below). Calculated are regions of interest in the same size.

useless. Concerning the total concentration the normal and pathological values were superimposed. The reason of these insufficient results seems to be the bend of the curve after the initial rise, which some times hardly can be determined by the computer.

According to these results we conclude

1. the semiquantitative evaluation of the functional curves should take place optically by the expert, the additional evaluation by the computer can be helpful.
2. the peak time and the half time of the excretion phase are parameters pointing to a possible normal function.
3. by means of the computer the patients with certain normal function are to select.

4. further we must interpret dubious and pathological cases by ourselves.

The hitherto existing program does not estimate the renal extraction rate of Radiohippuric acid. We will check for an improved program because as above mentioned we saw corresponding changes in some special cases. This information obtained as a routine may be helpful in the clinical work.

Conclusions

According to the presented experimental and clinical results the sequential scintigraphy performed with the scintillation camera is a helpful method, which inform about the inflow, concentration, intrarenal transport and evacuation of radiopharmaceuticals distinguished by a renal affinity. In this way new

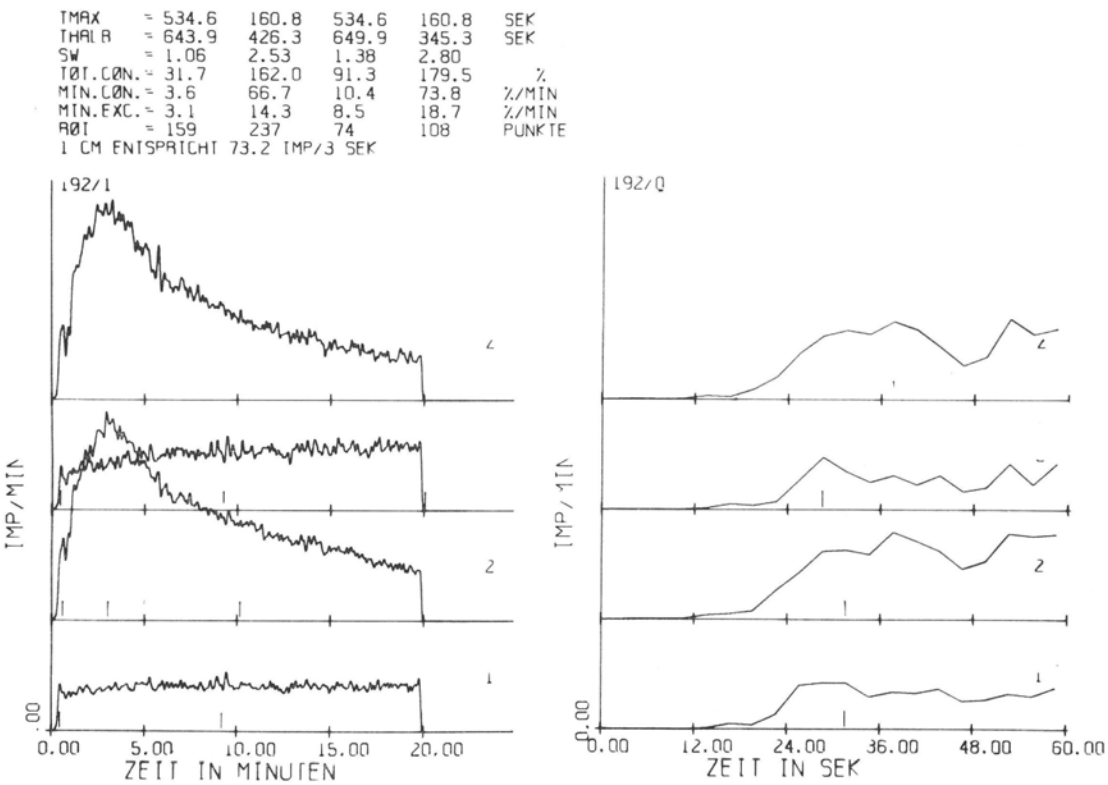


Fig. 13. Computer calculating (in same regions of interest as in figure 12) in a patient with hydronephrosis of the left kidney. Note the probably reduced extraction rate for Radiohippuric acid of the left kidney as seen in the curves demonstrated in the right side.

functional and morphological results can be obtained. The informations are improved and detached by using a storage system as a multichannel analyser and a digital tape which allows the functional analysis of the whole kidney or parts of it, respectively. With this arrangement the examination can be adapted to the individual conditions. In proving patients with nephrologic or uologic diseases a lot of pathophysiologic studies in an animal and in human must be done to make the best of the obtained results. In that direction our experimental and clinical findings may be helpful and can be concluded as following

1. the inflow corresponds with the renal vascularization, it needs 6 sec from the renal artery via

cortex to the renal vein.

2. the extraction rate of Hippuric acid is diminished in rejection of renal transplants.
3. the flow of the compounds through the loop Henle can be proved.
4. the movement of compounds toward the renal medulla and renal pelvis is to verify, inflammatory diseases cause a delayed intrarenal transport.
5. the evacuation of the renal pelvis is to observe, its delay occurs in a disturbed empty of the upper urinary tract and in a reduced urinary flow.
6. it is to differentiate between dirturbed intrarenal and postrenal transport.

Of course the combination of the described findings

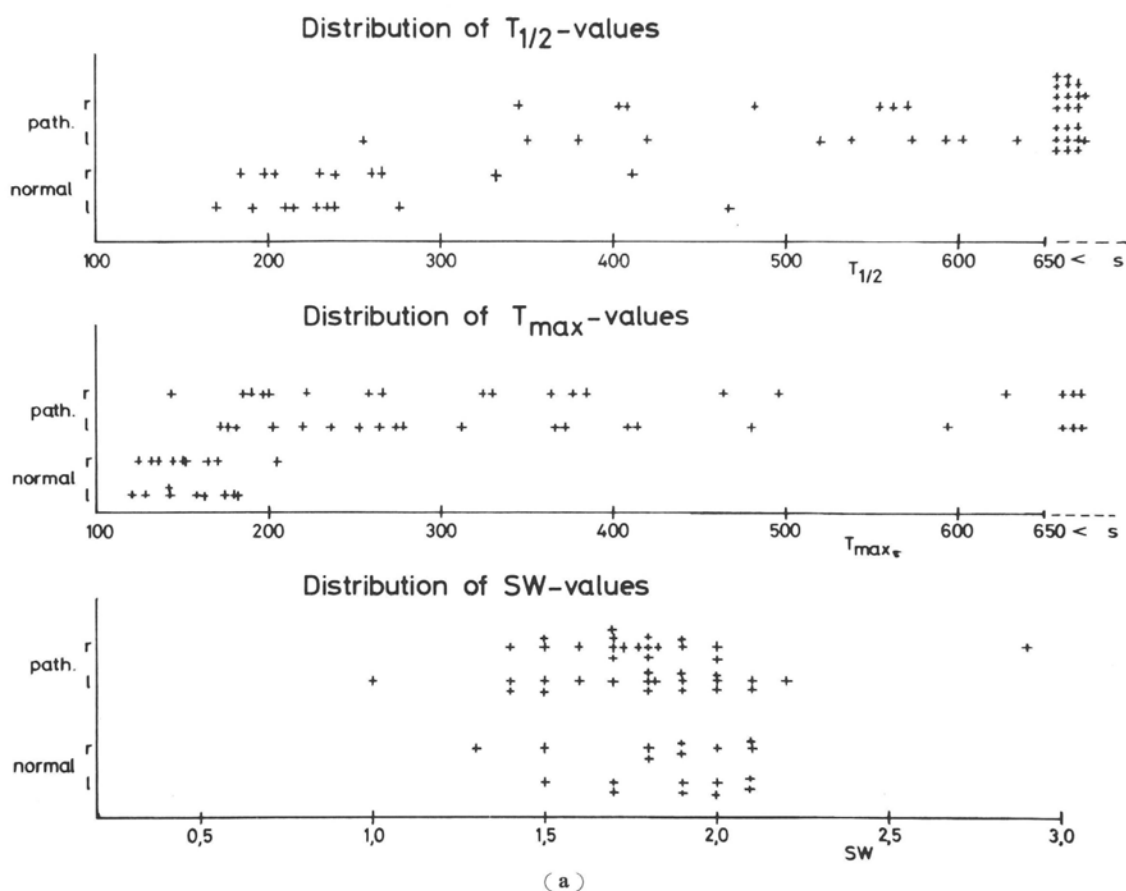


Fig. 14. a) and b) results of the parameter calculating by using the computer in patients with normal and pathological renal function, separated in in each of the left and the right kidney.

open more possibilities in clinical diagnostic. Some more should be done in future. Still, a fascinating field of morphologic and functional studies is opened.

Summary

Experimental and clinical studies are performed to improve the diagnosis of renal diseases by means the scintillation camera and data processing system. For this reason the comprehension of the renal kinetics of radiopharmaceuticals seems to be very important. After intra-arterial application the inflow, the concentration, the intra-renal transport and the evacuation

was proved in human and in dogs under physiologic and pathophysiologic conditions. Numerous examinations were formed in patients with reduced renal blood flow, inflammatory diseases, disturbed evaluation of the upper urinary tract and renal transplantation, whose results may facilitate the interpretation and lead to new and more complete informations about the functional and morphologic status of the kidney.

References

- Anger, H. O., Powell, M. R., van Dyke, D. K., Schaer, L. R., Fawwaz, R., Yano, Y. :
Recent application of the scintillation camera.

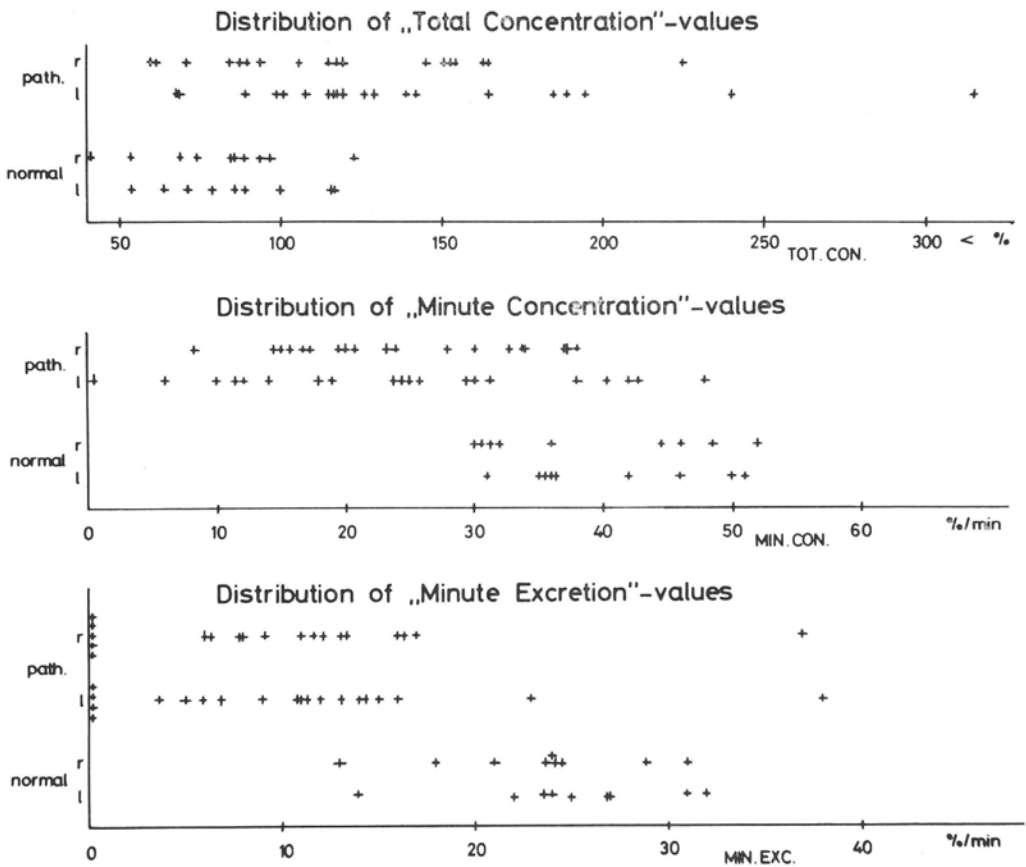


Fig. 14. (b)

- In : Radioaktive Isotope in Klinik und Forschung, Vol. 7. Urban & Schwarzenberg, Muenchen 1967
- Feine, K., zum Winkel, K. :
Nuklearmedizin-Szintigraphische Diagnostik. G. Thieme, Stuttgart 1969
- Haubold, U., Jost, H., zum Winkel, K. :
Sequenzszintigraphien der Nieren mit ^{131}J -o-Jodhippursäure und $^{135\text{m}}\text{In}$ -EDTA. Strahlentherapie 140, 89 (1970)
- Krueger, R. P., Sanders, A. P. De Maria, W., Baylin, G. J. :
Analysis of the radio-renogram curve. Amer. J. Roentgenol. 86, 819 (1961)
- Motzkus, F., Bachmann, D. :
Entstehung und Deutung des Radio-Renogrammet. Nucl.-Med. 7, 46 (1968)
- Müller-Beissenhirtz, Ziegler, M., zum Winkel, K., Seduhn, D., Encke, A., Pöplau, Rulad, S. :
Die Sequenzszintigraphie und die Angiographie zur Diagnostik der Abstossungskrisen von experimentellen Nierentransplantaten. Fortschr. Roentgenstr. 113, 148 (1970)
- Nagel, R., zum Winkel, K., Neide, E. L., Jost, H., Sonderkamp, H. M., Frisius, H., Marx, F. :

- The diagnosis of renal lesions by serial scintigraphy and angiography.
Intern. Sympos. Radionuclides in Nephrology, New York Januar 1971
- Rosenthal, L. :
Radionuclide diagnosis of malignant tumors of the kidney.
Amer. J. Roentgenol. 101, 662 (1967)
- Scheer, K. E., zum Winkel, K. :
Studies of renal function, blood flow and morphology.
In : Radioisotopes in Medical Diagnosis. Ed. E. H. Belcher and H. Vetter. Butterworths, London 1971
- Sigman, E. M., Bender, M., Blau, M. :
Radiohippuran renography and radiohippuran renal autofluoroscopy.
J, Urol. 92, 153 (1964)
- Steinhausen, M. :
personal communication
- zum Winkel, K. :
Nierendiagnostik mit Radioisotopen.
G. Thieme, Stuttgart 1964
- zum Winkel, K. :
Radiopharmaceuticals in kidney investigation.
Ann. Congr. Brit. Inst. Radiology, London March 1967
- zum Winkel, K., Hardst, H., Schenck, P., Franz, H. E., Ritz, E., Röhl, L., Ziegler, M., Amman, W., Maier-Borst, W. :
Sequential scintigraphy in renal transplantation.
In : Medical Radioisotope Scintigraphy. Intern. Atomic Energy Agency, Vienna 1968
- zum Winkel, K., Hallwachs, O., Steinhausen, M. :
Kameraszintigraphie und Isotopennephrographie an der Hundeniere und deren Überprüfung durch die Intravitalmikroskopie.
Fortschr. Roentgenstr 108, 382 (1968)
- zum Winkel, K., Jost, H., Motzkus, F., Golde, G. :
Renal function studies with radioisotopes.
In : Dynamic Studies with Radioisotopes in Medicine.
Intern. Atomic Energy Agency, Vienna 1971
- zum Winkel, Jost, H., Motzkus, F., Venohr, H., Golde, G. :
Dynamic and morphologic examination with the scintillation camera and data processing.
Intern. Sympos. Radionuclides in Nephrology, New York, Januar 1971
- zum Winkel, K., Sonderkamp, H. M., Jost, H., Marx, F., Hermann, H.-J. :
Angiography and scintigraph of the kidney.
Sympos. Angiography-Scintigraphy. Ass. Radiol. Europ., Mainz Oct. 1970

* * * * *

* * * * *