Clinical experience with ^{99m}Tc-MAG3, mercaptoacetyltriglycine, and a comparison with ^{99m}Tc-DTPA

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Abstract. The preparation, application and clinical usage of ^{99m}Tc-mercaptoacetyltriglycine, MAG3, a tubular secreted compound, is described in the first 225 patients in a phase III study. Image quality, relative renal function, and renal transit times were compared with a 4 fold greater administered activity of ^{99m}Tc-DTPA in 11 patients. Correlation coefficients of 0.94 for relative function, 0.83 for parenchymal transit time index and 0.82 for whole kidney transit time index were found. Frusemide responses were similar. ^{99m}Tc-MAG3 is an efficacious radiopharmaceutical for routine renal radionuclide studies, giving excellent image quality in patients with hypertension, poor renal function, obstructive nephropathy or a renal transplant.

Key words: ^{99m}Tc-MAG3 – ^{99m}Tc-DTPA

Since its introduction into clinical use in 1970 (Hauser et al. 1970), technetium labelled diethylenetriamine penta-acetic acid (⁹⁹Tc-DTPA) has played an unchallenged role as the main radiopharmaceutical for detecting functional abnormalities in the urinary tract in routine clinical use.

^{99m}Tc-DTPA is cleared by glomerular filtration and provides an excellent alternative to iodine labelled orthoiodohippurate, OIH, because of its physical properties and reduced radiation exposure (Taylor et al. 1980; Barbour et al. 1976). Disadvantages, however, stem from the fact that its low extraction efficiency (20%) gives rise to a proportionately low target to background ratio, a fact that should be taken into account when interpreting results in cases of reduced renal function. A high extraction efficiency, up to 87% (Britton and Brown 1971), can be achieved with orthoiodohippurate, OIH, labelled with ¹³¹I or ¹²³I, but the disadvantages of the former include a high radiation dose, especially in the presence of outflow obstruction (Elliott and Britton 1978) and poor spatial resolution and sensitivity of images, while the higher cost and reduced availability of the latter precludes its use as a routine renal imaging agent.

Recently, a new and promising series of technetium complexes were synthesized as potential replacements of OIH in kidney function studies (Davison et al. 1981). The new chelating agents were based on an amide nitrogen and thiolate sulphur donor groups.

A preliminary member of the series, ^{99m}Tc-N, N'-bis (mercaptoacetyl) ethylenediamine (^{99m}Tc-DADS) showed rapid extraction and clearance by the kidney but was inferior to OIH as regards to its biological properties (Fritzberg et al. 1981; Fritzberg et al. 1982; Klingensmith et al. 1982, 1983, 1984).

Efforts to avoid sterioisomer formation resulted in the development of a new (N3-S) ligand, ^{99m}Tc-mercaptoace-tylglycylglycylglycine (^{99m}Tc-MAG3) which was shown to be a potential replacement of OIH in animals (Fritzberg et al. 1986). Preliminary studies with volunteers (Taylor et al. 1986) and patients (Taylor et al. 1987; Jafri et al. 1988) has shown ^{99m}Tc-MAG3 to be a single radiochemical agent with fast renal excretion.

As outlined in recent work from this department (Jafri et al. 1988), phase I and II studies were done to compare the simultaneous clearance of ^{99m}Tc-MAG3 and ¹³¹I-OIH and to compare renal handling of ^{99m}Tc-MAG3 with ¹²³I-OIH. In this work (phase III), a clinical evaluation of ^{99m}Tc-MAG3 involving 225 patients has been undertaken. In a sub group, the results obtained in 11 patients with ^{99m}Tc-MAG3 have been compared with those obtained within 4 weeks with ^{99m}Tc-DTPA. This work is undertaken to evaluate whether ^{99m}Tc-MAG3 meets the requirements of the ultimate renal radiopharmaceutical which should be safe, cheap, readily available, easy to prepare and clinically useful.

Materials and methods

A total of 225 patients referred to the Nuclear Medicine Department for routine radionuclide renography were selected for this study (males 135, females 90 mean age: 47 years range 9 to 75 years). The majority of patients came from either the hypertension clinic or the Urology Department at St. Bartholomew's Hospital, London. The causes for referral were hypertension (94), assessment of a renal transplant (42), possible urinary tract obstruction (75) and (14) for various other reasons, Table 1, 33 of these studies were follow-up tests in the same set of patients.

The studies with MAG3, being approved by the City and Hackney District Ethical Committee for routine use, were carried out with a thorough explanation given before each routine procedure and most patients were willing to try a new imaging agent in preference to the existing one.





Fig. 1

The study was approved by the Governmental Administration of Radioactive Substances Advisory Committee.

Preparation of ^{99m}Tc-MAG3. MAG3 was supplied by Mallinckrodt Diagnostica, Holland, as a freeze dried white powder in multidose vials (Code MP600). Under aspetic conditions, when required 925 MBq (25 mCi)^{99m}Tc eluate, from an Ultratechneknow FM generator, in a volume less than 1 ml was added to the vial. Before addition, the activity was diluted with saline to 4 ml and attention was paid

Fig. 1a-c. JH 56-year-old male with renal colic and a radiolucent renal stone in the left ureter. Renal radionuclide study. a^{99m} Tc-DTPA 400 MBq Posterior abdominal views. Left 60–90 s, Right 15 min. High background is seen on the 1st image and a dilated left pelvis and upper ureter is seen in the left kidney on the 15 min image. Transit times in s.

| | PTTI | WKTTI | MTT | Relative function |
|-----------------|------------|------------|-------------|-------------------|
| Left | 198 | 294 | 278 | 46% |
| Right Normal | 63 <156 | 86 <170 | 193 <240 | 54% |

 b^{99m} Tc-MAG3 100 MBq Posterior abdominal views. Left 60–90 s, Right 15 min. Lower background is seen on the 1st image than in 1a and better definition on the 15-min image. Transit times in s.

| | PTTI | WKTTI | MTT | Relative function |
|--------|------|-------|------|-------------------|
| Left | 182 | 544 | 282 | 45% |
| Right | 70 | 120 | 150 | 55% |
| Normal | <156 | <170 | <240 | |

Abnormal PTTI demonstrates obstructive nephropathy. c Activity time curves: vertical axis, counts/s, horizontal axis, time in min. A normal right kidney curve is seen (*light dots*). The left kidney curve rises to a plateau (*dark dots*) and shows a good response to frusemide in spite of renal colic and an obstructing stone clinically and radiologically

Table 1. Results of 99mTc-MAG3 studies in 225 patients

| Reason for request | Diagnosis | | |
|---------------------------------------|---|----|--|
| Hypertension (94) | Normal | | |
| •• | Small kidney, no RVD | 5 | |
| | Symmetrically function RVD | 12 | |
| | Renal artey stenosis | 2 | |
| | Normal single kidney | 1 | |
| Possible obstructive nephropathy (75) | Symmetrical function, no obstructive nephropathy | 15 | |
| | Single kidney, no obstructive nephropathy | 2 | |
| | Not analysable | 2 | |
| | Computer failure | 1 | |
| | Equivocal | 2 | |
| | Bilateral obstructive nephropathy | 2 | |
| | Unilateral obstructive nephropathy | 15 | |
| Assess renal transplant (42) | | 42 | |
| Miscellaneous (14) | Normal | 3 | |
| | Acute renal failure | 3 | |
| | Chronic renal failure | 3 | |
| | Acute aneurysm | 3 | |
| | Renal carcinoma | 1 | |
| | Systemic lupus erythematosis | 1 | |

Key: RVD Renovascular disorder

to technique to ensure that no air was introduced into the preparation. The mixture was then shaken, and after measuring the total activity the vial content was aliquoted (1 ml) into nitrogen filled vials. These aliquots were boiled for ten min, as and when required, up to four h after reconstitution. These modifications have been shown to give a radio-chemical purity always greater than 90% ^{99m}Tc-MAG3, even in an aliquot 4 h after reconstitution. An injection of accidentally unboiled ^{99m}Tc-MAG3 resulted in good quality analogue images and transit times but much reduced effective renal plasma flow (ERPF) estimation as compared

with the expected value Jafri et al. (1988). The patients' dose was about 2.5 mCi (92.5 MBq) of ^{99m}Tc-MAG3.

Preparation of ^{99m}*Tc-DTPA*. ^{99m}*Tc-DTPA* was prepared according to the manufacturers instructions (Mallinckrodt, Holland). The dose for the patient was about 10 mCi (370 MBq).

Quality control of radiopharmaceuticals. 99m Tc-MAG3 kits – these were assayed using the recommended chromatography, glass TLC plates coated with RP18 (Merck 15683) and developed over 3 h in a mixture of methanol:saline:acetic acid, 45:55:1. Radiochemical purity range was 90%–96% with a mean of 94%.

 99m Tc-DTPA Kits – a twin ITLC-SG chromatography system run in acetone and water was used to assay these. The radiochemical purity range was 98%–99.8% with a mean of 99%.

Procedure. Normal intake of fluid and food was encouraged and a further 180 ml water was given prior to the test. The patients were seated in a modified reclining backless chair with the detector head of the gamma camera (IGE 400AT) under the back, equipped with a low energy general purpose parallel hole collimator and covering the area between the bladder and the heart. Either 99m Tc-DTPA or ^{99m}Tc-MAG3 was injected via a three way connector to a butterfly line and flushed with saline. The data were collected in the form of analogue images at 30, 60, 90 and 120 s, and then at 5, 10, 15 and 20 min postinjection. A further ten min acquisition was done after an injection of frusemide in cases of suspected obstruction. The data was also acquired by the camera linked computer (Nodecrest V76) in ten s frames. During the MAG3 studies, vital signs were monitored before and after injection.

Transplant studies were acquired in the supine position with the camera head positioned over the transplant area and bladder anteriorly.

Eleven patients were examined with both ^{99m}Tc-MAG3 and ^{99m}Tc-DTPA. The duration between the two tests



ranged from a few days up to a month where no change in function was thought to have occurred. Dosimetry calculations showed an effective whole body dose equivalent of about 0.5 millisieverts per study using 100 MBq (2.7 mCi) ^{99m}Tc-MAG3.

In the hypertensive patients, clinical signs were monitored before and after the MAG3 injection and in a sub group of 20 patients standard haematological and biochemical profiles were taken before and within a week after MAG3 injection.

Data analysis

1. Obstructive nephropathy. After the study, the data was redisplayed on the computer monitor using a 64×64 matrix. Regions of interest (ROI) were selected over the kidneys at 2 min (before any tracer had left), the left ventricle from an early frame and two background regions superior and medial to each kidney but avoiding the central vessels. From the renal and background regions, the relative renal function as a percentage was derived. The normal range



a ^{99m}Tc-MAG3 100 MBq Posterior abdominal views. Left 5 min, Right 30 min. Left kidney is just visualised at 5 min. An empty pelvis is still evident at 30 min after frusemide given at 20 min, to which there is no response.

b Activity time curves: vertical axis, counts/s; horizontal axis, time in min. Right kidney is normal (*light dots*). Left kidney shows a slowly rising curve (*dark dots*) and no response to frusemide at 20 min. Transit times

| | PTTI | WKTTI | MTT | Relative function |
|--------|------|-------|------|-------------------|
| Left | 359 | 364+ | 479 | 6% |
| Right | 41 | 71 | 101 | 94% |
| Normal | <156 | <170 | <240 | |

Conclusion: left obstructive nephropathy

which is the same for filtered and for tubularly secreted compounds was established at $50\% \pm 7\%$ (Britton 1980).

Separation of parenchyme from pelvis is required to obtain the tracer transit time through the renal parenchyma. A mean time image is obtained from analysis of the activity time curves of each pixel. Since pelvic activity is usually delayed by about 100 s compared to the parenchyma, the scaling of this functional image makes the parenchymal region easily distinguished from the pelvic one (Britton and Maisey 1983). This pure parenchymal activity time curve was then used for deconvolution analysis with the left ventricular activity time curve to give the mean parenchymal transit time MPTT (Nimmon et al. 1981). The MPTT may be divided into a part common to all nephrons, the minimum transit time (Min. TT), and residual transit times the mean of which is called parenchymal transit time index (PTTI). Thus MPTT = Min. TT + PTTI.

The Min. TT represents the minimum obligatory time taken for the activity to pass the length of the nephron and collecting ducts and this depends on medullary concentration and urine flow. To reduce the interpatient variation in hydration and urine flow, both the MPTT and whole



Fig. 3a, b. DB A 20-year-old male with asymptomatic proteinuria was shown to have a right hydronephrosis on intravenous urography. Renal radionuclide study. a 99m Tc-MAG3 100 MBq Posterior abdominal views. Frusemide given at 18 min. Left 90–120 s, Middle 15 min, Right 30 min. A small right kidney with a response to frusemide is seen into a dilated ureter displaced laterally. b Activity time curves: vertical axis, counts/s; horizontal axis, time in min. The left kidney curve is normal (*dark dots*). The right kidney curve is a low plateau. Transit times

| | PTTI | WKTTI | MTT | Relative function |
|--------|------|-------|------|-------------------|
| Left | 48 | 83 | 148 | 95% |
| Right | 22 | 188 | 82 | 5% |
| Normal | <156 | <170 | <240 | |

Conclusion: Poorly functioning right kidney without obstructive nephropathy

kidney transit time (WKTT) were corrected for this obligatory Min. TT leading to parenchymal transit time index (PTTI) and whole kidney transit time index (WKTTI) respectively (Britton et al. 1980). Normal ranges are:

PTTI – 10–156 s MPTT – 100–240 s WKTTI – 20–170 s

The data sampling rate of 10 s is such that the very short time for, and the slight difference in timing between, the filtration of ^{99m}Tc-DTPA into and the secretion of ^{99m}Tc-MAG3 into the proximal tubular lumen is totally lost. Thus the transit times of these two compounds along the nephron are expected to be similar. In interpreting the response to frusemide, the persistence of a rise of the activity time curve was taken to indicate obstructive uropathy while a rapid fall indicated the absence of such obstruction. When renal function is reduced, a normal response is that rate of fall appropriate to the previous rate of rise of the renal activity time curve (Britton et al. 1987).

2. Hypertension cases. Applying the same analytic procedure, the presence of renovascular disorder likely to be due to renal artery stenosis as a cause of hypertension was concluded if the relevant kidney appeared smaller in size, showed reduced relative function less than 40% of total and a delay of more than 60 s in MPTT compared with the normal kidney. In kidneys with symmetrical uptake and



Fig. 4a, b. RH A 49-year-old man with a right ureteric calculus. Renal radionuclide study. a^{99m} Tc-MAG3 100 MBq posterior abdominal views. Frusemide given at 18 min. Left 60–90 s, Middle 15 min, Right 25 min. Right kidney has a dilated pelvis with a moderate response to frusemide. b Activity time curves: vertical axis, counts/s; horizontal axis, time in min. The left kidney curve shows a normal second phase and a slower falling uneven third phase (*dark dots*). The right kidney curve shows a slow rise until the response to frusemide causes a fall. Transit times

| | PTTI | WKTTI | MTT | Relative function |
|--------|------|-------|------|-------------------|
| Left | 61 | 124 | 161 | 63% |
| Right | 126 | 545 | 246 | 37% |
| Normal | <156 | <170 | <240 | |

Conclusion: no evidence of obstructive nephropathy

a prolonged MPTT (over 240 s), renovascular disorder likely to be due to small vessel disease or as a consequence of severe hypertension was discovered. In all cases of renovascular disorder, pelvic transit time is normally less than 40 s.

3. Transplant cases. The concept of perfusion index (PI) was adopted (Hilson et al. 1978). Acute tubular necrosis was suggested by the absence of calyceal activity usually with good early perfusion, and a reduced PI improving with time from operation. A rise in PI together with a reduction of a previously satisfactory early perfusion of the transplant usually indicated deterioration due to a rejection episode.

Data interpretation. Besides the computer analysed data, the analogue images were considered visually, to determine the size, shape and perfusion of both kidneys, the presence of pelvi-calcyceal retention, and its response to frusemide. The physicist undertaking the transit time analysis was unaware of the clinical condition of the patient, and since the results were numerical, no bias was introduced.

Results

The reasons for requesting the renal radionuclide study and the consequent diagnoses in the 225 patients are summarised in Table 1. Only 2 patients with renal artey stenosis confirmed radiologically were found in the 94 hypertensives





Fig. 5a, b. N-M A 19-year-old woman received a living donor renal transplant. a Renal radionuclide study one day later with ^{99m}-Tc-MAG3 100 MBq Anterior abdominal views. Left hand images Top 0-30 s, Middle 30-60 s, Bottom 60-90 s. Right hand images Bottom 90-120 s, Middle 4.5-5 min, Top 9.5-10 min. Conclusion: a normal renal transplant study with good early perfusion and bladder and urinary catheter activity at 5 min. b Activity time curves: vertical axis, counts/s; horizontal axis, time in min. 1 Renal transplant; 2 Iliac artery distal to the transplant. Perfusion index 88 ± 6 . Conclusion: Normal perfusion

whereas 12 with symmetrical function and a prolonged mean parenchymal disorder characteristic of small vessel disease due to glomerulonephritis or as a consequence of severe hypertension were found. These frequencies accord with published data (Page and McCubbin 1968). In the possible obstructive nephropathy group (75), the usual request was in a patient with either pain thought to be renal in origin, or dilated renal outflow tract or the presence of stone disease on intravenous urography or ultrasound, or combinations of these. Some requests were for postsurgical or postlithotripsy follow up (Bomanji et al. 1987). Unilateral obstructive nephropathy meeting the criteria of both a prolonged parenchymal transit time index with a prolonged pelvic transit time and subsequently confirmed by other investigations, surgery and follow up was present in 15 (Figs. 1 and 4) and bilateral in a further 5 patients. In two patients with less than 4% of total function in one kidney, the transit time analysis could not be performed and computer failure lost the data in one patient. Equivocal results with borderline PTTI values were noted in two patients. Frusemide responses were uninterpretable in six patients and misleading in two.

The serial studies of renal transplants were particularly efficaceous with ^{99m}Tc-MAG3. In this situation the high resolution, high uptake, low background pictures were generally superior to previous experience with ^{99m}Tc-DTPA. The same criteria for acute tubular necrosis and for rejection were found to apply and similar changes in perfusion index with recovery and with rejection were noted. There is also none of the slight hepatic uptake in the field of view. As a result of this excellent initial experience all renal transplants are now being monitored using ^{99m}Tc-MAG3, Figs. 5 and 6. In the miscellaneous group, the visualisation of the kidneys in acute or in chronic renal failure were better than with ^{99m}Tc-DTPA used previously.

A more detailed comparison was performed in 11 patients. The images obtained with ^{99m}Tc-MAG3 in these patients were without exception of better quality and provided improved detail of the kidneys with a higher target to background ratio as compared to ^{99m}Tc-DTPA studies done with four times the administered activity. Some clinical examples are illustrated in Figs. 1 to 6.

A comparison of ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 is made in a 56-year-old man with renal colic due to a radioluscent ureteric stone, Fig. 1. Note the much better definition of renal and calyceal detail and the lower tissue background when using MAG3 at one quarter of the administered activity, Fig. 1b, compared with Fig. 1a. Both these studies show a prolonged parenchymal transit time index, indicating obstructive nephropathy and yet there is a normal response to frusemide, Fig. 1c. Ureteric obstruction was confirmed radiologically and lead to operative intervention. A false frusemide response may be seen in the presence of obstructive nephropathy when renal function is very good (Britton et al. 1987).

A 59-year-old female had a left hydronephrosis with very poor function, 6% of the total, as shown by ^{99m}Tc-MAG3, Fig. 2. PTTI shows left obstructive nephropathy and there is no response to frusemide, Fig. 2b, but at this level of function this lack of response may occur due to an inability to induce a diuresis. A further illustration of this is given by the results of a ^{99m}Tc-MAG3 study shown in Fig. 3. A normal PTTI is seen in the right kidney which contributes 5% of total function. Visual response to fruse-



Fig. 6a, b. GS A man aged 48 years received a cadaveric renal transplant on 19 February 1987. Renal radionuclide studies with ^{99m}Tc-MAG3 100 MBq showing the early perfusion image 0–30 s on an anterior abdominal view. a Left 6 March 1987, Middle 10 March 1987, Right 20 March 1987. Poor early perfusion typical of rejection is seen on the first image with subsequent recovery demonstrated in the later images. b Activity time curves: vertical axis, counts/s; horizontal axis, time in min. 1 Renal transplant; 2 iliac artery distal to the transplant. Left 6.3.87 Perfusion index 263 ± 24 ; Middle 10.3.87 Perfusion index 213 ± 16 ; Right 20.3.87 Perfusion index 145 ± 9

mide only, and it was shown radiologically not to be obstructed. A concordant finding of a prolonged renal PTTI and an impaired and inappropriate response to frusemide is shown by the left kidney in the ^{99m}Tc-MAG3 study illustrated in Fig. 4. In this case the right kidney contributed 37% of the total function.

Two ^{99m}Tc-MAG3 results in patients with renal tranplants are illustrated in Figs. 5 and 6. The first patient received a living related donor transplant and shows a normal series of images. Fig. 5a, and activity time curves, Fig. 5b, with a normal perfusion index. Stages in the recovery of another patient from a severe rejection episode, after a cadaver renal transplant, is illustrated in Fig. 6. The day before the 1st image, on the left side of Figure 6a, a ^{99m}Tc-DTPA study was performed using 400 MBq and the kidney could not be visualised on the transparent film record.

The comparative analysis of transit times of 99m Tc-MAG3 and 99m Tc-DTPA showed for PTTI a correlation coefficient, r=0.83, P<0.05 and for WKTTI a correlation coefficient, r=0.82, P<0.05. The comparison of relative renal function gave a correlation of r=0.94, P<0.01. Renogram curves obtained with the two agents were similar.

Discussion

In a previous study from this department (Jafri et al. 1988), phase I and II studies were done to compare the simultaneous clearance of a new renal radiopharmaceutical, mercaptoacetyltriglycine (MAG3) labelled with ^{99m}Tc with that of ¹³¹I labelled orthiodohippurate (OIH) and to compare the renal handling of 99m Tc-MAG3 with that of 123 I-OIH in serial studies.

The purpose of this study (phase III) was to evaluate the clinical usefulness and robustness of ^{99m}Tc-MAG3 in routine practice and to make a comparison with technetium labelled diethylenetriamine penta-acetic acid ^{99m}Tc-DTPA.

The study involved a total of 225 patients with a wide range of renal function impairment, and the results of 11 patients were compared with those obtained, within 4 weeks, with ^{99m}Tc-DTPA, given 4 times the activity of that used for ^{99m}Tc-MAG3. Visual analysis and interpretation of analogue images obtained with ^{99m}Tc-MAG3 were clearly superior to those obtained with ^{99m}Tc-DTPA with higher target to background ratio, particularly in cases where the renal function was so depressed as to render DTPA images difficult to evaluate.

The extraction efficiency of MAG3 was determined recently in rats (Fritzberg et al. 1986) and was found to be about 85% compared to 69% for ¹³¹I-OIH, and as MAG3 was predominantly protein bound at 77% compared to 33% for OIH, the corrected tubular cell extraction was found to be 75% for MAG3 and 43% for OIH. Protein binding, however, showed different values in different studies. A value of 88% was found in volunteers (Taylor et al. 1986) and 91% in patients (Bubeck et al. 1987). while our measurements produced a value of 78%. These differences may simply reflect different techniques used, and further evaluation of this point is clearly needed.

A good DTPA substitute should be able to assess accurately the percentage contribution by each kidney to the total renal function. A comparison of such values obtained with MAG3 and DTPA showed a highly significant correlation of r=0.94. Comparative computer analysis for transit time values showed a good correlation between MAG3 and DTPA for parenchymal transit time index (PTTI) of r=0.83 and for whole kidney transit time index (WKTTI) of r=0.82. As expected, slight time differences between tubular secretion and glomerular filtration are lost when the whole nephron transit time is of the order of three min and the sampling is at 10 s intervals.

Renogram curves obtained with MAG3 and DTPA were basically similar, as were the frusemide response curves. The correlation between the perfusion indices in transplant cases were not measured as these parameters change rapidly, in numerical terms, within a short period of time depending on the clinical improvement or deterioration of the transplant status, and a useful comparison with DTPA was not feasible.

The need to boil the ^{99m}Tc-MAG3 complex beforehand and to use it within one h thereafter was one of the disadvantages met with during the clinical work. This step was necessary to remove the benzoyl group already mentioned under preparation of MAG3. Work is being done in this department to optimise this procedure and modify the labelling and boiling procedures to get the maximum benefit from each kit. The preliminary findings show that the boiling step can be separated by as much as four h from the time of addition of 99mTc to the MAG3 without increase in the lipophilic liver secreted components particularly when the radiopharmaceutical is kept cold. At each of these preparative steps, one may divide the kit into pairs of doses to give finally four doses arranged at times convenient for the patient studies during a morning or afternoon session. Another minor disadvantage was a 4% hepatobiliary excretion of MAG3 which did not interfere with data processing or interpretation and was shown to be unrelated to the state of kidney function. No untoward changes in vital signs were noted after the MAG3 injection. No side effects were observed and there were no unexpected haematological or biochemical findings.

We conclude that ^{99m}Tc-MAG3 is an excellent renal radiopharmaceutical in routine use. It has some advantages over ^{99m}Tc-DTPA with comparable relative function and transit time studies and it is particularly suitable for the evaluation of renal transplants.

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