^{99m}Tc-EDDA/HYNIC-TOC: a new ^{99m}Tc-labelled radiopharmaceutical for imaging somatostatin receptor-positive tumours: first clinical results and intra-patient comparison with ^{111}In-labelled octreotide derivatives

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Abstract. [^{111}In-diethylene triamine penta-acetic acid-D-Phe[1]]-octreotide (DTPA-octreotide) scintigraphy has gained widespread acceptance as a diagnostic clinical procedure in oncology for imaging somatostatin receptor-positive tumours. However, indium-111 as a radiolabel has several drawbacks, including limited availability, suboptimal gamma energy and high radiation burden to the patient. We have recently reported on the preclinical development of ^{99m}Tc-EDDA/HYNIC-TOC, a new octreotide derivative which showed promising results both in vitro and in vivo. We now report our initial clinical experiences with this new radiopharmaceutical in ten oncological patients. The clinical diagnoses were: carcinoid syndrome (*n*=5), thyroid cancer (*n*=3), pancreatic cancer (*n*=1) and pituitary tumour (*n*=1). The biodistribution and kinetics of ^{99m}Tc-EDDA/HYNIC-TOC were compared with those of ^{111}In-DTPA-octreotide in six cases, and with those of ^{111}In-DOTA-TOC in five cases. With the new tracer tumours were imaged within 15 min after injection and showed the highest target/non-target ratios 4 h after injection. Tumour uptake persisted up to 20 h p.i. The rate of blood clearance was similar to that of ^{111}In-DTPA-octreotide but faster than that of ^{111}In-DOTA-TOC, while urinary excretion was lower compared with the ^{111}In derivatives. Semi-quantitative region of interest analysis showed that ^{99m}Tc-EDDA/HYNIC-TOC produced higher tumour/organ (target/non-target) ratios than the ^{111}In derivatives, especially in relation to heart and muscle. Significantly more lesions could be detected in ^{99m}Tc images. We conclude that ^{99m}Tc-EDDA/HYNIC-TOC shows better imaging properties for the identification of somatostatin receptor-positive tumour sites than currently available ^{111}In-labelled octreotide derivatives.

Key words: Technetium-99m – Somatostatin – HYNIC – Tyrosine-octreotide – Scintigraphy

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Introduction

Imaging somatostatin receptor-positive tumours with [^{111}In-diethylene triamine penta-acetic acid-D-Phe[1]]-octreotide (DTPA-octreotide) has become a widely used diagnostic procedure in clinical nuclear medicine [1, 2,3]. The major limitations of this procedure are related to the use of indium-111 as the radiolabel, with its limited availability, high cost, medium gamma energy leading to suboptimal image resolution and relatively high radiation burden to the patient. Because small peptides are usually rapidly taken up in the target and cleared from non-target tissue, technetium-99m would be expected to be the preferred radiolabel for octreotide derivatives. Recently Maecke and Behe described the possible use of hydrazinonicotinamide (HYNIC) as a bifunctional chelator (BFC) for these compounds [4]. In a recent study we showed that HYNIC has considerable advantages over other BFCs and that the choice of co-ligand is crucial if the imaging properties of the radiolabelled peptide are to be optimised [5]. Among the co-ligands studied, we found that ethylene diamine *N*,*N*'-diacetic acid (EDDA) produced the most stable and hydrophilic complexes. In an animal tumour model we compared ^{111}In-DTPA-

octreotide with HYNIC-conjugated Tyr^3-octreotide (HYNIC-TOC) labelled with ^{99m}Tc using a number of co-ligand systems. In these studies ^{99m}Tc-EDDA/HYNIC-TOC produced higher tumour uptake values compared with ^{111}In-DTPA-octreotide and lower levels of uptake in normal tissues than HYNIC-TOC labelled with co-ligands based on tricine [6]. In this report we present the first human studies of this new radiopharmaceutical, ^{99m}Tc-EDDA/HYNIC-TOC, in a series of ten patients. We include data on biodistribution, pharmacokinetics and tumour uptake in comparison with ^{111}In-labelled octreotide derivatives.

Materials and methods

Radiopharmaceuticals. ^{99m}Tc-EDDA/HYNIC-TOC was prepared as recently described [7]. For the first three patient studies, briefly, 20 µg HYNIC-TOC was incubated with 10 mg *N*,*N*' ethylene diamine diacetic acid, 15 µg of stannous chloride dihydrate and 1 GBq of ^{99m}Tc-pertechnetate in 2 ml 0.05 *N* phosphate buffer pH 6 at room temperature for 1 h. For all other studies 20 µg HYNIC-TOC was heated with 10 mg *N*,*N*'-ethylene diamine diacetic acid, 20 mg tricine, 15 µg of stannous chloride dihydrate and 1 GBq of ^{99m}Tc-pertechnetate in 2 ml 0.05 *N* phosphate buffer pH 6 at 70°C for 30 min. The solution was purified using a SepPak mini cartridge (Waters, Milford, Mass., USA) eluted with 80% ethanol and diluted with 5 ml saline. The purified radiolabelled peptide was sterilised by filtration and 200–300 MBq of the resulting solution was used for each patient study. Radiochemical purity was greater than 95% using analytical techniques based on high-performance liquid chromatography (HPLC) and thin-layer chromatography (TLC) as described elsewhere [6].

^{111}In-DTPA-octreotide was prepared from a commercial kit (Octreoscan, Mallinckrodt Inc., Petten, The Netherlands). The injected dose per patient was 150 MBq. ^{111}In bound to peptide exceeded 95% as analysed by TLC using the recommended instant thin-layer chromatography (ITLC) method with 0.1 *N* citrate buffer pH 5 as solvent.

^{111}In-[1,4,7,10-tetraazacyclododecane-*N*,*N*',*N*'',*N*'''-tetra-acetic acid, D-Phe^1,Tyr^3]-octreotide (DOTA-TOC) was prepared at the Forschungszentrum Seibersdorf (Seibersdorf, Austria). The administered dose per patient was 185 MBq. ^{111}In bound to peptide exceeded 95%,as analysed by TLC using the ITLC method described above.

Patients. This clinical study was approved by the local ethical committee and all patients gave their informed consent prior to inclusion. Scintigraphy with ^{99m}Tc-EDDA/HYNIC-TOC was performed in ten patients, details of whom are given in Table 1. Comparative imaging with ^{111}In-DTPA-octreotide alone was performed in five patients and with ^{111}In-DOTA-TOC alone in four patients, while one patient underwent all three imaging modalities. The time between comparative studies normally ranged from 2 to 30 days, although in one patient the ^{111}In study was performed on

Table 1. Summary of patient data and comparative studies performed

Patient	Age (years)	Sex	Diagnosis	Comparison with:	Time interval between studies (days)
A	46	M	Oncocytic anaplastic thyroid carcinoma with known cervical and lung metastases	DOTA-TOC	32
B	60	F	Carcinoid of the papilla with liver metastases and a tumour mass in the upper abdomen	DOTA-TOC	14
				DTPA-octreotide	20
C	54	M	Carcinoid of the ileocecal valve with known liver and GI metastases	DTPA-octreotide	2
D	51	F	Carcinoid of the rectum with known liver metastases	DTPA-octreotide	25
E	32	F	Medullary thyroid carcinoma	DOTA-TOC	2
F	55	M	Oxyphilic thyroid carcinoma with low degree of differentiation, cervical lymph node involvement, lung metastases	DOTA-TOC	2
G	50	F	Endocrine pancreatic cancer with known liver metastases, unclear histology	DTPA-octreotide	2
H	57	F	Colorectal carcinoid recently treated by surgery, follow-up pending	DOTA-TOC	7
I	66	F	Carcinoid of the ileum with liver and lung metastases	DTPA-octreotide	3
K	55	F	Recurrence of TSH-producing pituitary adenoma	DTPA-octreotide	1

the day following the ^{99m}Tc study. Patients were not treated with cold somatostatin analogues within 1 month before the imaging studies.

Imaging. Planar imaging was performed with a double-head camera (Elscint HELIX, Haifa, Israel). All patients were imaged at 4 h post injection. Seven patients were additionally imaged at 1–2 h, and in two patients additional imaging was performed at 15 min and 20 h. For ^{99m}Tc studies the camera was equipped with a low-energy all-purpose parallel-hole collimator, window setting 140 keV, width 10%. ^{111}In images were obtained using a high-energy parallel-hole collimator, with window setting over both ^{111}In peaks at 172 and 246 keV and a window width of 20%.

Single-photon emission tomography (SPET) imaging of areas of interest was performed 4 h post injection and in some patients additionally at 20 h. For ^{99m}Tc tomographic acquisition, the same double-head camera as described above was used. Acquisition parameters were: 60 projections, 25 s/projection, matrix 64×64, zoom 1. SPET for ^{111}In studies was performed on a Siemens single-head camera (ZL3000, Siemens, Erlangen, Germany) equipped with a medium-energy parallel-hole collimator using 60 projections, 35 s/projection, matrix 64×64. This camera system was also used for SPET of brain and neck regions of interest (ROIs) for ^{99m}Tc studies using a low-energy parallel-hole collimator. In general, imaging parameters were chosen that produced comparable whole-body counts for both ^{111}In and ^{99m}Tc studies. Total whole-body counts (arithmetic mean of anterior and posterior images ± SD) were 2056±244 kcounts for ^{111}In studies and 1764±428 kcounts for ^{99m}Tc studies (decay-corrected to the time of injection).

For SPET analysis raw data were transferred to a Hermes system (Nuclear Diagnostics, London, UK). Before reconstruction data were filtered (Wiener filter). All images underwent clinical evaluation by three independent viewers, all experienced in the interpretation of Octreoscan studies.

Blood and urine analysis. In eight patients heparinised blood samples were taken at 5 and 15 min and 1, 2, 4 and 20 h post injection and radioactivity was determined in plasma and cells after centrifugation. Protein binding was determined using Microspin G-50 columns (Pharmacia Biotech) as previously described [8]. Urine was collected over 24 h in patients A, E, F, G and I for both the ^{99m}Tc- and the ^{111}In study and the cumulated excretion was calculated. Excreted urinary radioactivity at early time points (2–4 h) after injection of ^{99m}Tc-EDDA/HYNIC-TOC was analysed by HPLC in three patients.

Image analysis. All data were analysed on the Hermes system (Nuclear Diagnostics, London, UK) using an ROI technique for semi-quantitative analysis of main organ and tumour uptake. ROIs were drawn over whole body, tumour sites, kidneys, liver, spleen, heart and a right thigh area (as an ROI for muscle) on both the planar anterior and posterior views of the corresponding ^{111}In and ^{99m}Tc images. For evaluation of kidney uptake the left kidney was selected to avoid interference from liver superimposition. Parts of organs showing tumour infiltration or superimposition were excluded from evaluation of organ uptake. Total counts and counts per pixel in all ROIs were calculated. For the evaluation of uptake in malignant tissue the lesion with the maximum uptake in counts/pixel was selected and tumour/organ ratios for this lesion were calculated from the respective counts/pixel values in various organs. The view with the highest tumour/organ ratios was selected (anterior or posterior) and used for the direct comparison between ^{111}In and ^{99m}Tc in the same patient.

In seven patients the organ or lesion uptake was evaluated by calculation of the organ uptake (in counts/pixel) as a percentage of whole-body uptake (calculated from early images, 15 min or 1–2 h before voiding) using the conjugated views from anterior and posterior images. The resulting ratios again formed the basis for a direct comparison of the ^{99m}Tc and ^{111}In studies in the same patient.

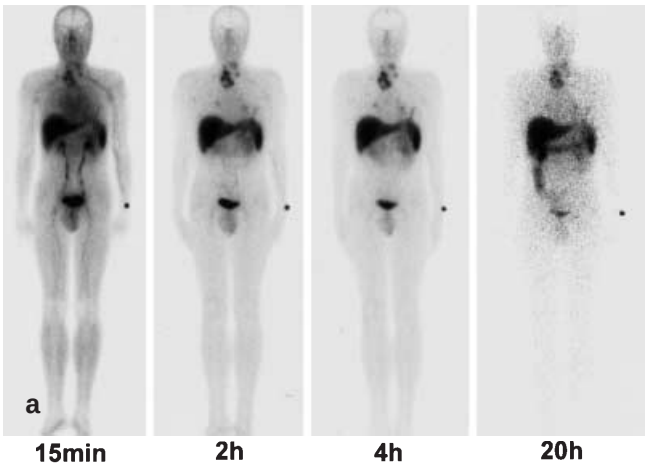
Statistical differences between the ^{99m}Tc and the ^{111}In studies were calculated using a paired *t* test; *P* values <0.05 were considered to be significant.

Tumour uptake was also evaluated from SPET images. Slices where lesions were clearly visualised were selected. ROIs were drawn over the lesion and a defined background or organ region (lung in the case of thorax or abdominal images, bone and base of the skull in the case of brain images) and ratios calculated.

Results

^{99m}Tc-EDDA/HYNIC-TOC showed a pharmacokinetic behaviour which was very similar to that of ^{111}In-Octreoscan. An example of the pattern observed in serial images at different times after injection is shown for patient A in Fig. 1a. By 15 min the main organs of tracer uptake, i.e. liver, spleen and kidneys, were clearly visible, the rapid renal clearance could be visualised and tumour uptake in various cervical lesions was already seen. These lesions were seen more clearly at 2 and 4 h, at which time muscle and blood activity is markedly reduced. After 20 h the lesions are still visible and some gastrointestinal excretion is observed, although the image quality is compromised owing to the low count rate caused by the rapid decay of ^{99m}Tc. The results of semi-quantitative analysis of this patient study are shown in Fig. 1b. Maximum tumour/organ ratios were observed 4 h after injection. Images of the SPET study of the chest (sagittal and coronal slices) in patient A (thyroid carcinoma) are shown in Fig. 2. Multiple tumour lesions in the neck are clearly visualised, but lesions with lower uptake in the left thorax can also be detected. Tumour/liver ratios and tumour/lung ratios in the SPET study were 1.4 and 12, respectively while the corresponding ratios calculated from anterior planar images were 0.81 and 3.61.

^{99m}Tc-EDDA/HYNIC-TOC showed a rapid bi-exponential plasma clearance. As shown in Fig. 3, the ^{111}In derivatives showed a very similar pattern although significantly higher plasma levels (*t* test, $P<0.05$) were found 2 and 4 h post injection with ^{111}In-DOTA-TOC. Cell-associated activity was lower than 5% irrespective of time after injection or radiotracer used. Protein binding was lower at early time points (e.g. 2%–11% at 5 min post injection) compared with late time points (33%–51% at 20 h) with no significant difference between ^{99m}Tc and ^{111}In studies. The cumulative 24-h urinary excretion rate of ^{99m}Tc-EDDA/HYNIC-TOC was between 24% and 64% ID and is summarised for five patients in Fig. 4a. A higher urinary excretion was found for ^{111}In-labelled derivatives. HPLC analysis of urine samples showed single peaks with retention times corre-



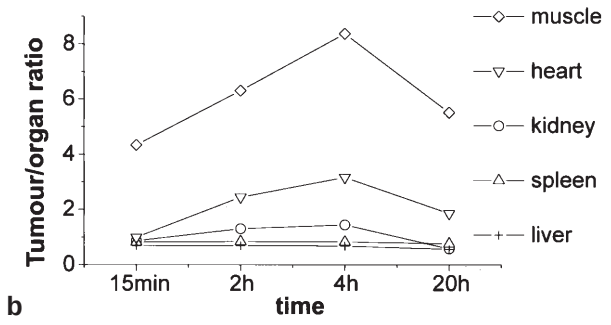


Fig. 1. a Anterior whole-body images of patient A (anaplastic thyroid carcinoma with cervical and lung metastases) at 15 min to 20 h post injection of 300 MBq of ^{99m}Tc-EDDA/HYNIC-TOC. Note the rapid uptake in liver, spleen, kidney and tumour and renal excretion. **b** Tumour/organ ratios over time for patient A; maximum ratios were obtained 4 h p.i.

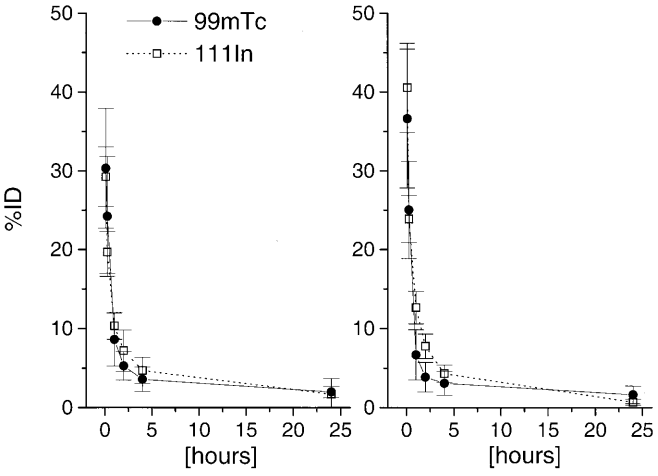


Fig. 3. Time-activity curves in plasma. Comparison of mean values ± SD between ^{99m}Tc-EDDA/HYNIC-TOC and ^{111}In-labelled octreotide derivatives in the same patients. *Left:* DTPA-octreotide (*n*=4); *right:* DOTA-TOC (*n*=5)

sponding to those of the injected standard and no signs of peptide degradation or complex instability (Fig. 4b).

Figure 5 shows a comparison of planar imaging results obtained using ^{111}In-DTPA-octreotide and ^{99m}Tc-EDDA/HYNIC-TOC in a patient with a pancreatic tumour of unclear histology (patient G). A very similar pattern of distribution is seen in both studies, with high uptake of the tracer in several focal tumour sites in the liver. Spleen and left kidney are clearly visualised. Visually both studies show high tumour uptake. However, semi-quantitative analysis showed considerably higher tumour/organ ratios for the ^{99m}Tc study than for the ^{111}In study, with the greatest differences in tumour/kidney (^{99m}Tc vs ^{111}In = 5.13 vs 2.23) and tumour/heart (13.00 vs 5.63) ratios, and the smallest difference in the tumour/liver ratio (2.44 vs 2.17). Additionally, focal lesions showed better individual separation and one additional lateral lesion could be detected in the ^{99m}Tc scan.

A direct comparison between ^{99m}Tc-EDDA/HYNIC-TOC and both ^{111}In-labelled octreotide derivatives was performed in patient B (carcinoid syndrome, Fig. 6). Again a very similar pattern of biodistribution can be observed for all three radiopharmaceuticals, with high up-

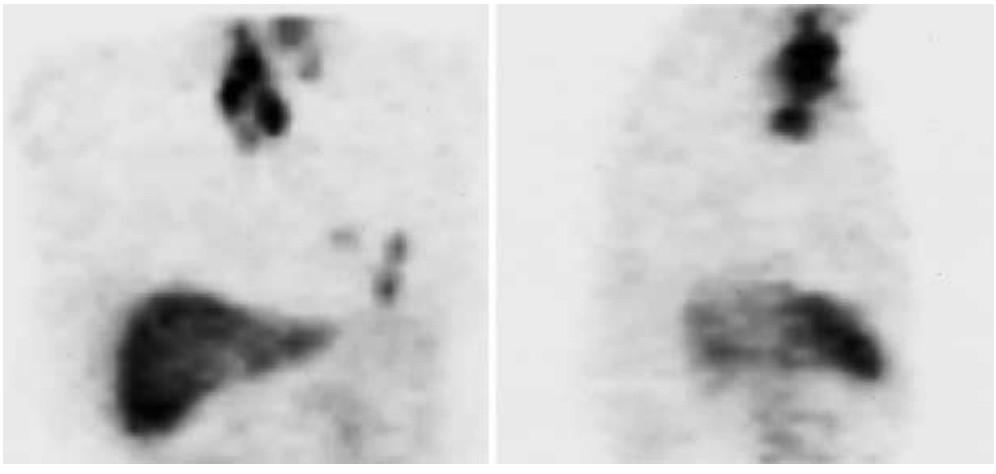


Fig. 2. SPET images [coronal (*left*) and sagittal slices (*right*)] of patient A 4 h post injection of ^{99m}Tc-EDDA/HYNIC-TOC. Note the high uptake in multiple tumour lesions in the neck and upper abdomen compared with the low activity in heart and soft tissue. Additional lung lesions in the left thorax which could not be detected in the planar images are visible in the coronal slice

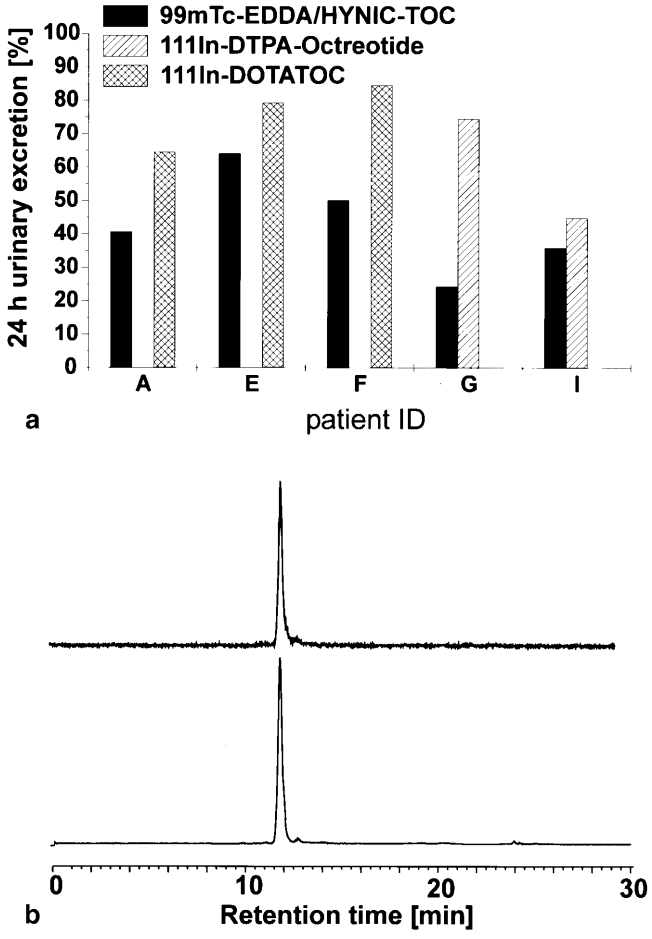


Fig. 4. a Urinary excretion of radioactivity in five patients. Percentage of radioactivity excreted within 24 h. **b** HPLC radioactivity profiles of a urine sample (*upper profile*, patient C, 4 h p.i.) in comparison with the injected tracer (*lower profile*). Method: Beckman Ultrasphere ODS 5 µm, 4.6×250 mm column, flow rates of 1 ml/min acetonitrile/0.01 *N* phosphate buffer pH 6.2, gradient as described in [7]

take in tumour in the hepatic and intestinal areas. Semi-quantitative analysis revealed similar tumour/organ ratios in liver and spleen for all tracers, but considerably higher ratios for ^{99m}Tc-EDDA/HYNIC-TOC for heart and muscle.

Figure 7 shows images of SPET studies of a patient with a pituitary adenoma (patient K, sagittal slices). Comparison of the ^{99m}Tc-EDDA-HYNIC-TOC and ^{111}In-DTPA-octreotide images shows the considerably lower background activity of the ^{99m}Tc study, with tumour/bone and tumour/skull base ratios of 6.58 and 1.89 compared with ratios of 2.94 and 1.06, respectively, for the ^{111}In study.

A comparative evaluation of the mean values of tumour/organ ratios between ^{99m}Tc-EDDA/HYNIC-TOC and both ^{111}In-DTPA-octreotide (n=6) and ^{111}In-DOTA-TOC (n=3) is summarised in Fig. 8. In the ^{111}In-DTPA-octreotide comparison, significantly higher ratios were found for the ^{99m}Tc tracer in kidney, heart and muscle. In comparison with ^{111}In-DOTA-TOC, higher heart and muscle ratios were also found but, due to the small number of patients (n=3) in this group, statistical analysis could not be performed.

Semi-quantitative measures of organ or lesion uptake in relation to injected dose are summarised in Fig. 9. Although there was a tendency towards higher uptake of ^{99m}Tc than ^{111}In in several tissues, notably tumour lesions, the differences were not statistically significant in either the ^{111}In-DOTA-TOC or the DTPA-octreotide group.

Of the ten patients included in this study, two showed no pathological uptake (patients E and H), two showed a single lesion (patients D and I) and six showed multiple lesions in the ^{99m}Tc scan. A comparison of ^{111}In and ^{99m}Tc with regard to the number of lesions detected in planar images from patients with multiple lesions is shown in Fig. 10. Variations in the number of lesions dependent on individual reporting were observed. However, overall, most reporters found a higher number of lesions in the ^{99m}Tc images for most patients.

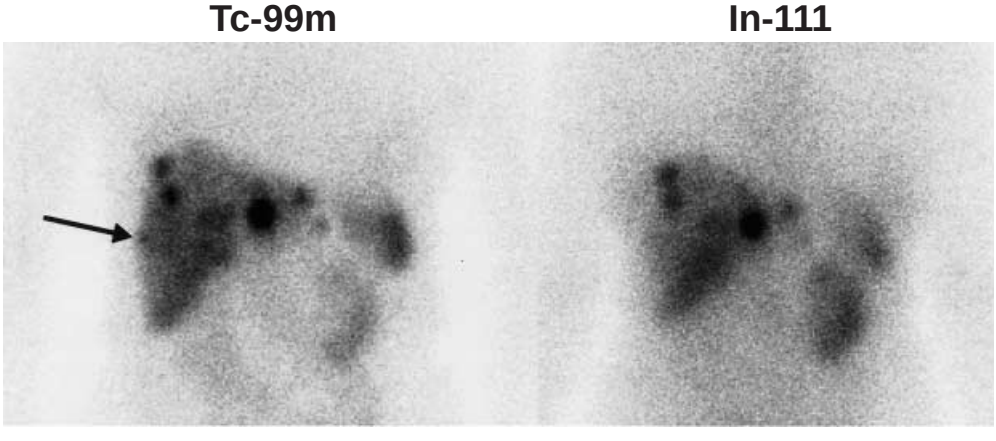


Fig. 5. Comparison of planar abdominal images of patient G, 4 h post injection. *Left:* ^{99m}Tc-EDDA/HYNIC-TOC; *right:* ^{111}In-DTPA-octreotide. Note the additional lateral liver lesion (*arrow*) visible in the ^{99m}Tc-scan

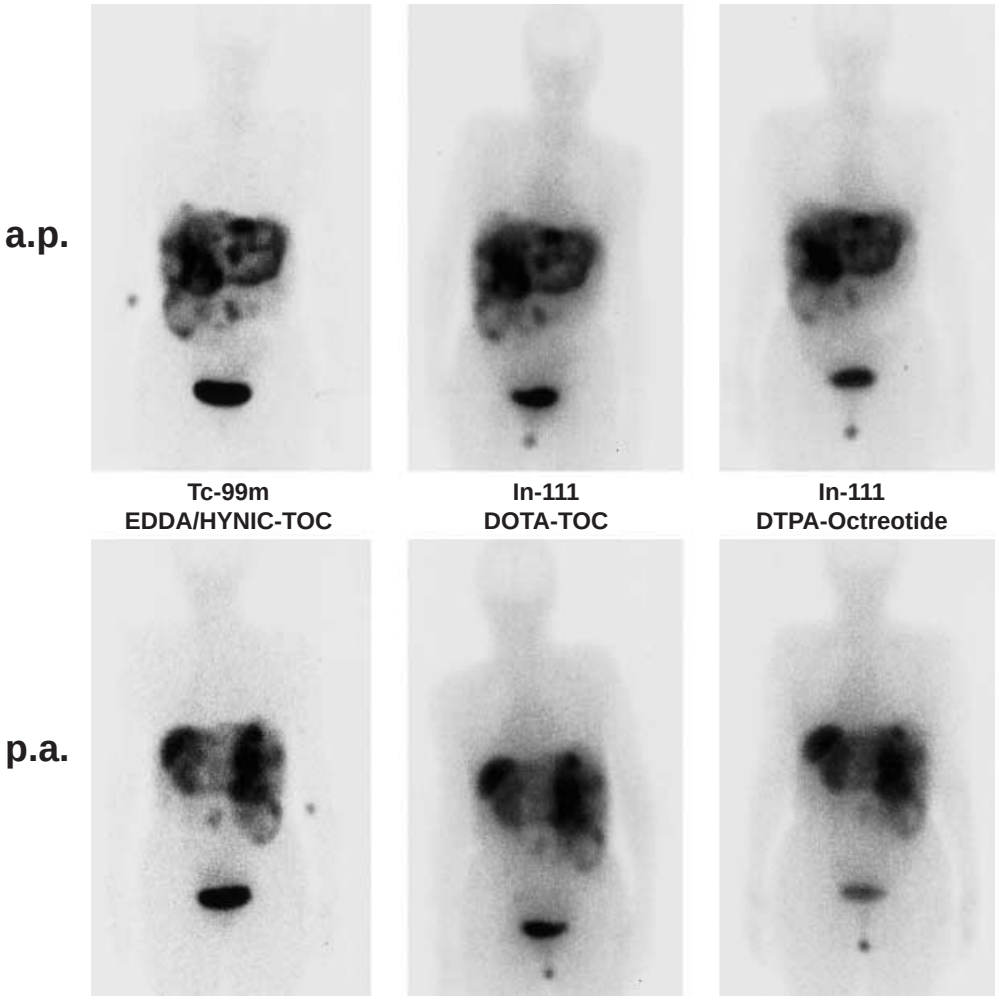


Fig. 6. Comparison of all three tracers studied. Planar images of patient B (carcinoid) 4 h p.i.: anterior view (*top row*) and posterior view (*bottom row*)

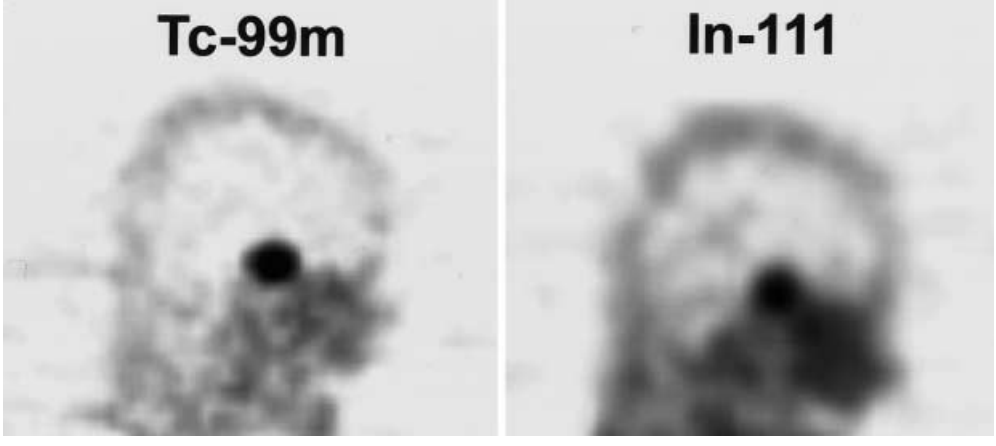


Fig. 7. Sagittal SPET slices of a patient with a pituitary adenoma 4 h post injection. *Left:* ^{99m}Tc-EDDA/HYNIC-TOC; *right:* ^{111}In-DTPA-octreotide. Note the lower uptake in tissue adjacent to tumour in the ^{99m}Tc image as compared with the ^{111}In image; see text for tumour/tissue ratios

Discussion

In a preclinical study ^{99m}Tc-EDDA/HYNIC-TOC has previously shown very promising properties as a new imaging agent for somatostatin receptor-positive tissue [6]. Compared with other bifunctional chelators such as mercaptoacetyltriglycine, we found HYNIC to be a superior complexing agent for labelling octreotide analogues but its performance depended very much on the co-ligand system employed. Thus, in a somatostatin receptor-positive mouse tumour model [6], the use of tricine, a very frequently used co-ligand for the HYNIC system [9], resulted in much higher residual activity in blood, muscle, kidneys and liver than the best co-ligand, EDDA, owing to a greater degree of instability of the tricine complex that resulted in high plasma protein bind-

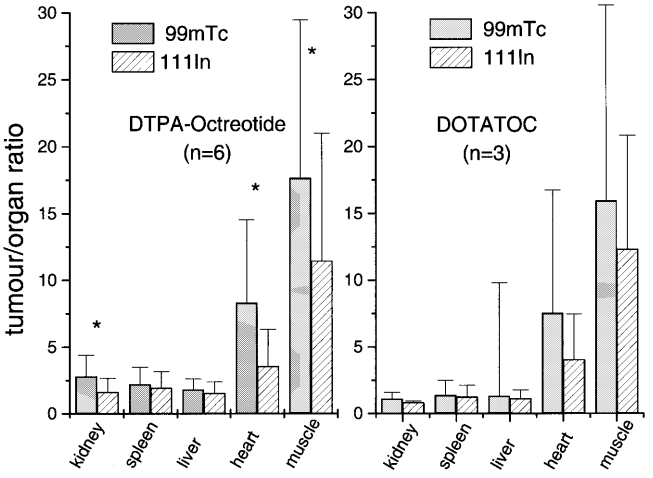


Fig. 8. Mean values (±SD) of tumour/organ ratios from planar images directly comparing ^{99m}Tc-EDDA/HYNIC-TOC with either ^{111}In-DTPA-octreotide (*left*, six patients) or ^{111}In-DOTA-TOC (*right*, three patients). **t* test, $P<0.05$

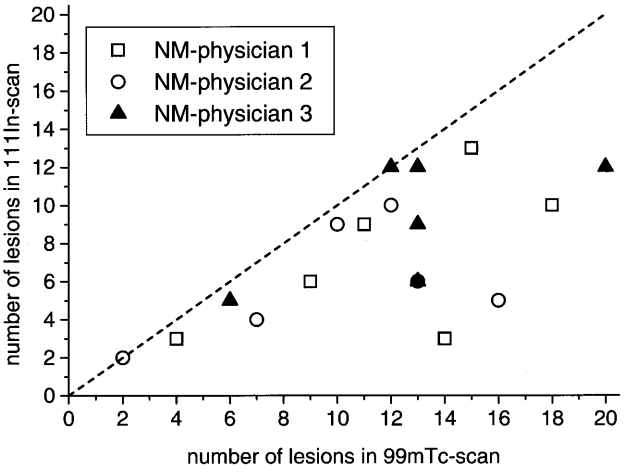


Fig. 10. Lesion detectability with ^{99m}Tc-EDDA/HYNIC-TOC compared with ^{111}In-labelled derivatives. Lesions detected in the ^{99m}Tc scan plotted against lesions detected in the ^{111}In scan for each patient and each of three independently reporting physicians. Note the higher number of lesions detected in the Tc scan by all reporters

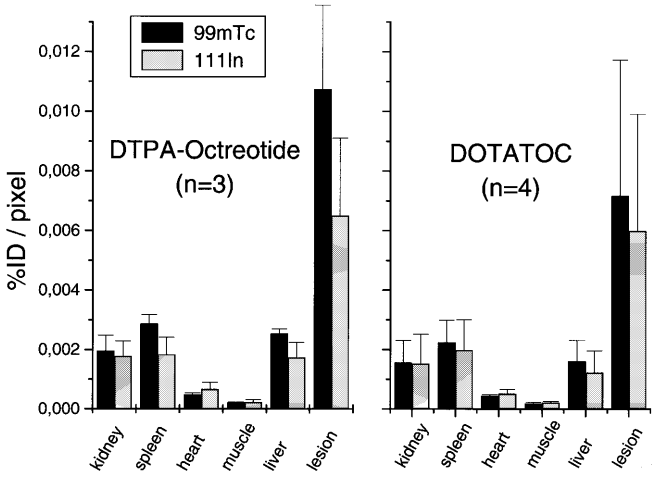


Fig. 9. Organ and lesion uptake (mean ± SD) relative to injected activity calculated from the conjugated views of planar images expressed in comparison with ^{111}In-DTPA-octreotide (*left*, three patients) and ^{111}In-DOTA-TOC (*right*, four patients)

ing. Although ^{99m}Tc-tricine/HYNIC-TOC showed good results for imaging somatostatin receptor-positive tumours in a preliminary clinical study by Bangard et al. [10] on seven patients, the superior preclinical results we obtained with EDDA persuaded us to choose this coligand system for our first clinical studies.

Our promising preclinical results have been largely supported in humans. Thus ^{99m}Tc-EDDA/HYNIC-TOC produced a very similar pattern of biodistribution to ^{111}In-labelled octreotide derivatives in the ten subjects studied so far. A very rapid uptake of the radiopharmaceutical in somatostatin receptor-positive tumours was observed, with lesions being imaged as early as 15 min after injection. The main organs of tracer uptake were liver, spleen and kidneys, with kidneys being the predominant route of excretion and only minimal hepatobiliary clearance being observed in late images.

One important difference was, however, seen between the clinical and preclinical studies. While in mice the blood clearance of ^{99m}Tc-EDDA/HYNIC-TOC was considerably slower than that of ^{111}In-DTPA octreotide, leading to higher "background" levels of radioactivity, in man the rates of blood clearance were almost identical, with a typical biphasic pattern in accordance with previous studies of ^{111}In-labelled somatostatin analogues [11,12]. The 24-h urinary excretion in humans was significantly lower for ^{99m}Tc-EDDA/HYNIC-TOC than for its ^{111}In-labelled counterparts and this factor, combined with the similar rate of blood clearance, indicates that the ^{99m}Tc must have a greater degree of retention in both target and non-target tissues. However, it seems unlikely that this is caused by a significant degree of in vivo instability, since HPLC analysis of urine revealed no breakdown products therein.

In terms of tumour localisation in this study, the two radionuclides performed very similarly. Thus, two patients did not show any pathological uptake of either the ^{99m}Tc or the ^{111}In tracer; one had uncertain staging of the disease (patient H) and one (patient E) had medullary thyroid carcinoma, a disease which rarely shows expression of somatostatin receptors [13,14]. Two patients with only a single lesion also revealed matching results, although, as can be seen in Fig. 7, the ^{99m}Tc image was clearly superior. However, in patients with multiple lesions, the ^{99m}Tc tracer detected a greater number of lesions than its ^{111}In counterparts.

In addition to this subjective comparison, attempts were made to compare the tracers more objectively through a semi-quantitative approach. ROI analysis revealed that when the organ or lesion ROI was related to

the injected dose (whole-body ROI before excretion) a tendency towards greater uptake of technetium could be seen although no statistically significant differences were observed. However, when the tumour uptake was compared with uptake by normal tissues, significantly higher uptake ratios were obtained for ^{99m}Tc-EDDA/HYNIC-TOC. One can therefore conclude that, at least in this small pilot study, ^{99m}Tc-EDDA/HYNIC-TOC performed better than ^{111}In-Octreoscan at imaging somatostatin receptor-positive tumours, at least at early time points p.i.

The question of why the technetium-labelled tracer should be superior can only be answered definitively by a more controlled study. This superiority cannot be related to a higher counting statistics, as these were considerably better in the ^{111}In images. It is likely that the superiority depends upon a number of factors including: the better physical decay properties of the radionuclide, the enhanced affinity of the Tyr^3-octreotide peptide to somatostatin subtype 2 receptors [15] and perhaps a better pharmacokinetic profile of the labelled complex. These and other important issues will form the basis of a more extensive clinical trial, which will also address the question of how 4-h p.i. imaging of the ^{99m}Tc compound compares with later (24–48 h p.i.) imaging of the^{111}In radiopharmaceuticals. However, we would suggest that the evidence presented herein is at least sufficient to suggest that ^{99m}Tc-EDDA/HYNIC-TOC can be usefully clinically employed for imaging neuroendocrine tumours, thereby taking advantage of the greater availability and lower cost of this radionuclide.

A more distant but still more exciting possibility is raised by the potential to replace technetium with the beta-emitting radionuclide rhenium-188 in order to develop a new therapeutic radiopharmaceutical. The high tumour uptake of ^{99m}Tc-EDDA/HYNIC-TOC combined with the apparently good retention of the radionuclide by the tumour suggests that this is a prospect worth pursuing.

Conclusion

The imaging properties of ^{99m}Tc-EDDA/HYNIC-TOC appear to be advantageous for investigating somatostatin receptor-positive tumours in man. This new preparation has a rapid tumour uptake and a similar biodistribution to ^{111}In-DTPA-octreotide but produced higher tumour to organ ratios and detected a greater number of lesions. Finally, the easy availability of ^{99m}Tc from generators and the low cost of this radionuclide make ^{99m}Tc-EDDA/HYNIC-TOC a promising candidate to replace currently used ^{111}In-octreotide derivatives in diagnostic nuclear medicine in oncology.

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