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THREE-DIMENSIONAL OCTREOSCAN111 SPECT OF ABDOMINAL MANIFESTATION OF NEUROENDOCRINE TUMOURS

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In the present study we have investigated the three-dimensional (3D) reconstruction of OctreoScan111 SPECT (single photon emission tomography) images in 20 patients with neuroendocrine tumours. All patients had at least 2 tumour lesions as assessed from computerized tomography (CT) and SPECT. The 3D rendering was performed using a software, which produces images by implementing direct rendering from voxels without an intermediate surface data structure. The software has options for a free choice of thresholding and possibilities of clipping in coronal, transversal and sagittal planes. The results obtained showed that 3D reconstruction with volume rendering (3Dvr) gave a superior topographical localization of tumour uptakes when compared with SPECT. The 3Dvr technique was also combined with transversal clipping in rendered volumes (3Dvr + c). The major advantage with the 3Dvr + c technique was found to be an improved visualization of anatomical references as well as improved diagnostic information in a particular, selected, transversal slice, thus facilitating the identification and comparison of individual tumour lesions.

Somatostatin, which was discovered in 1973, has a wide range of biological actions (1, 2). Apart from its physiological functions in normal cells, the hormone also binds to neuroendocrine tumours, which have been demonstrated to express large numbers of somatostatin receptors (3–5). Natural somatostatin has a short half-life in humans. Thus, somatostatin analogues that have a longer half-life in serum have been developed for therapeutic purposes. The treatment of neuroendocrine tumours using such somatostatin analogues has been shown to have a good effect on the patients' symptoms (6–9). Tyr-3-octreotide radiolabelled with ^{123}I has been successfully used for the scintigraphic visualization of neuroendocrine tumours in humans (10–12). Further development has resulted in the synthesis of (^{111}In-DTPA-D-Phe^{1})-octreotide (^{111}In labelled pentatreotide, OctreoScan111), a substance even more suitable for scintigraphic use in the in vivo localization of neuroendocrine tumours (13, 14). We have previously reported the results from a study of OctreoScan111 in 40 patients with abdominal neuroendocrine tumours (GEP tumours) (16). OctreoScan111 is rapidly cleared from blood. However, background activity is too weak to visualize normal organs, thus making the exact topographical localization of different tumour uptakes difficult in reconstructed transversal SPECT images. In the present study, we have investigated whether 3D volume rendering together with different clipping planes can add information to images, especially as regards distinguishing between different types of uptakes. We also wished to answer whether additional information could be obtained with respect to the topographical localization of pathological uptakes in cranio-caudal projections.

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Material and Methods

Patients

Fifty-two patients entered the GEP-study. Twenty of these (7 males and 13 females) were shown to have more than 2 uptakes in the abdomen and were selected for further investigation using the 3D-technique. Two patients suffered from metastasizing foregut carcinoid tumours, 6 from metastasizing endocrine pancreatic tumours and 12 patients from metastasizing midgut carcinoid tumours. In order to avoid artifacts from the accumulation of OctreoScan111 in the intestine, the patients were routinely given laxatives, starting on the day of the administration of the Octreoscan111 and continuing throughout the study.

Imaging procedures

The OctreoScan111 was delivered by Mallinckrodt Medical, Petten, the Netherlands. The labelling procedure and the control process of the labelling yield have been described elsewhere (13). Briefly, the ^{111}In-chloride (240 MBq) was added to the lyophilized (DTPA-D-Phe^{1})-octreotide (20 μg) and incubated for 30 min at room temperature. The labelling yield was controlled with reversed phase chromatography using SEP-PAK (15). The labelling yield always exceeded 97%. Each patient received 200–240 MBq of OctreoScan111 as an intravenous bolus injection. Four hours post administration static images were collected, covering the body from head to knees in frontal and dorsal projections. If intra-abdominal uptake was seen in the 4-h postinjection study, a 24-h postinjection SPECT (Single Photon Emission Tomography) study was performed over the abdomen. A gamma scintillation SPECT-camera delivered by Nuclear Diagnostics (Hägersten, Sweden and London, U.K.) was used. The collection of original data for SPECT images was performed using a 64-step rotation of 360° in a 64 × 64 word matrix. For the reconstruction of the SPECT images a Wiener filter was applied to original data and reconstruction was performed in 64 transversal slices.

3D-rendering

The three-dimensional rendering was performed using 'Hermes' software, working under X-Windows in a SUN-Sparc station, developed by nuclear Diagnostics (Hägersten, Sweden and London, U.K.). The volume rendering has earlier been shown to be superior to surface rendering techniques and to minimize threshold artifacts (17, 18). The 'Hermes' software produces images by direct rendering from voxels without an intermediate surface data structure (19, 20). The software has options for a free choice of thresholding, and possibilities of clipping in coronal, transversal and sagittal planes. Rendered images can be displayed with one colour table for the rendered surface and with another colour table in the clipping plane, thus producing a view of the selected volume and information about the distribution of radioactivity in selected clipping planes in relative or absolute scaling. The software allows a free choice of rotation of the rendered volume. Typically, a lower threshold of 15–30% and an upper threshold of 100% was used to render the volume images. To achieve a better view of different uptakes, rotations were performed individually, as was transversal clipping in rendered volumes. In order to control that exactly the correct level in the craniocaudal projections was handled in transversal SPECT images and in rendered 3D images, transversal clipping of the rendered volume was used together with rotation. The evaluation of different uptakes in reconstructed SPECT images and 3D-rendered images was performed blindly. Thereafter, each uptake was compared individually.

Comparison entailed:

1. transversal SPECT vs. 3D volume rendering (3Dvr) and
2. 3Dvr vs. 3D volume rendering + transversal clipping (3Dvr + c).

In transversal SPECT, absolute as well as relative scaling was used. During evaluation, identical colour tables were used but the upper and the lower thresholds were adjusted individually. Colonic uptakes were not considered when comparing 3Dvr versus 3Dvr + c, since all colonic uptakes except in the case of patient No. 11, were assessed as physiological after evaluation of the comparison between transversal SPECT and 3Dvr.

Results

The results from the comparison of transversal SPECT versus 3Dvr and 3Dvr + c are summarized in the table. A typical example of the 3D technique is shown in Fig. 1. In 7/17 patients there was no difference in the number of uptakes when the three techniques were compared. In total, 147 uptakes were detected using transversal SPECT images whereas only 115 uptakes were detected using the 3Dvr technique. Of the differing 32 uptakes, 18 were located in the colon, 9 in the liver and 5 in abdominal lymph nodes. In addition, transversal SPECT, in comparison with the 3Dvr technique, showed 5 additional pathological uptakes located in abdominal lymph nodes. When compared with transversal SPECT, the 3Dvr technique resulted in a superior topographical localization, with the uptakes in the colon excluded, of 10 pathological uptakes (3 in the pancreas, 1 in the pleura, 1 in a skeletal metastasis and 5 in abdominal lymph nodes). With respect to disease, a superior localization was achieved in 4/6 patients with endocrine pancreatic tumours whereas an improved tumour localization was seen in 3/14 of the carcinoid patients. In one patient (No. 7) with an endocrine pancreatic tumour, a

Table

Comparison transversal SPECT v.s. 3D-SPECT (Volume rendering + Clipping planes). Abbreviations used: fc, fore-gut carcinoid; mc, mid-gut carcinoid; ept, endocrine pancreas tumour

Patient No.	Diagn.	Lesions transv. SPECT n	Lesions 3D vol. rendering n	Lesions 3D vol. rendering + transv. clipping n	Reasons for discrepancies
1	fc	10	9	9	one colonic uptake assessed as 1 in trv. SPECT
2	fc	5	3	3	colonic uptake assessed as 2 in trv. SPECT
3	ept	3	3	3	
4	ept	9	5	6	one liver met assessed as 2 and colonic uptake as 2 in trv. SPECT uptake in lymph nodes shown as 1 in 3Dvr
5	ept	9	5	5	colonic uptake assessed as 4 in trv. SPECT
6	ept	4	4	4	
7	ept	7	6	6	one liver met assessed as 2 in trv. SPECT
8	ept	3	3	3	
9	mc	14	10	10	one liver met assessed as 2, colonic uptake assessed as 3 in trv. SPECT
10	mc	4	4	4	
11	mc	12	9	12	three liver met assessed as 2 in trv. SPECT uptake in lymph nodes shown as 1 in 3Dvr
12	mc	12	10	10	two liver met. assessed as 2 in trv. SPECT
13	mc	10	6	7	one liver met assessed as 2 and colonic uptake as 2 in trv. SPECT uptake in lymph nodes shown as 1 in 3Dvr
14	mc	7	6	6	colonic uptake assessed as 1 in trv. SPECT
15	mc	2	2	2	
16	mc	4	3	3	colonic uptake assessed as 1 in trv. SPECT
17	mc	2	2	2	
18	mc	12	10	10	colonic uptake assessed as 2 in trv. SPECT
19	mc	15	12	12	two liver met assessed as 2, one colonic uptake assessed as 2 in trv. SPECT
20	mc	3	3	3	
SUM		147	115	120	

better topographical localization was achieved in one lesion located in the pleura in front of the cardiac apex and in a skeletal metastasis located in a rib (Fig. 2). This skeletal metastasis was also verified by bone-scan using ^{99}Tc-HDP.

When comparing 3Dvr with 3Dvr + c, the 3Dvr-technique detected 115 uptakes whereas the 3Dvr + c technique detected 120 uptakes. 3Dvr + c showed that minor uptakes had disappeared when trying to find the correct level for the lower threshold in separating uptakes in 3Dvr in 5 locations. In patient No. 10, 3Dvr + c revealed that the abdominal uptake, assessed as single in 3Dvr, in reality comprised 3 separate uptakes.

Discussion

The liver parenchyma expresses somatostatin receptors. This results in a weak OctreoScan111 background activity, thus enabling the localization of uptakes in the liver in the reconstructed transversal SPECT images. However, it is difficult to distinguish between the head of the pancreas and the liver due to the absence of background activity in these slices. In these areas we have found the 3Dvr to be of value. It is also difficult to find the exact location of an uptake in front of the right kidney due to the low background activity in these transversal slices. The 3D rendering technique also facilitated the localization of uptakes in these areas. Most of the patients accumulated OctreoScan111 in the colon; sometimes in the whole colon transversum and sometimes only in one single area. If this area is located in front of the kidney or in an area adjacent to the kidney, the 3Dvr technique is of value, especially when a neuroendocrine pancreatic tumour is suspected or when the distinguishing between uptakes located in the colon and the right liver lobe is required.

We also found that it was possible to achieve a quick overview of volume distribution in the patient together with anatomical information in one single image. This has proven to facilitate the interpretation of uptake distribution in transversal slices. It is also easier to visualize

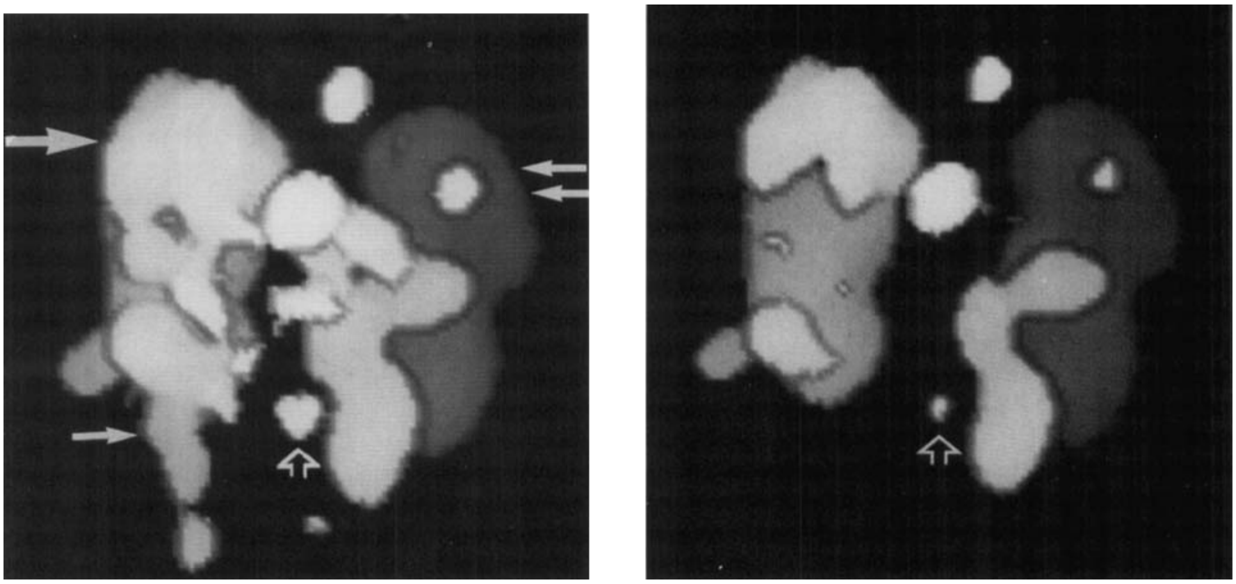

Fig. 1. 3D generated images using volume rendering on reconstructed SPECT data from patient No. 11. These images from this study show the effect of too high a lower threshold. The abdominal uptakes are viewed slightly from the right side. Left image: Nuclide uptakes are seen in the colon (small arrow), in the liver (big arrow), in mesenteric lymph nodes (unfilled arrow), and in the spleen (double arrows). In the right image, generated using a higher lower threshold, the liver uptake is lower. In this image low uptakes in abdominal lymph nodes have diminished or disappeared (unfilled arrow).

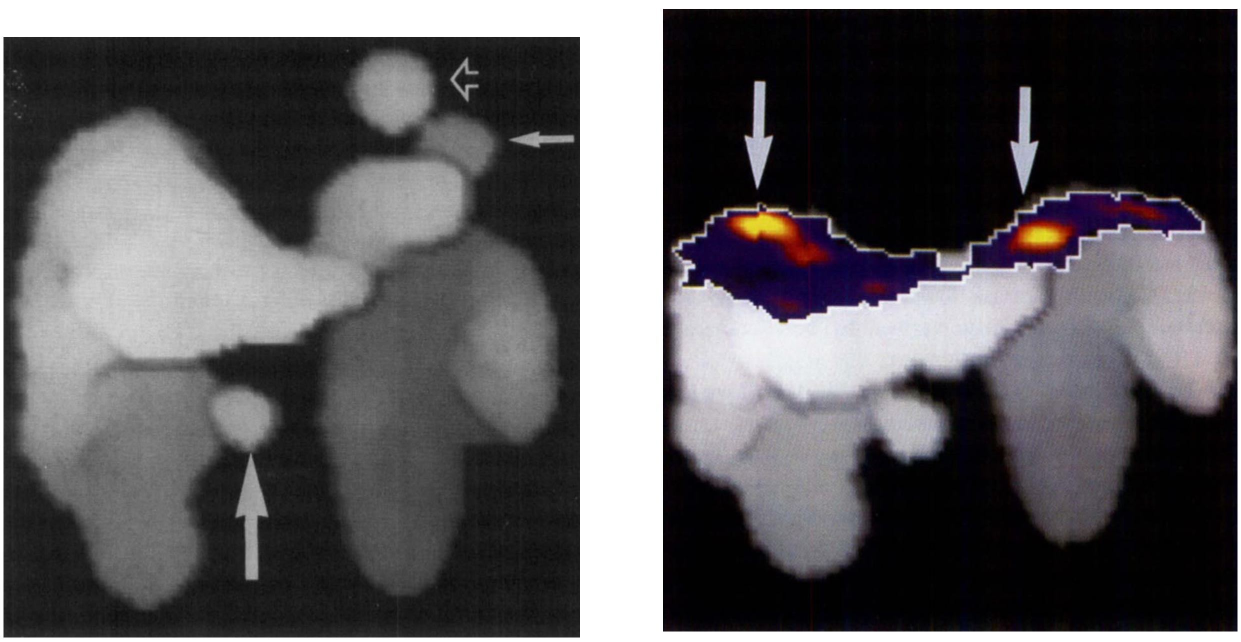

Fig. 2. OctreoScan111 scintigraphy data from patient No. 7. Left image: This study demonstrates the effect of clipping in a 3D rendered image using volume rendering and transversal clipping. The volume rendered image to the left shows the abdominal uptake slightly from the patient's right side. The patient's tumour is seen under the liver (big arrow). Uptakes in the pleura (small arrow) and in skeleton (unfilled arrow) are also seen. Right image: By applying a transversal clipping plane and a slight forward rotation, additional information on uptake distribution within the rendered volume is displayed in the 3Dvr + c. Two liver metastases are seen (arrows). The 3Dvr + c technique reveals that the uptake in the center of the left image is located in the left liver lobe. Both images were rendered using the same lower threshold.

elongated 'tube-like' structures, such as the ascending colon, the descending colon and retroperitoneal lymph nodes, in the sagittal plane. These are in transversal SPECT spuriously often regarded as multiple uptakes, whereas in 3Dvr these uptakes are shown to be part of the same structure.

Our interpretation of this study is that the differences between lesions detected in transversal SPECT and lesions detected in 3Dvr, or the differences between lesions detected when comparing 3Dvr and 3Dvr + c, are due to the 3Dvr technique itself. The lower threshold is critical when attempting to separate small uptakes located closely together. Too high a lower threshold makes the smallest uptakes disappear and too low a lower threshold cannot distinguish between the uptakes. In cases like these, discrepancies are seen between transversal SPECT and 3Dvr and between 3Dvr and 3Dvr + c. In a previous study comparing transversal SPECT with CT, we found that metastases with a diameter <1.5 cm and located closely together, could not be distinguished from each other in transversal SPECT. Also the number of uptakes, 18, assessed as pathological in transversal SPECT, but disclosed as located in the colon with the 3Dvr technique, is high. The localization of intra-abdominal lymph node metastases and the distinction between pathological lesions and physiological colonic uptakes are extremely difficult in transversal SPECT since the intensity of an uptake depends on the size as well as the intensity of the uptake in the tumour. In such cases, the 3Dvr technique is of value.

A superior topographical localization, regardless of the colonic uptakes, was achieved, when comparing 3Dvr with transversal SPECT in a total of 10 uptakes, where the most important ones were located in the pancreas and the abdomen.

When comparing 3Dvr with 3Dvr + c, the latter technique disclosed 5 additional uptakes. The major advantage in using 3Dvr + c is that this technique shows anatomical references together with diagnostic information in a particular, selected transversal clipping plane thus facilitating the comparison of each particular uptake. The human mind has difficulties in integrating consecutive transversal slices into a 3D volume. Thus, the integration of multiple tumour uptakes located close to each other can lead to an over-diagnosis when assessing the number of tumour lesions. Our results show that there is a risk of 'over evaluation' when using only transversal SPECT. In these cases, a combination of 3Dvr and 3Dvr + c is superior, especially when evaluating consecutive studies in one and the same patient. Possibly the 3D technique is of minor value when tracers giving a higher background activity are utilized, but progress in tracer technology will most probably result in more tracers such as the OctreoScan111, which gives very little background activity on the ability of the nuclear medicine specialist in exactly locating uptakes and evaluating consecutive studies of individual patients. In these cases, the 3D techniques will become a valuable tool in understanding the distribution of radioactivity. The 3D techniques also make it easier for non-nuclear medicine specialists to interpret uptake distributions and may have a future impact on the presentation of nuclear medicine investigations, especially when surgery is considered. The new generation of computers offers a high degree of performance and the time to generate a 3D image is constantly decreasing. In our computer (SUN Sparc Station, IPC), the generation of a typical 3D image takes less than 10 s and it is thus practical to use in clinical praxis. Our impression is that clinicians, using the images as a basis for therapy decisions, have found 3D images of value in better understanding the anatomic localization of a tumour lesion before planned surgical intervention.

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