Meta-iodobenzylguanidine (MIBG) is an analogue of noradrenaline which concentrates in adrenergic vesicles. Studies performed with an iodine-131 radiolabelled form (131I-MIBG) have shown that it can be used as an imaging agent for the adrenal medulla (Fischer et al., 1984) and its neoplasms (phaeochromocytoma and neuroblastoma) (Hoeftagel et al., 1987; Kimmig et al., 1984). 131I-MIBG has also been shown to localise in paraganglioma, another tumour arising from the sympathetic nervous system (Pease & Polak, 1978), and in medullary carcinoma of the thyroid (Shapiro et al., 1985). These tumours show a common APUD (amine precursor uptake and decarboxylation) mechanism (Sisson et al., 1981). Carcinoid tumours also possess a number of APUD properties, including in particular neuroscience (dense core) granules and the ability to produce a variety of biogenic amines. Preliminary studies have suggested that carcinoid tumours may also take up 131I-MIBG (Sisson et al., 1984; Smit et al., 1984).

If carcinoid tumours were shown to take up this radio-pharmaceutical with sufficient concentration then it might be possible to achieve therapeutic doses of 131I-MIBG, a technique successfully employed with malignant phaehromocytoma (Sone et al., 1985).

We describe a study to investigate further the uptake of 131I-MIBG for diagnostic imaging in 11 patients with confirmed metastatic carcinoid tumours.

Eleven patients known to have metastatic carcinoid tumours were studied. In 5 patients secondary deposits were histologically confirmed as carcinoid. The remaining 6 patients had metastatic tumours diagnosed by CT scanning or ultrasound and elevated urinary 5 hydroxyindoleacetic acid (5HIAA) levels, the original primary tumour had been diagnosed histologically. Ten of the 11 patients had abdominal CT scan or ultrasound to document metastases. An NMR scan was performed in one patient (10). Bone scans were only performed in patients with bone pain. Patient details are shown in Table I.

The patients received 0.3 ml of Lugol's iodine 3 times a day for 3 days prior to and 3 days after administration of 131I-MIBG to prevent thyroid uptake of the radioiodide.

131I-MIBG (20-40 mBq) was injected intravenously. Imaging was performed at 24 and 48 h following injection for all patients, and at 72 h in 6 patients, using a Siemens ZLC75 Gamma camera.

A medium energy collimator was used with the peak set at 350 KeV and a window of 15%. Images were acquired over 600 seconds. Planar anterior and posterior views of the chest and abdomen were taken with selective views of clinically involved areas.

| Table I | Patient characteristics. |
|---------|--------------------------|
| Age     | 41–72 (Median 60)        |
| Sex     | M: 5, F: 6               |
| No. of sites of disease | 1–3 (Median 1) |
| 5HIAA levels        | 115–1,198 (Median 845) µmol 24 h⁻¹ |
| Sites of primary tumour | Ileum 4, Ovary 1, Lung 2, Unknown 4 |

Uptake at tumour sites was compared with normal uptake both in the liver and the myocardium.

The levels of 131I-MIBG in the areas involved by carcinoid tumour in relation to the myocardial and liver uptakes are summarised in Table II together with the sites of disease, symptoms experienced and urinary 5HIAA levels for individual patients.

In 8 (73%) patients unequivocal abnormal uptake was seen. One patient (8) had abnormal uptake in a single area within the liver, whereas CT scan showed multiple metastases. One patient (2) demonstrated a mixture of 'hot' and 'cold' areas in the liver. In 3 patients no abnormal uptake was seen. No sites of disease were identified on 131I-MIBG scintigraphy that were not also detectable by other tests. One patient (5) with a negative 131I-MIBG scintigram was the only patient in our group to have bone metastases (histologically proven) and he also suffered no 'carcinoid' symptoms. A 90Ymethylene diphosphonate bone scintigram showed multiple areas of increased uptake, and this appearance was shown to be gradually progressing over a 4-year period. A second patient with a negative 131I-MIBG scintigram (11) had only moderately elevated 5HIAA levels and was asymptomatic. The third had a lung primary with hepatic metastases, an elevated 5HIAA and marked symptoms. The liver metastases were documented by ultrasound and CT scanning.

We found no correlation between the urinary 5HIAA levels and 131I-MIBG uptake in the tumours. One patient (6) had levels only modestly raised at 132 µmol 24 h⁻¹ (N<75 µmol 24 h⁻¹) but an unequivocally positive scintigram and marked symptoms while another patient with 5HIAA levels 5 times this level had a negative scintigram.

We also found no relationship between 'carcinoid' symptomatology and 131I-MIBG uptake. Patient 5 suffered florid carcinoid symptoms (with elevated urinary 5HIAA levels) but no uptake of the 131I-MIBG was seen.

We did not observe an increase in uptake of the 131I-MIBG after 48 h and therefore scanning at 72 h was discontinued. Compared with other studies we saw low levels of myocardial activity at 48 h (none in 6/11 patients).

Our results confirm that 131I-MIBG is preferentially taken up by the majority of metastatic carcinoid tumours, with a 73% positive uptake in this study compared with 63% in Hoefnagel's series (Hoefnagel et al., 1987). However, this incidence is lower than in malignant phaeochromocytoma where more than 90% of lesions take up 131I-MIBG (Wieland et al., 1981). In keeping with other authors we found no correlation between urinary 5HIAA and 131I-MIBG uptake. However, we were unable to confirm the relationship between carcinoid symptomatology and 131I-MIBG uptake reported by Hoeftagel et al. (1987).

We were unable to demonstrate preferential uptake of radiolabelled MIBG in particular sites. Although our only patient with bony metastases did not show any uptake of 131I-MIBG, Hoeftagel found that 2 of 3 patients with bone involvement showed abnormal uptake.

In 2 patients the uptake varied from lesion to lesion. The 131I-MIBG scintigram suggested a solitary hepatic metastasis, while the CT scan showed multiple lesions. It is possible that these appearances represent a mixture of func-
tioning and non-functioning lesions, or alternatively poorly functioning lesions may not be seen due to the low activities used and the limitations of planar imaging. This variability of uptake may have implications in future attempts at therapy.

The preferential uptake of $^{131}$I-MIBG by pheochromocytomas has led to successful attempts at radiotherapeutic ablation using larger doses of this radiopharmaceutical (Sone et al., 1985). A small number of patients with carcinoid have also been treated in this way and although some symptomatic improvements have been seen, no tumour regression has so far been reported (Hoefnagel et al., 1987). Nevertheless the frequency of positive uptake suggests that the therapeutic potential merits further investigation.

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Table II

| Urinary 5H1AA N<75 μmol 24 h$^{-1}$ | Sites | 'Carcinoid' symptoms | $^{131}$I-MIBG uptake | Myocardial uptake | Confirmatory tests |
|---|---|---|---|---|---|
| 1 | 845 | Li, P | D | Li = 3, P = 2 | 0 | CT Histo |
| 2 | 208 | Li | D | Li = 3 and 0 | 0 | CT |
| 3 | 957 | Li | D, F, B | Li = 3 | 1 | US |
| 4 | 986 | Li | Nil | Li = 3 | 0 | CT Histo |
| 5 | 658 | Li | D, F, B | No abnormal uptake | 0 | US Histo |
| 6 | 132 | Li | D, F, B | Li = 3 | 1 | CT |
| 7 | 115 | B | Nil | No abnormal uptake | 0 | XR Bone scan |
| 8 | 1,198 | Li, S, N | D | Li = 3, S = 2, N = 0 | 0 | CT US Histo |
| 9 | 517 | Li | F | Li = 3 | 1 | US CT |
| 10 | 871 | Lu, M, N | D, F | Li = 3, M = 3* | 2 | CT NMR Histo |
| 11 | 177 | Li, Lu | Nil | No abnormal uptake | 1 | CT Histo |

N obscured by liver.

Sites: Li = Liver | N = Nodes | Symptoms: F = Flushing |
Lu = Lung | P = Pelvic mass | D = Diarrhoea |
B = Bone | M = Mesentery | B = Bronchospasm |
S = Spleen

Uptake grade: 0 No activity |
1 Less than normal liver |
2 Similar to normal liver |
3 Greater than normal liver

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