## CASE REPORTS

# Scintigraphy of a Neuroblastoma with I-131 Meta-iodobenzylguanidine

B. Kimmig, W. E. Brandeis, M. Eisenhut, B. Bubeck, H. J. Hermann, and K. zum Winkel

*Klinikum der Universität Heidelberg, Heidelberg, FRG*

**Radioiodinated *m*-iodobenzylguanidine has been applied mainly for the diagnosis of pheochromocytoma and blastoma. In this paper we show that an ontogenetically related tumor, the neuroblastoma, is also scintigraphically visualized by its high uptake of I-131 MIBG. Because of the kinetic findings and the high uptake of more than 30% of the injected activity, it is likely that the neuroblastoma, by analogy with pheochromocytoma, is susceptible to specific radionuclide therapy.**

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The development of a radiopharmaceutical that is taken up by adrenergic tissue has permitted the scintigraphic visualization of benign and malignant neoplasia of the adrenal medulla and of ectopic pheochromocytoma. In the opinion of its developers, this agent, meta [$^{131}$I] iodobenzylguanidine (I-131 MIBG), resembles norepinephrine in molecular structure and behavior (*1–4*).

The results of other groups support the value of I-131 MIBG as a tool for the diagnosis and location of pheochromocytoma (*5–7*).

An ontogenetically related tumor occurring in very young children is the neuroblastoma, which in more than 90% of cases produces homovanillic acid, vanillylmandelic acid, and other catecholamine metabolites (*8*). Its excretion of norepinephrine and epinephrine is rather rarely, if ever, detected. It originates from a malignant disorder of the neural crest, which is the first stage of developing sympathetic ganglion cells. Because of these characteristics, radioiodinated MIBG should show some affinity allowing scintigraphic visualization of a neuroblastoma.

## CASE REPORT

A 2.5-yr-old girl was admitted for investigation of an intraabdominal tumor. Clinical and biochemical data supported the suspicion on neuroblastoma. Blood pressure and heart rate were always within the normal range. The systolic blood pressure did not exceed 110 mm Hg and heart rate ranged between 130 and 90/min.

The 24-hr urinary excretion of vanillylmandelic acid (VMA) and homovanillic acid (HVA) were 196 μmole and 126 μmole, respectively. These values were obtained at the time of imaging. Eighteen weeks later, after ineffective therapy, the 24-hr excretions became: VMA 96.9 μmole (10.7), HVA 108.1 μmole (25.5), epinephrine 111 nmol (55), and norepinephrine 92 nmol (136). (Parentheses indicate upper limits of normal.) This pattern of catecholamine and its metabolites is typical for neuroblastoma (*9*).

Transmission computerized tomography (TCT) showed a large, somewhat inhomogeneous, and partially calcified abdominal tumor (Fig. 1). Its volume was calculated to be ~630 cm$^3$. Laparotomy and histological study of the biopsy (Fig. 2) revealed an inoperable undifferentiated neuroblastoma, Stage 3 according to Evans (*10*) and Grade 3 according to Hughes (*11*).

## SCINTIGRAPHY

An MIBG was labeled with Na$^{131}$I by isotope exchange (*12*, unpublished data M. Eisenhut and B. Kimmig). A dose of 0.2 mCi I-131 MIBG (2 mCi/mg) was given intravenously. Although the thyroid had been blocked by injected contrast agents during the preceding TCT, sodium perchlorate was also given for safety. Scintiphotos were made with a scintillation camera at 29, 95, and 143 hr after injection (Fig. 3). Calibration was performed by comparison of the tumor activity with a similar size of known activity in a water phantom. From the plot in Fig. 4 the maximum activity uptake of the tumor was estimated at >30%. The effective half-life of I-131 MIBG in the tumor was 56 hr.

## DISCUSSION

The scintigraphy of a neuroblastoma, and the extraordinarily high uptake therein, represent another impressive example of the high affinity of I-131 MIBG for adrenergic tissue. At this stage however, we cannot say what meaning scintigraphy with I-131 MIBG will have for the diagnosis, therapeutic control, and follow-up of this tumor. More cases of this kind must establish the

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For reprints contact: Dr. Ds. B. Kimmig, Klinikum der Universität Heidelberg, Zentrum Radiologie, Abt. für Klinische Nuklearmedizin, Voßstr. 3, 6900 Heidelberg, FRG.

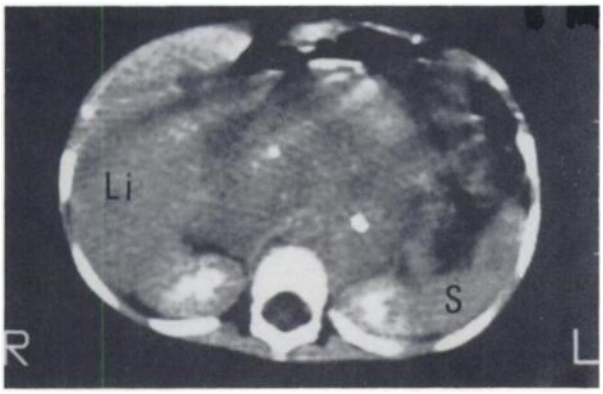


**FIG. 1.** TCT of neuroblastoma at level of porta hepatis.

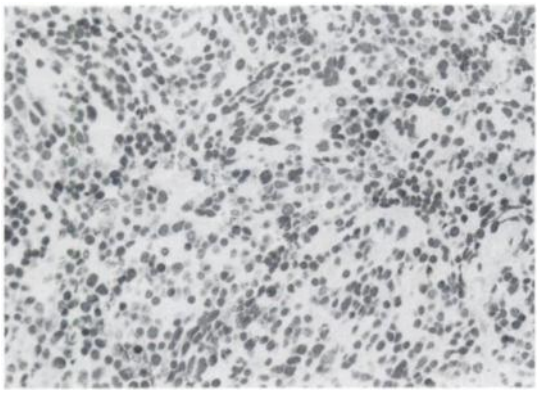

**FIG. 2.** Microscopic appearance of neuroblastoma showing typical rosette formation. Hematoxilin-eosin staining (magnification ×250).

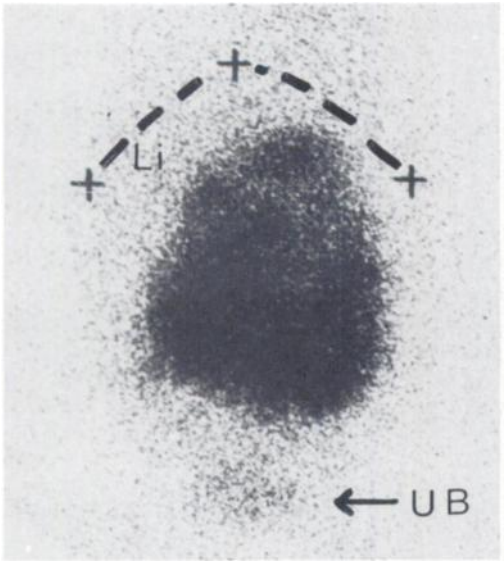


**FIG. 3.** Anterior I-131 MIBG scintigram of neuroblastoma, made at 143 hr after injection. Li = liver, UB = urinary bladder.

accuracy of the method, the connection between uptake and histology, and the influence of chemotherapy on the uptake behavior.

According to our uptake data, radionuclide therapy lies within

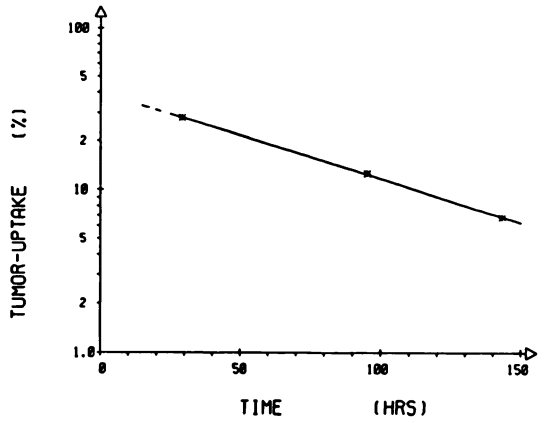


**FIG. 4.** Relative uptake of I-131 MIBG in tumor as function of time.

the range of possibility. The recommended tumor dose for Stage 3 neuroblastoma is 2000 rad (*13*), and we estimate roughly that this could be achieved with an administered dose of ~80 mCi.

We have had the opportunity to investigate two other patients with histologically proven neuroblastoma. Both showed a similar uptake of I-131 MIBG in the tumor.

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