Iodine-123-MIBG SPECT Versus Planar Imaging in Children with Neural Crest Tumors

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Iodine-123-metaiodobenzylguanidine (MIBG) SPECT was compared with ^{123}I-MIBG planar imaging in 35 studies of 25 children with neural crest tumors. **Methods:** Iodine-123-MIBG (0.070–0.140 mCi/kg intravenously) was followed at 24 hr by whole-body planar imaging and triple-detector, high-resolution thoracoabdominal SPECT. At 48 hr, thoracoabdominal planar imaging was performed whenever a high-tissue background or gut activity interfered with the interpretation of the 24-hr planar images. SPECT views included a cine loop presentation of multiple volume-rendered projections. Two reviewers enumerated the number of abnormal sites on the planar and SPECT studies and rated the certainty of interpretation for each study on a scale from 0.1 (low certainty) to 1.0 (high). **Results:** Abnormal uptake was noted on planar or SPECT imaging in 13 studies (seven patients). The average number of abnormal sites detected per study for all 35 studies was 2.7 for planar imaging and 2.9 for SPECT (p = not significant) (and 7.2 and 8.4 for planar and SPECT, respectively, for the 13 abnormal studies). The certainty ratings for all 35 studies were 0.74 for planar studies, 0.82 for SPECT ($p = 0.05$, chi-square, compared with planar) and 0.86 for planar and SPECT combined ($p = 0.01$ compared with planar alone). On volume-rendered images, gut activity was seen as diffuse and/or linear intraluminal activity. **Conclusion:** When ^{123}I-MIBG SPECT is used, the number of lesions detected is not increased, but there is a significant improvement in the certainty of interpretation over planar imaging.

Key Words: iodine-123-metaiodobenzylguanidine; neuroblastoma; SPECT

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The tracer ^{123}I-metaiodobenzylguanidine (MIBG) has been exceedingly valuable in the diagnosis of neural crest neoplasm (*1–4*). It can be administered in much larger activities than ^{131}I-MIBG, and the images demonstrate greatly improved spatial resolution and information content (*5–7*). When ^{123}I-MIBG is used, SPECT can be performed at 24 hr postinjection. With SPECT, gastrointestinal tract activity can be separated from focal retroperitoneal uptake, and abnormal foci of radiopharmaceutical uptake are accurately localized within the abdomen and chest.

In the authors' laboratory, when a high-resolution multidetector SPECT camera became available, SPECT was added to the routine planar imaging protocol. In this study, the diagnostic utility of ^{123}I-MIBG SPECT was evaluated as a supplement to planar imaging. Two hypotheses were tested (1) that ^{123}I-MIBG SPECT detects more foci of abnormal uptake than does planar imaging and (2) that the scans done with ^{123}I-MIBG SPECT can be interpreted with greater certainty than those with ^{123}I-MIBG planar imaging.

METHODS

The drug ^{123}I-MIBG was prepared according to the method of Mangner et al. (*8*) as modified by Mock and Weiner (*9*). According to the known stage of disease, patients received 0.070 or 0.140 mCi/kg of ^{123}I-MIBG by slow intravenous injection. Patients with stage III and IV neuroblastomas received a dose of 0.140 mCi/kg. A saturated solution of potassium iodide at an oral dose of one to three drops, according to the patient's age, was given prior to and for 2 days after radiopharmaceutical administration to block thyroid uptake of free iodide. The study was performed with parental informed consent after approval of the hospital's investigational review board. The ^{123}I-MIBG was used under a physician's investigational new drug exemption.

Thirty-five imaging studies were performed in 25 pediatric patients (neuroblastoma = 20; suspected pheochromocytoma = 4; paraganglioma = 1). Whole-body planar images were obtained at

TABLE 1
Acquisition and Processing Parameters of Triple-Detector SPECT Camera

Acquisition
40 increments
40 sec/frame (24.5-cm axial field of view) or 30 sec/frame (49-cm axial field of view)
Body contouring
20% window around 159 keV
Low-energy, ultrahigh-resolution collimator
Processing
Hanning filter
0.70–0.80 cycles/cm cutoff
Coronal, sagittal and transaxial displays
Cine and static displays of volume-rendered images

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TABLE 2
Iodine-123-MIBG Planar and SPECT Imaging: Abnormal Sites Detected

	Mean no. of abnormal sites per scan	
	All studies (n = 35)	Abnormal studies (n = 13)
Planar*	2.7	7.2
SPECT†	2.9	8.4

*For planar imaging at 24 and 48 hr (when available).
†For SPECT imaging at 24 hr.
p = not significant.

TABLE 3
Certainty Rating in Planar, SPECT and Both Types of Imaging

	Certainty rating*
Planar	0.74†‡
SPECT	0.82‡
Planar + SPECT	0.86†

*The derivation of the certainty rating is explained in the Methods section.
†p = 0.01, chi-square.
‡p = 0.05, chi-square.

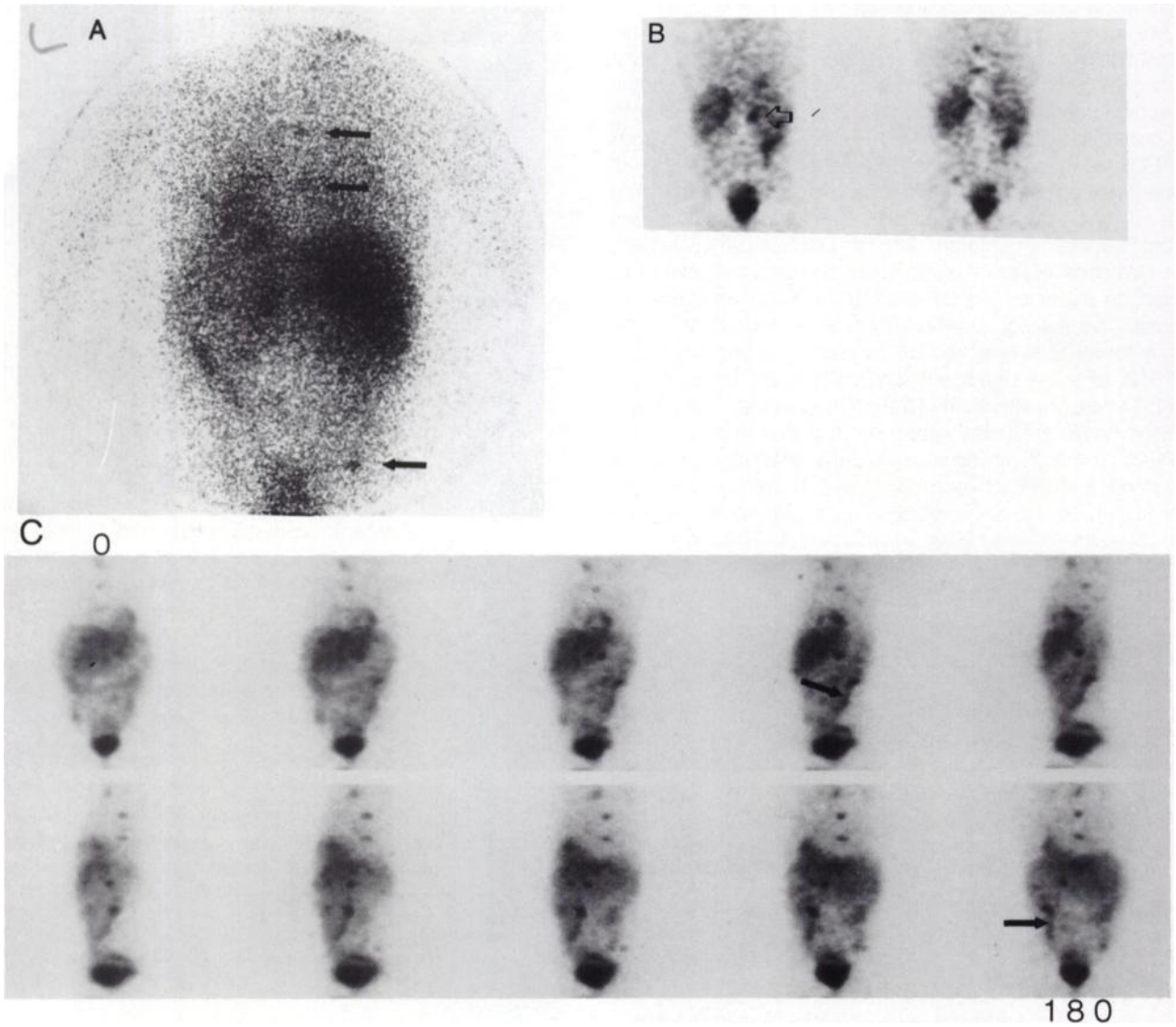

FIGURE 1. This 8-yr-old boy was examined 2 yr after bone marrow transplant (BMT) for advanced neuroblastoma. Since BMT, two foci of uptake in the spine and one in the right ilium (closed arrows) have consistently been unchanged on ^{123}I-MIBG scintigraphy during a period when the patient received no additional therapy. These foci of uptake are visible on planar imaging (A), but they are better localized and more clearly seen on coronal SPECT (B). A left adrenal gland is also identified (open arrow). On the basis of prolonged clinical observation, it is believed that the foci of uptake in the spine and pelvis had probably matured to ganglioneuromas, and biopsy was deferred. Volume-rendered images (C) from 0° (anterior) to 180° at 20° intervals. Activity in the colon is identified. As the projection is rotated, the edge of the veil of minimal, diffuse small-bowel activity (closed arrows) rotates, allowing the reader to inspect the retroperitoneum.

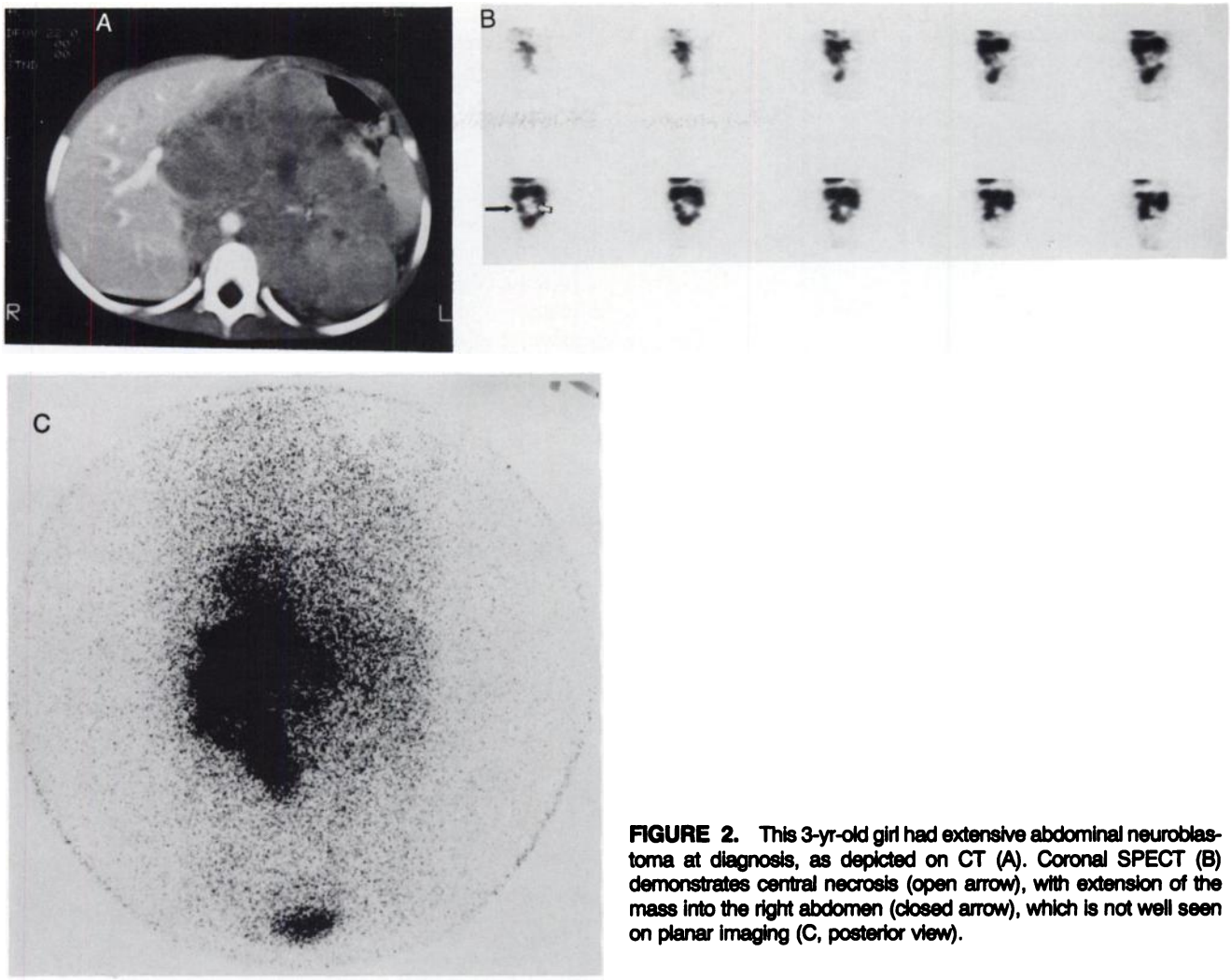

FIGURE 2. This 3-yr-old girl had extensive abdominal neuroblastoma at diagnosis, as depicted on CT (A). Coronal SPECT (B) demonstrates central necrosis (open arrow), with extension of the mass into the right abdomen (closed arrow), which is not well seen on planar imaging (C, posterior view).

24 hr postinjection for 300,000 counts/image (Siemens Orbiter, Siemens Gammasonics, Iselin, NJ or Basicam, general-purpose collimator), or at scan speeds of 7.2 cm/min (Trionix TRIAD, high-resolution collimator Trionix Research Laboratories, Twinsburg, OH) or 11.1 cm/min (GE XR/T, high-resolution collimator, GE Medical Systems, Milwaukee, WI). Planar images were also obtained at 48 hr postinjection in all patients who were able to return for repeat imaging. The imaging protocol at 48 hr was individualized for each patient and included 10-min images of the abdomen, chest (particularly if the primary tumor arose in the chest) and any other locations where the findings on the planar study at 24 hr were difficult to interpret.

SPECT imaging of the abdomen was performed at 24 hr postinjection with a Trionix Triad triple-detector SPECT camera, and the acquisition and processing parameters are listed in Table 1. SPECT acquisition included the upper and midabdomen and the site of the primary tumor or, when feasible, the entire torso. When sedation was required, oral chloral hydrate or intravenous pentobarbital (occasionally supplemented with intravenous fentanyl) was administered and monitored by a registered nurse trained in pediatric sedation.

All studies were retrospectively reviewed by two experienced readers. The numbers of sites of abnormal uptake within the field of view of the SPECT study were enumerated separately for the planar and SPECT examinations, respectively. The certainty of identification of these abnormal sites was evaluated for each planar examination, for each SPECT examination and for the combined planar and SPECT studies. The certainty of the readings was rated from 0.1 (low) to 1.0 (high) on a linear scale.

Nonparametric tests of association were used to assess the statistical significance; the chi-square method was used for the number of sites of abnormal uptake and for proportions for the certainty ratings.

RESULTS

Abnormal uptake was noted on planar and SPECT imaging in 13 studies in seven patients; 12 of these studies in six patients were performed in patients with neuroblastomas. The other abnormal study finding occurred in a patient with a paraganglioma.

The mean number of abnormal sites per scan detected by planar and SPECT imaging did not differ significantly. For all 35 studies, there were 2.7 abnormal sites per examination on planar images and 2.9 on SPECT images (Table 2). For 13 abnormal study results, the respective numbers of abnormal sites were 7.2 on planar images and 8.4 on SPECT.

In contrast, the certainty rating for SPECT imaging was higher than that for planar imaging alone, and the combination of planar and SPECT imaging was also superior to

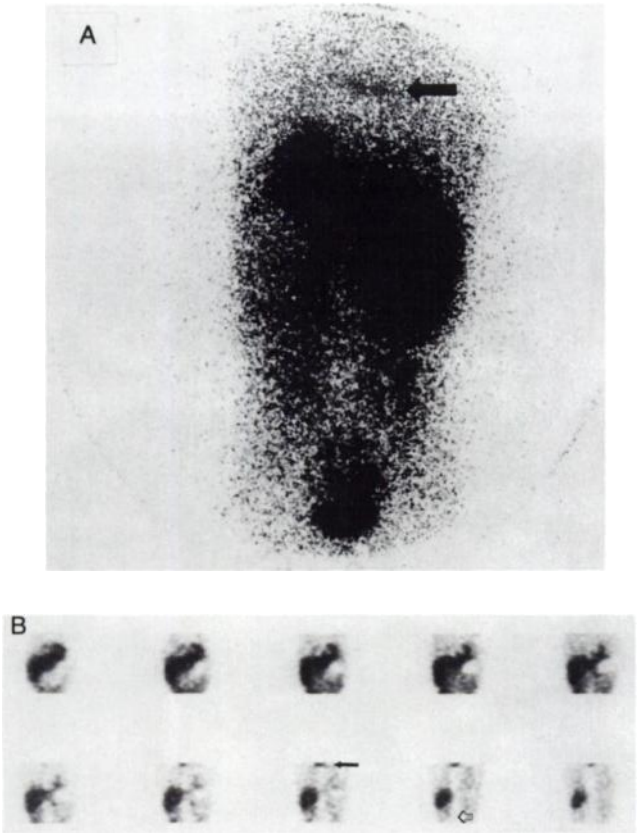

FIGURE 3. This 3-yr-old girl with treated neuroblastoma was being evaluated for BMT. Uptake in the thoracic spine (closed arrows), seen on planar (A) and coronal SPECT (B) imaging, is consistent with an unsuspected metastasis. SPECT precisely localizes the abnormal uptake to the spine. Uptake in unaffected spine is less than soft-tissue background activity (open arrow).

planar imaging (Table 3). Selected SPECT and planar images are illustrated in Figures 1–3.

Coronal and sagittal views through the spine demonstrated that the spine has much less ^{123}I-MIBG uptake than does surrounding normal soft tissue (Fig. 3).

Volume-rendered SPECT images, viewed individually and as a cine loop, provided a useful image display. Abdominal activity appeared as linear activity that followed the course of the large bowel and/or as a slight diffuse increase in uptake with the appearance of a "veil" in the distribution of large and small bowel (Fig. 1). The use of the volume-rendered images in multiple projections allowed the reader to "peek" behind this "veil" from posterior and posterior oblique projections and examine the retroperitoneum.

DISCUSSION

The value of SPECT imaging in the diagnosis of tumors in the chest and abdomen was first demonstrated by Tumeh et al. (*10*) who showed ^{67}Ga SPECT to be more sensitive than planar gallium imaging in Hodgkin's disease and non-Hodgkin's lymphoma. This observation was confirmed in a pediatric population by Rossleigh et al. (*11*). Other SPECT studies have evaluated the use of ^{201}Tl and ^{99m}Tc-sestamibi in pediatric brain tumors (*12,13*). PET has recently been used in a variety of pediatric soft-tissue tumors (*14*). Emission CT improves the visualization of uptake abnormalities by separating the image into its component planes. The ratio of abnormal uptake in the lesion-to-normal uptake in surrounding tissue is enhanced, and the lesion is localized to its precise location in each of the orthogonal planes that pass through it.

In studies with ^{67}Ga, the sensitivity of SPECT for the detection of foci of abnormal uptake was greater than that achieved by planar imaging (*10,11*). In this study, the authors were unable to demonstrate a significant improvement in the number of lesions detected, but the certainty with which lesions were detected was significantly enhanced by SPECT imaging.

An interesting view of the distribution of ^{123}I-MIBG was provided by the multiple volume-rendered reprojections of the SPECT images. When viewed as a 360° cine loop, the distribution of gastrointestinal activity became obvious and easily separable from retroperitoneal activity. Gastrointestinal activity was usually seen as a diffuse low count level veil of activity that corresponded to the small and large bowel, often with a linear colonic activity of an increased count level superimposed. Because most primary neuroblastomas arise from retroperitoneal sites in the adrenal gland or sympathetic ganglia, this cine presentation was helpful in deciding whether abnormal activity was present in the abdomen.

MIBG uptake in bone or bone marrow is abnormal and, when present, is a sign of focal bone involvement and/or diffuse bone marrow infiltration (*2*). Although planar ^{123}I-MIBG findings often suggest that the spine has less MIBG uptake than does the adjacent soft tissue, SPECT clearly demonstrates that the normal spine has much less uptake of MIBG than do adjacent tissues.

In conclusion, ^{123}I-MIBG SPECT does not increase the number of lesions detected in the torso compared with the results of planar imaging, but SPECT alone or in combination with planar imaging does significantly increase the certainty with which ^{123}I-MIBG studies are interpreted. Volume-rendered reprojections of SPECT images aid the reader in separating abdominal activity from foci of normal and abnormal uptake in the retroperitoneum.

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