pass operation) and perception is improved further by edge enhancement (a high-pass operation). It is possible to present even more information by combining cine displays with color and intensity to represent different parameters, and hence extra information. Techniques such as those of Wallis and Miller should be welcomed because they continue to enhance the information conveyed, as well as exploiting the intrinsic ability of the human visual system. However, we feel that incorporating the effects of motion in their assessment of the technique would further substantiate the benefits of the method.

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Iodine-125-MIBG Therapy for Neuroblastoma

TO THE EDITOR: It is with great interest that we have read of the use of [^{125}I]MIBG for the treatment of neuroblastoma published in the preliminary report of Sisson et al. (*1*) in the September issue of the *Journal*. We are pleased to see that the therapeutic application of this agent is being studied elsewhere and in general we support this article.

We would, however, draw the Editor's attention to the fact that the MIBG group at The Netherlands Cancer Institute has used [^{125}I]MIBG to treat neuroblastoma since 1987 and has reported low toxicity with this radiopharmaceutical at the Society of Nuclear Medicine meeting in San Francisco in 1988 (*2*). Preliminary results were published in 1989 (*3,4*). Sisson et al. make no reference to this.

In order to complete the published experience, we report again the three treatments in two patients that we have conducted.

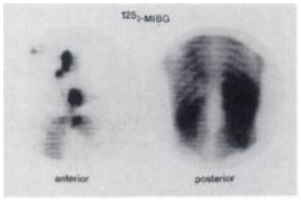

FIGURE 1
Post-therapeutic [^{125}I]MIBG scintigrams of Patient 1 shows intense concentration in the tumor in the neck.

Case 1

In November 1987, a 24-yr-old male with recurrent neuroblastoma was treated with 7.4 GBq (200 mCi) [^{125}I]MIBG, which was administered by i.v. infusion over 4 hr. The patient had originally been referred to our institute from the U.S. in April 1984 for [^{131}I]MIBG treatment of six large recurrent tumors in the lumbar region, which no longer responded to conventional treatment. In contrast to the pessimism expressed by Sisson et al. (*1*) concerning the use of [^{131}I]MIBG as a therapeutic agent, this patient was one of the best (2.5 yr) responders to [^{131}I]MIBG therapy in our series of 75 patients and initially attained complete remission of disease. After 2.5 yr, however, he developed a recurrence in the neck, which was arrested but did not regress following subsequent [^{131}I]MIBG therapy. At that time, it was decided to use [^{125}I]MIBG for treatment. Figure 1 shows the post-therapeutic scintigrams that demonstrate the specific concentration of [^{125}I]MIBG by the tumor and the attenuation of the 35-keV photons by the overlying bones. The treatment was repeated in January 1988, resulting in an objective regression (>50% of tumor volume) of the tumor mass. At the same time, there was progression of disease in the mediastinum, which led us to discontinue treatment. No adverse effects were observed on either occasion.

Case 2

In November 1988, a 4-yr-old girl, in whom previous [^{131}I]MIBG treatment had been successful for Stage IV neuroblastoma (bone metastases after chemotherapy), presented with bone marrow relapse. As no autologous bone marrow was available, further [^{131}I]MIBG therapy was contraindicated. Despite subsequent chemotherapy with carboplatin and 4-Epiadriamycine, the bone marrow disease progressed dramatically. Treatment was therefore attempted using 3.7 GBq (100 mCi) [^{125}I]MIBG. Figure 2 demonstrates the use of all three radioiodine labels of MIBG (^{131}I, ^{123}I, and ^{125}I) for scintigraphy in this patient performed within 4 wk. Iodine-125-MIBG therapy was well tolerated and relieved the patient's pain, but, except for halting the rapid progression of disease for 6 wk, did not induce an objective remission. No hematologic side effects occurred, again demonstrating that therapeutic doses of [^{125}I]MIBG can be given safely, even when the bone marrow is infiltrated by tumor.

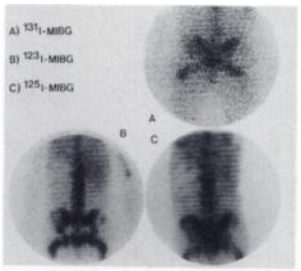

FIGURE 2
Scintigrams using [^{131}I]MIBG (A), [^{125}I]MIBG (B), and [^{125}I]MIBG (C) of Patient 2, each of which shows the diffuse bone marrow invasion by neuroblastoma.

On the basis of this experience, we would like to raise the following points with regard to the article by Sisson et al. (*1*):

1. We agree that [^{125}I]MIBG has a place in the treatment of neuroblastoma micrometastases and bone marrow infiltration, particularly as the results of [^{131}I]MIBG treatment under these circumstances are poor. We have used lower activities than Sisson et al., but have observed no toxicity whatsoever. The use of [^{125}I]MIBG for therapy, especially at higher doses, does pose a problem of radioactive waste, which requires responsible attention from nuclear medicine specialists.
2. In contrast to Sisson et al., the images accompanying this letter demonstrate that post-therapeutic scintigraphy using [^{125}I]MIBG is feasible and that the images obtained are also of acceptable quality.
3. In discussing the rationale for using [^{125}I]MIBG to treat neuroblastoma, Sisson et al. have overlooked the fundamental observations by Smets et al. (*5*), which indicate the most promising basis for this radiopharmaceutical, particularly in neuroblastoma, in that extragranular storage contributes significantly to total MIBG retention. The cytoplasmic and homogeneous distribution of [^{125}I]MIBG may result in a lethal radiation dose to the nucleus.
4. Finally, we do wish to stress that by pursuing [^{131}I]MIBG therapy at our institute (230 therapeutic applications in 75 patients to date), we have observed complete remissions and long-term responses, despite the fact that most of these patients had progressive Stage IV neuroblastoma and were only treated with [^{131}I]MIBG after all other treatment options had failed. We are convinced of the efficacy and safety of [^{131}I]MIBG in children, provided that the bone marrow is not involved by tumor. The observed response in advanced neuroblastoma, the non-invasive nature of the procedure, and the high metabolic activity of untreated tumors have permitted us to use preoperative [^{131}I]MIBG successfully instead of combination chemotherapy for inoperable neuroblastoma (*6*). The advantages of this approach are that the child's general condition is usually good prior to surgery and that chemotherapy is reserved to treat minimal residual disease, when it is likely to be most effective. Iodine-125-MIBG therapy may also be indicated in these circumstances.

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REPLY: We thank Dr. Hoefnagel and colleagues for the references to their work. We, too, reported part of our work in abstract form (Eur Assoc Nucl Med Congress, 1989; *J Nucl Med* 1990;31:804) but elected not to quote abstracts in our recent paper (*1*). Moreover, this paper described the initial toxic effects of [^{125}I]MIBG as a single agent in a dose-escalation program which differs from the apparent purpose of Hoefnagel et al.

Images of neuroblastoma can be made with [^{125}I]MIBG as shown by Hoefnagel et al. But quantification of MIBG within regions of the body, including the tumors under treatment, has been difficult using [^{131}I]MIBG, and this goal becomes a formidable challenge when MIBG is labeled only with ^{125}I.

We agree with the Dutch investigators that [^{131}I]MIBG has effects on neuroblastoma. However, the optimum use of [^{131}I]MIBG, and of [^{125}I]MIBG, will remain uncertain until there is a controlled trial of therapy with these agents.

Our hypothesis for the treatment of neuroblastoma with [^{125}I]MIBG is: at acceptable levels of toxicity, [^{125}I]MIBG will be more effective in destroying micrometastases than [^{131}I]MIBG. We have shown that per mCi or MBq administered [^{125}I]MIBG is less toxic (*1*). Nevertheless, [^{125}I]MIBG will be toxic as doses are increased, and it is likely that optimum treatment of neuroblastoma will require the highest doses possible. Therefore, a dose-escalation study of [^{125}I]MIBG is a prerequisite to testing our hypothesis. Such a study is also a necessary foundation for optimum therapy with [^{125}I]MIBG under any circumstance.

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Effective Background Correction on Separate Technetium-99M-DTPA Renal Clearance

TO THE EDITOR: In a recent paper on the measurement of individual kidney glomerular filtration rate (IKGFR) from the technetium-99m-DTPA (^{99m}Tc-DTPA) renogram, Piepsz