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AJNR Am J Neuroradiol 1985, 6 (4) 533-536

<http://www.ajnr.org/content/6/4/533>

This information is current as of June 5, 2025.

CT of Multiple Sclerosis: Reassessment of Delayed Scanning with High Doses of Contrast Material

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A prospective study involving 87 patients was carried out to evaluate the necessity for a high dose of contrast material in addition to delayed computed tomographic (CT) scanning for optimal detection of the lesions of multiple sclerosis in the brain. In patients with either clinically definite multiple sclerosis or laboratory-supported definite multiple sclerosis, CT scans were obtained with a uniform protocol. Lesions consistent with multiple sclerosis were demonstrated on the second scan in 54 patients. In 36 of these 54 patients, the high-dose delayed scan added information. These results are quite similar to those of a previous study from this institution using different patients, in whom the second scan was obtained *immediately* after the bolus injection of contrast material containing 40 g of organically bound iodine. The lack of real difference in the results of the two studies indicates that the increased dose, not just the delay in scanning, is necessary for a proper study.

Computed tomographic (CT) scanning of the brain has been used for the assessment and diagnosis of multiple sclerosis. On the basis of a presumed mild blood/brain barrier (BBB) disruption, patients with suspected multiple sclerosis have had high-dose delayed (HDD) CT scanning of the head [1, 2]. It was assumed that the high dose of contrast material is as necessary as the delayed scan for proper assessment of the lesions of multiple sclerosis in the brain. This study was designed to demonstrate the need for the high dose of contrast material.

Subjects and Methods

Using a protocol set up at University Hospital, University of Western Ontario, we examined 87 patients with clinically definite multiple sclerosis or laboratory-supported definite multiple sclerosis [3]. A CT scan was obtained before the injection of contrast material. A second scan was commenced 20 min after a rapid bolus injection of contrast material containing 40 g of organically bound iodine (Conray 400), administered within 1 min. Immediately after the completion of the second scan, a rapid infusion of contrast material containing 42.3 g I (Reno-M-Dip) was administered over 40 min, and a third HDD CT scan was obtained 1 hr after the start of the infusion.

All these studies were performed on a GE 8800 scanner using a 9.6 sec, high-resolution mode. Similar window settings were used for filming the standard and the HDD scans. No major reactions to the contrast material or decreases in renal function occurred in this group of patients. The patients' charts were reviewed before undergoing the examination to exclude those with multiple myeloma, diabetes mellitus, and decreased renal function. Two neuroradiologists evaluated the CT scans, paying special attention to the differences in information displayed between the second and third scans.

Results

All of the patients in this study had either clinically definite multiple sclerosis or laboratory-supported definite multiple sclerosis. The results of this protocol could

This article appears in the July/August 1985 issue of *AJNR* and the September 1985 issue of *AJR*.

Received July 18, 1984; accepted after revision November 1, 1984.

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AJNR 6:533-536, July/August 1985

0195-6108/85/0604-0533

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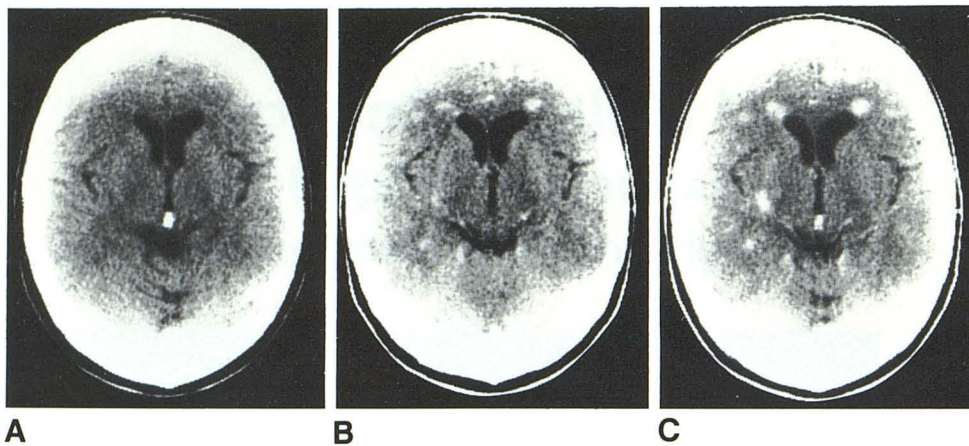


Fig. 1.—Axial CT scans. **A**, Without contrast. **B**, With standard volume of contrast material and 20 min delay. **C**, With high dose of contrast material and delay. Lesions in **C** are more enhanced and some are more readily apparent.

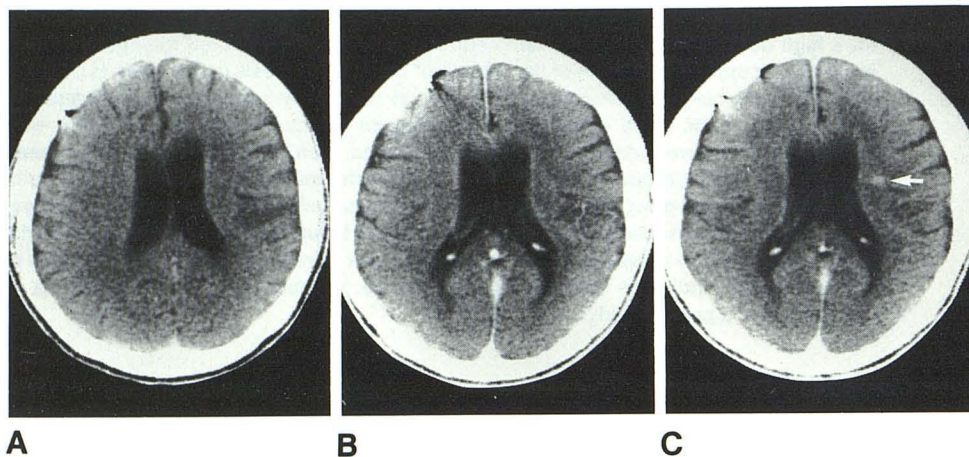


Fig. 2.—Axial CT scans. **A**, Without contrast. **B**, With standard volume of contrast material and delay. **C**, With high dose of contrast material and delay. Enhancing lesion (arrow) not demonstrated in **A** or **B**.

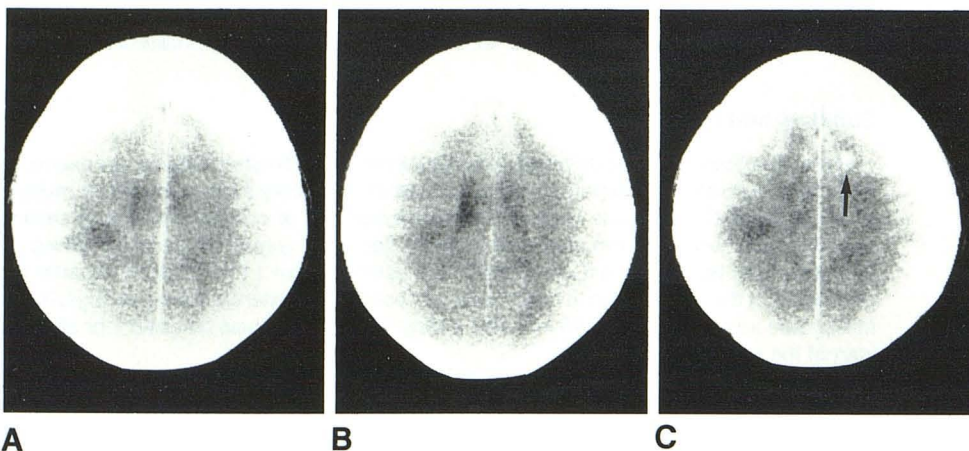


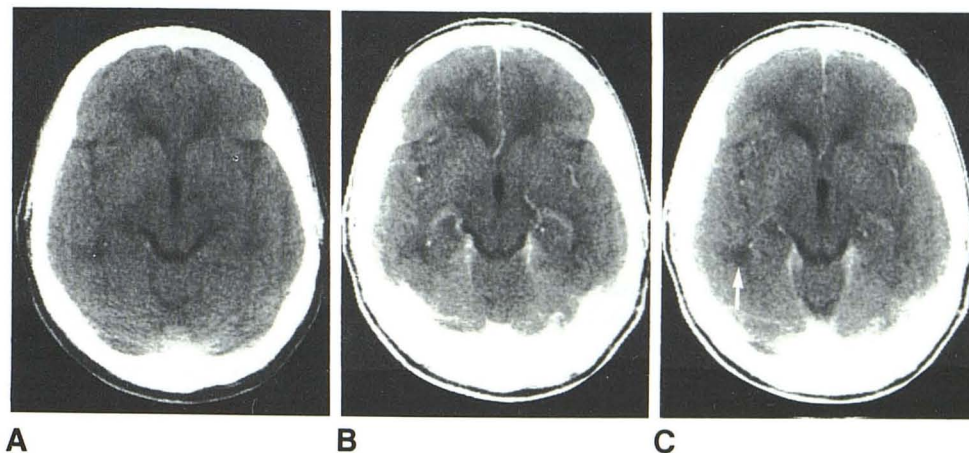
Fig. 3.—Axial CT scans. **A**, Without contrast. **B**, With contrast. Low-density lesion in right frontoparietal region is seen less well in **B** than in **A**. **C**, With high dose of contrast material and delay. Enhancing lesion in left frontal region (arrow) was not demonstrated in **A** or **B**.

be divided into three groups. The first group consisted of those patients whose first and/or second CT scans demonstrated findings compatible with multiple sclerosis and whose third scans (HDD) displayed additional information. The second group consisted of those patients whose first and/or second CT scans demonstrated findings compatible with

multiple sclerosis, but whose third scans added no new information. The third group consisted of those patients whose three CT scans demonstrated no findings compatible with multiple sclerosis.

In the first group were 36 cases (42%). Of these 36 cases, 35 had enhancing lesions in the white matter. The third scan

Fig. 4.—Axial CT scans. **A**, Without contrast. **B**, With standard volume of contrast material and delay. **C**, With high dose of contrast material and delay. Low-density lesion in right temporoparietal region (arrow) was not seen in **A** or **B**.



demonstrated additional enhancing lesions, which were not present on the second scan (standard volume of contrast material and delay) (figs. 1–3). There was a low-density lesion that was not demonstrated as well on the scan with the standard volume of contrast material (fig. 3B). This may be due to sufficient enhancement of the lesion so that it is indistinguishable in density from brain parenchyma. Alternatively, the scans were at slightly different levels, and the lack of demonstration may have been from partial-volume effect. In one case, however, the sole findings were low-density lesions in the white matter, and they were appreciated only on the third scan (fig. 4). We postulated that white-matter lesions have a density very similar to brain parenchyma. It is only in the HDD scan that there is sufficient difference in enhancement between the brain parenchyma and the white-matter lesion to render the latter detectable.

In the second group, there were 18 cases (21%). Of these, 11 demonstrated low-density white-matter lesions that did not enhance on either the second or the third scans. The other seven cases demonstrated enhancing white-matter lesions, without additional information being noted on the third scan.

There were 33 cases (38%) in the third group. In these cases, no enhancing or low-density white-matter lesions were demonstrated on any of the three scans.

Of the 54 cases in this study with positive findings on either the first or second CT head scan, 36 (66%) had additional information displayed on the third scan. In none of the cases was information obscured on the third scan.

Discussion

CT head scanning using the HDD protocol has been shown to be of use in the diagnosis and assessment of multiple sclerosis [1]. This protocol demonstrated lesions that were not detected on the standard CT scan. The accepted mechanism for the enhancement of lesions of multiple sclerosis is the presence of a disruption of the BBB. It is postulated that those lesions demonstrating enhancement only on the scan with a high dose of contrast material and a delay have less BBB disruption than those lesions enhancing on the scan

with a standard volume of contrast material. The HDD protocol uses both an increased amount of contrast material and a delay in scanning to cause further enhancement of these lesions.

Our results have demonstrated that the delay in scanning after a bolus injection of contrast material is not as effective in imaging enhancing lesions as is the addition of a high dose of contrast material with a delay. The chosen interval of 20 min between the bolus injection and the second CT scan was based on the accepted mechanism of contrast enhancement. It has been shown that with a bolus injection of contrast material, the degree of enhancement is related to the blood level of organically bound iodine at 10 min after injection [4]. Between 20 min and 1 hr after a bolus injection of contrast material, there is little increase in enhancement [5]. After an infusion of contrast material, however, the peak effect occurs at about 40 min [4]. It has been shown that for enhancement to occur, contrast material has to be present in the extravascular space [6]. Presumably, this explains the need for a delay between the injection of contrast material and CT scanning. The interval of 20 min between the bolus injection and the second CT scan as well as the delay of 1 hr between the end of the infusion and the third CT scan is quite consistent with these observations.

The results of this study are quite similar to those of a previous study from our institution [1]. In the previous study, the contrast-enhanced scan was obtained immediately after the bolus injection of contrast material, whereas in this study the second scan was obtained 20 min after the bolus injection. This difference in the protocol was designed to demonstrate that merely delaying the contrast-enhanced scan does not add information. As explained before, 20 min seems to represent the time of peak enhancement after a bolus injection [5]. In this study, the HDD scan added information in 66% of the studies. In the previous study information was added in 72% of the cases [1]. The rate of lesion detection in this study is somewhat less than in that of the previous study, which can be explained by the difference in patient populations studied. The previous study was performed on patients with known or a strong clinical suspicion of acute or relapsing multiple sclerosis. This study was concerned with patients

who had definite multiple sclerosis regardless of their clinical status at the time the CT head scans were obtained. There were more patients in clinical remission in our current study than in our previous study.

This study demonstrated an increased detectability of the lesions of multiple sclerosis in the brain with a high dose of contrast material and a delay. Delaying the CT scan after a bolus injection of a standard amount of contrast material was not as effective in demonstrating these lesions. Therefore, we consider the HDD CT scan as being necessary for a proper study in a patient with multiple sclerosis.

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