

Title	Administration and dosage of iohexol, a nonionic contrast medium, for dynamic renal computed tomography
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Citation	泌尿器科紀要 (1993), 39(8): 687-693
Issue Date	1993-08
URL	<a href="http://hdl.handle.net/2433/117915">http://hdl.handle.net/2433/117915</a>
Right	
Type	Departmental Bulletin Paper
Textversion	publisher

# ADMINISTRATION AND DOSAGE OF IOHEXOL, A NONIONIC CONTRAST MEDIUM, FOR DYNAMIC RENAL COMPUTED TOMOGRAPHY

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We investigated the optimal method of administering iohexol, which contains 300 mg iodine/ml (Omnipaque 300®), a nonionic contrast medium, to maintain adequate renal contrast while reducing artifacts during dynamic CT scanning. In this study, 76 patients with renal disease received 10~50 ml of iohexol as follows: group I (14 patients), 20 ml injected as an intravenous bolus for 5 sec, followed by 30 ml intravenous drip infusion for 5 min; group II (18 patients), bolus of 20 ml injected for 5 sec; group III (13 patients), 20 ml diluted with sterile water (total volume 40 ml), and injected as a bolus for 8 sec; group IV (15 patients), 20 ml injection for 5 sec followed by intravenous drip infusion of 200 ml of Hartmann-Ringer's solution given at maximum speed; and group V (14 patients), 10 ml diluted with sterile water (total volume 20 ml) injected as a bolus for 5 sec. We found that corticomedullary differentiation was most distinct on the images obtained from group IV. We concluded that a lower concentration of iohexol (150 mg iodine/ml) given by intravenous fluid loading can provide superior CT images.

(Acta Urol. Jpn. 39: 687-693, 1993)

**Key words:** Kidney, Renal dynamic CT, Iohexol, Dosage

## INTRODUCTION

Nonionic contrast media, which produce fewer adverse effects than conventional ionic contrast media, are widely used<sup>1,2)</sup>. Because nonionic agents achieve excellent contrast, the renal pelvis and calyces tend to be represented too strongly on computed tomographic (CT) scans of the kidney; consequently, artifacts are common. Renal lesions with a local reduction in blood flow, such as acute pyelonephritis with subtle changes in which CT scans show wedge-shaped low-density zones and finely striated low-density zones from the

collection system to the renal capsule, appear as artifacts in the hyper-dense renal pelvis and renal calyces<sup>3)</sup>. Diagnosis of such lesions can therefore be difficult.

Using conventional ionic contrast media, we conducted a previous CT study of the healing of pyelonephritis<sup>4)</sup> and of the development of renal cortical scarring in patients with acute pyelonephritis<sup>5)</sup>. Because no studies of artifacts appear to have been conducted on renal CT scans, we performed a dynamic CT scan study, using a nonionic contrast medium and various methods of administration to identify which combinations would provide adequ-

ate renal contrast while reducing artifacts.

### MATERIALS AND METHODS

A total of 76 patients requiring a CT scan for the assessment of renal disease were examined at the Department of Urology of either the Kamo Hospital or the Mitsubishi Hospital. They were 50 men and 26 women between 19 and 81 years old (mean  $\pm$ SD: 50.8  $\pm$  14.0 years). Weight ranged from 37.2 kg to 75 kg (mean  $\pm$ SD: 58.9  $\pm$  9.7 kg). At the Kamo Hospital a Toshiba TCT-60SX scanner was used (Toshiba Co., Tokyo); at the Mitsubishi Hospital a General Electric CT/T9000 was used (General Electric, Milwaukee, WI, U.S.A.)

Plain CT scanning was initially carried out on slices 1 cm wide. The exposure of the post-contrast CT scans in the dynamic study was: (1) 5.5 sec; (2) 12.0 sec; (3) 18.5 sec; (4) 25.0 sec; (5) 32.5 sec; (6) 60.0 sec; (7) 2 min and 25.0 sec; and (8) 5 min and 31.5 sec after infusion. Serial exposures were made immediately thereafter, from the upper to the lower pole of the kidney, and were completed in about 16 minutes.

The contrast medium used was iohexol containing 300 mg iodine/ml (Omnipaque 300®, Daiichi Pharmaceutical Co., Tokyo). The patients were divided into five groups according to dosage (10~50 ml iohexol) and method of administration. All patients underwent dynamic CT scanning. There were no significant differences in the body weight or age between the groups.

The following five methods of administration were carried out. Group I (14 patients) received 20 ml of iohexol injected as an intravenous bolus for 5 sec, followed by an intravenous drip infusion of 30 ml of iohexol administered over 5 min for obtaining sufficient contrast after the bolus injection. Group II (18 patients) received a bolus of 20 ml of iohexol injected in 5 sec as a control. Group III (13 patients) received 20 ml of iohexol diluted with sterile water for injection (total volume 40 ml), injected as a bolus in 8 sec for assessing the effect of a low concentration. Group IV (15 patients) received an injection of 20 ml of contrast medium given in

5 sec followed by a 200 ml intravenous drip of Hartmann-Ringer's solution given at the maximum speed for assessing the diuretic effect of hydration. Group V (14 patients) received 10 ml of contrast medium diluted with sterile water injected as a bolus (total volume 20 ml) in 5 sec for assessing the effects of low concentration and low dosage.

Although we attempted to obtain serial measurements of the CT values for the renal cortex, renal medulla and renal pelvis or calyces, this was difficult to achieve at identical sites because of movements related to respiration. For this reason, in some cases (group I, 4 patients; group II, 7 patients; group III, 5 patients; group IV, 5 patients; group V, 8 patients) we measured the CT values of the renal cortex and renal medulla separately in the early contrast phase. We then determined the CT values of the renal parenchyma and renal pelvis or renal calyces only when adequate renal pelvic contrast had been achieved so that we could assess their enhancement in each group.

Using the images in which the corticomedullary differentiation was the most distinct in each kidney, the corticomedullary differentiation was classified in each kidney as follows: no differentiation (0); indistinct ( $\pm$ ); distinct (+); and highly distinct ( $\oplus$ ).

The severity of artifacts was classified

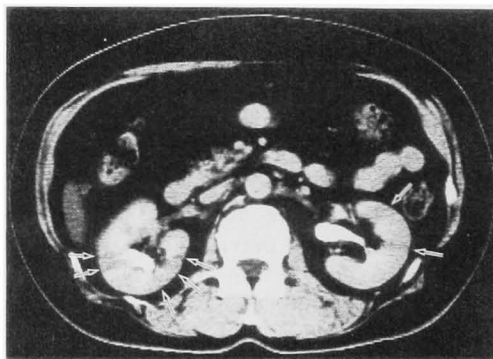


Fig. 1. Classification of severity of artifacts. Slight impairment by more than four artifacts was found in the CT scan of the right kidney, graded as (+). A slight impairment by two artifacts was noted in the left kidney, graded as ( $\pm$ ).

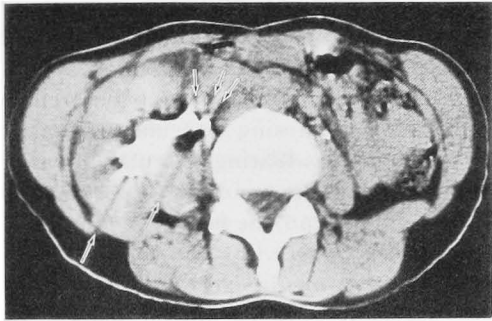


Fig. 2. Classification of severity of artifacts. Marked impairment by more than four artifacts was found in the right kidney on the CT scan, graded as (+).

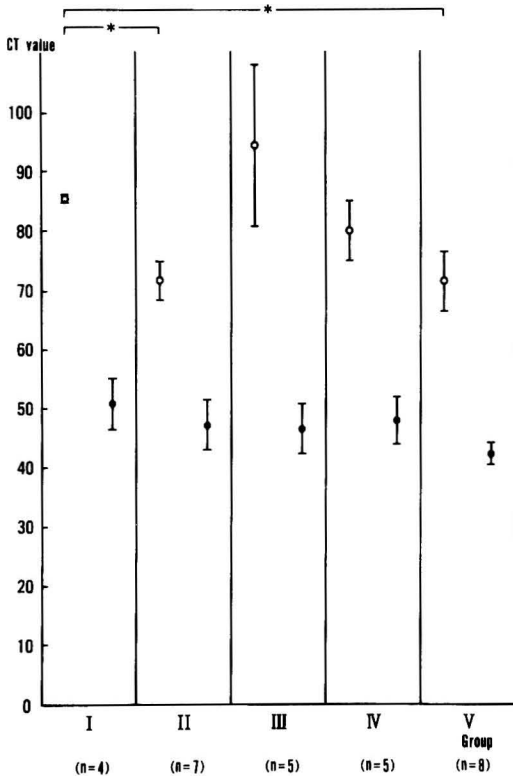


Fig. 3. CT values of renal cortex (○) and renal medulla (●) in each of five dosage groups (mean ± SD). CT values of the renal cortex in group I were high in the early phase (\*:  $p < 0.05$  vs groups II and V).

according to the extent of impairment of the image of the renal parenchyma in each kidney as follows: no impairment (0); slightly impaired (by less than 3) artifacts ( $\pm$ ); slightly impaired (by more than 4)

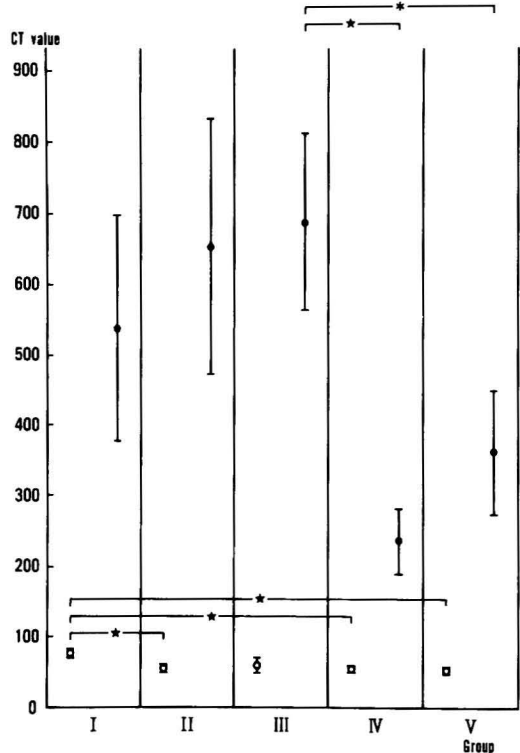


Fig. 4. CT values of renal parenchyma (○) and renal pelvis (●) in each group (mean ± SD). CT values of the renal parenchyma in group I were high in the late contrast phase (\*:  $p < 0.01$  vs groups II, IV, V). Those of the renal pelvis in group III were high in that phase (\*:  $p < 0.01$  vs group IV and\*:  $p < 0.05$  vs group V).

artifacts or markedly impaired (by less than 3) artifacts (+) (Fig. 1); markedly impaired (by more than 4) artifacts (++) (Fig. 2). Those classifications were blindly evaluated. The results were analyzed by the chi-square test and Student's t-test, with  $p < 0.05$  accepted as statistically significant.

### RESULTS

1. CT values of the renal cortex and medulla measured in the early contrast phase, and those of the renal parenchyma and the renal pelvis or calyces, measured in the late contrast phase

In group I, when given the 20 ml bolus of the contrast medium plus the subsequent infusion of contrast, the CT values of the renal cortex were high in the early

Table 1. Grading of corticomedullary differentiation. The distinctness of corticomedullary differentiation was classified as follows: no differentiation (0); indistinct ( $\pm$ ); distinct (+); and highly distinct ( $\#$ ). There were statistically significant differences between groups I, II and IV (\*:  $p < 0.05$ ), and between groups IV and V ( $\star$ :  $p < 0.01$ ). Number: renal units.

Group	Grade				Total	
	0	$\pm$	+	$\#$		
I	0	5	5	15	25	<div style="display: flex; align-items: center; justify-content: center;"> <div style="border-left: 1px solid black; border-right: 1px solid black; border-bottom: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border-left: 1px solid black; border-right: 1px solid black; border-bottom: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border-left: 1px solid black; border-right: 1px solid black; border-bottom: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border-left: 1px solid black; border-right: 1px solid black; border-bottom: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> <div style="border-left: 1px solid black; border-right: 1px solid black; border-bottom: 1px solid black; width: 20px; height: 20px; margin-right: 5px;"></div> </div>
II	1	9	7	18	35	
III	0	1	8	15	24	
IV	1	0	4	25	30	
V	0	4	13	10	27	

phase ( $p < 0.05$  vs. group II,  $p < 0.05$  vs. group V, Fig. 3), Those of the renal parenchyma were high after the late contrast phase (group II  $p < 0.01$ , group IV  $p < 0.01$ , group V  $p < 0.01$ , Fig. 4). No significant differences were found in the various groups between the early phase CT values for the renal medulla (Fig. 3). The renal pelvic or calyceal CT values were significantly lower in group IV than in group III ( $p < 0.01$ ), and were also significantly lower in group V than in group III ( $p < 0.05$ ) (Fig. 4).

## 2. Corticomedullary differentiation and image artifacts

The corticomedullary differentiation in group IV was significantly more distinct than in the other groups (group I  $p < 0.05$ , group II  $p < 0.05$ , group V  $p < 0.01$ , Table 1). Artifacts were more severe in group II. There were statistically significant differences between groups II and III ( $p < 0.05$ ), and between groups II and V ( $p < 0.01$ ). There were no severe artifacts ( $\#$ ) in groups II and IV. There were no significant differences between groups I, II and IV. No significant side effects were associated with the administration of iohexol in this series.

## DISCUSSION

In performing CT diagnostic studies of the upper abdomen, post-contrast scans are

performed using high-dose enhancement for increasing contrast in the lesion and for clearly outlining the vascular system. This method is reported to be extremely useful for diagnosing vascular lesions in the liver, for evaluating vascular invasion by hepatic tumors, and for observing the hepatic hilum and the head of the pancreas<sup>6,7</sup>). However, in the kidney, non-ionic contrast media exert an osmotic pressure which is only 1/2 to 1/3 that of the conventional ionized contrast media, and their osmotic diuretic effect is far less. Therefore, considerable fluid reabsorption, takes place in the proximal tubules.

The concentration of the nonionic contrast medium in the urine is good, and adequate contrast can easily be obtained to delineate the urinary tract<sup>8</sup>). For this reason, the effect of the contrast is too strong when high-dose enhancement is applied to the kidney and halation develops as a consequence of the artifacts produced by the excretion of the contrast medium into the renal pelvis and calyces. It then becomes difficult to detect subtle changes in the renal parenchyma. Because of such problems, we thought that low doses of a nonionic contrast medium could be used for post-contrast CT studies of the abdomen in patients with suspected renal disease.

In the case of tumors with a poor blood supply and necrotic tissue, the high-dose enhancement increases contrast in the lesion and thus can be very useful. When evaluating subtle changes in the renal parenchyma, however, as in the case of acute pyelonephritis (including acute focal bacterial nephritis or lobar nephronia), it becomes difficult to differentiate the findings from those of tumors. When the contrast enhancement is too strong, it becomes difficult to evaluate the lesion. For these reasons we decided to study the optimal dose and method of administering a non-ionic contrast medium for post-contrast renal CT.

The cortical CT values in group I exceeded those in groups II and V. The cortical CT values did not differ significantly among groups I, III and IV. Corticomed-

ullary differentiation was detectable in all but two of the 76 patients. This was less visible in group V because of the low dose (150 mg iodine/ml) and concentration of the contrast medium. The superior distinctness of corticomedullary differentiation identified in group IV may have been due to an increase in the volume of renal blood flow as a result of intravenous fluid loading. The cortical CT values and distinctness of the corticomedullary differentiation may be due to the volume of the contrast medium administered, rather than to its concentration.

We expected that artifacts would be the most severe in group I. The renal pelvic and calyceal CT values were significantly elevated in group I in which a large dose of contrast medium was used. Because the infusion was administered slowly after the bolus injection, this did not appear to have been an effect of administering the medium by intravenous drip infusion. Although artifacts were also observed in groups III and V, even though the medium was diluted by 50%, they were not severe, and good images were obtained. Thus, a low concentration of contrast medium appeared to be superior.

In intravenous urography (IVU), it is essential that the contrast medium possess an osmotic diuretic effect. Ionic contrast media are superior in terms of filling image of the renal pelvis, but large doses of nonionic contrast media are required to produce filling images of the bladder<sup>9)</sup>. On the other hand, CT scans have a high resolution; thus, one can shorten the time and obtain clear images of the kidney by administering lower doses of the contrast medium. In this study, good CT images of the kidney were obtained with a volume of 20 ml of the contrast medium which contained 300 mg iodine/ml. When bolus injections were used, the dilution of the medium reduced the severity of artifacts.

CT scanning plays a significant role in the field of urology, comparable to that of intravenous urography. It is possible to use a plain film of the kidney-ureter-bladder area (KUB) before and after post-contrast CT as a substitute for IVU. When

post-contrast CT scanning is prolonged, and some time has elapsed from the end of the post-contrast CT procedure to the KUB exposures, most of the contrast medium will be excreted, so that images of the renal pelvis will be indistinct. In the present study, we administered 20 ml of a 50 ml dose of the contrast medium (iohexol 300 mg/ml) for the CT scans and obtained KUB exposures, either when the post-contrast CT had been completed, or immediately before or after the administration of the drip infusion of the remaining 30 ml.

When intravenous urography is performed so that it is approximately equivalent to a 15-min image, distinct images of the renal pelvis can be obtained. By subsequently performing a supplementary post-micturition IVU with the patient in the standing position, it becomes possible to detect the presence or absence of residual urine as well as the presence of nephroptosis. When this combined method is employed, not only can detailed anatomical findings be detected in the kidney, but the procedure becomes applicable to the overall diagnostic examination of the urinary tract.

If a lesion is detected by ultrasound studies prior to CT scanning, and such an IVU procedure is combined with bolus injection CT scanning, it becomes possible to reduce both the dose of contrast medium and the amount of radiation exposure. Severe anaplylactic shock is uncommonly associated with nonionic contrast media, and these agents are quite safe<sup>1)</sup>. They are, however, quite expensive, and some institutions have restricted their use<sup>9)</sup>. If the dose of the contrast medium can be reduced, a cost savings can be achieved as well as a reduction in the risk of adverse effects. It is therefore desirable to obtain the maximum amount of information while administering the lowest effective dose.

In this study we assessed ways of administering iohexol more effectively and obtained good images by administering a low concentration of this agent with adequate fluid loading in renal CT scanning. Our

observations indicate that a low concentration of iohexol (150 mg/ml) may be used when bolus injections are administered.

#### REFERENCES

- 1) Wolf GL, Arenson RL and Cross AP: A prospective trial of ionic vs nonionic contrast agents in routine clinical practice: comparison of adverse effects. *AJR* **152**: 939-944, 1989
- 2) Palmer FJ: The Royal Australian College of Radiologists (RACR) Survey of Reactions to Intravenous Ionic and Nonionic Contrast Media. Proceedings of the Nycomed Scientific Symposium Elsevier Science Publishers Biomedical Division. Patient safety and adverse events in contrast medium examinations. I. Enges, J. Edgrem, eds., pp. 137-141, 1989
- 3) Gold RP, McClennan BL and Rottenberg RR: CT appearance of acute inflammatory disease of the renal interstitium. *AJR* **141**: 343-349, 1983
- 4) Tsugaya M, Hirao N, Sakagami H, et al.: Computerized tomography in acute pyelonephritis: the clinical correlations. *J Urol* **144**: 611-613, 1990
- 5) Tsugaya M, Hirao N, Sakagami H, et al.: Renal cortical scarring in acute pyelonephritis. *Br J Urol* **69**: 245-249, 1992
- 6) Murayama S, Bama H and Shimoda Y: Incremental dynamic CT for small hepatic tumors using high-speed, high resolution CT apparatus. *Radiation Med* **6**: 200-203, 1988
- 7) Foley WD: Dynamic hepatic CT. *Radiology* **170**: 617-622, 1989
- 8) Suzuki S and Yamazaki E: Urography using low-osmotic contrast media. *Rinsho Hoshasen* **32**: 253-262, 1987
- 9) Dawson P: Intravenous urography revisited *Br J Urol* **66**: 561-567, 1990

(Received on January 4, 1993)  
(Accepted on March 26, 1993)

## 和文抄録

腎ダイナミック CT における非イオン性造影剤  
(イオヘキソール) の投与方法に関する検討

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腎ダイナミック CT において非イオン性造影剤であるイオヘキソール 300 mg iodine/ml (オムニパーク 300) によるアーチファクトを軽減し, 腎の良好なコントラストをえるための至適投与方法を検討した. 対象は腎疾患を有する 76 症例に 10~50 ml のイオヘキソールを以下のように投与した. 第Ⅰ群 (14例) は 20 ml を 5 秒間で急速静注し, その後 30 ml を 5 分間で点滴静注した. 第Ⅱ群 (18例) は 20 ml を 5 秒間で急速静注した. 第Ⅲ群 (13例) は 20 ml を蒸留水で希

積 (全量 40 ml) し, 8 秒間で急速静注した. 第Ⅳ群 (15例) は 20 ml を 5 秒間で急速静注し, その後ハルトマン液 200 ml を全開で点滴静注した. 第Ⅴ群 (14例) は 10 ml を蒸留水で希積 (全量 20 ml) し, 5 秒間で急速静注した. 腎の皮髄境界は第Ⅳ群で最も明瞭となった. 低濃度のイオヘキソール (150 mg iodine/ml) でボリューム負荷をかけると良好な CT 画像がえられた.

(泌尿紀要 39 : 687-693, 1993)