Comparison of Iomeprol 300 and 350 mgI/ml Syringe Preparations for Contrast-Enhanced Helical Computed Tomography of the Liver Using Bolus-Tracking Technology

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Key Words: helical CT, bolus-tracking technology, abdominal CT

ABSTRACT

Purpose: To evaluate contrast enhancement with iomeprol in helical computed tomography (CT) using bolus-tracking technology.

Method: Helical CT examinations were performed on 114 patients using 100 ml of iomeprol administered via either a 300 mgI/ml syringe or a 350 mgI/ml syringe. After nonenhanced CT was performed, contrast-enhanced CT scans were obtained at optimal times during three phases, the early, late, and delayed phases, using bolus-tracking technology while infusing the contrast medium. Regions of interest were determined for the observed transverse sections of the aorta and liver, and the contrast index that was used for plotting time-density curves was defined as the difference in CT density before and after the administration of iomeprol. Time-density curves were plotted by body weight group to evaluate how the contrast enhancement was affected by different concentrations of the contrast medium.

Results: When time-density curves obtained using iomeprol preparations containing different iodine concentrations for the different body weight groups were compared, the contrast enhancement tended to be greater for the 350 mgI preparation than the 300 mgI preparation.

Conclusion: Contrast-enhanced CT can be performed with a 300 mgI preparation of iomeprol in patients weighing less than 60 kg; whereas a 350 mgI preparation is preferable for patients weighing 60 kg or more.

Introduction

Computed tomography (CT) is now an essential examination procedure in clinical practice. Equipment capable of helical scanning is currently so widely used that helical scanning can now be regarded as routine. Scan times are far shorter for helical CT than for conventional CT, but the former dictates a stricter selection of the flow rate, concentration and volume of the contrast medium to offset the shorter scan times. A new technology called bolus tracking has been developed to meet these challenges. Bolus tracking permits the continuous scanning of the same slice at a low dosage of X-ray and the measurement of CT values to determine the
optimal scan timing. In the present study, contrast-enhanced helical CT of the liver was performed with the aid of bolus-tracking technology to determine the optimal concentrations of the contrast medium for different body weight groups.

**Materials and Methods**

The drug used in this study was 100 ml of iomeprol (Eisai Co., Ltd., Tokyo, Japan), containing either 30 g of iodine (300 mgI/ml; iomeprol 300) or 35 g of iodine (350 mgI/ml; iomeprol 350), which was administered via a syringe. The subjects of this study were 114 patients: 61 outpatients and inpatients received iomeprol 300 and 53 patients received iomeprol 350 for abdominal CT at Osaka Medical College Hospital. There were 74 men and 40 women, ranging in age from 34 to 86 years (mean ± standard deviation: 66.6 ± 8.1 years). Patients with severe heart disease, nephropathy, or a past history of adverse reactions to an iodinated contrast medium were excluded from the study. Patients were required to provide their written informed consent prior to participation in the study. The patients were randomly assigned to iomeprol 300/100 ml and 350/100 ml groups (300 and 350 groups). Regarding the sex ratio in each group, the 300 group consisted of 41 men and 20 women, and the 350 group consisted of 33 men and 20 women. In terms of body weight distribution, the 300 group was composed of 9 subjects weighing less than 50 kg (<50 kg group), 20 subjects weighing 50 to less than 60 kg (≥50 <60 kg group) and 32 subjects weighing 60 kg or more (≥60 kg group); the 350 group was composed of 12 subjects weighing less than 50 kg (<50 kg group), 20 subjects weighing 50 to less than 60 kg (≥50 <60 kg group) and 21 subjects weighing more than 60 kg (≥60 kg group). There were no significant differences in the sex ratio or weight distribution between the two groups, as assessed by the $\chi^2$-test ($p = 0.339$ for body weight, $p = 0.580$ for sex). CT was performed using a Xvigor Real device (Toshiba, Tokyo, Japan) with a tube voltage of 135 kV, a tube amperage of 150 mA, a slice thickness of 7 mm, a time of tube rotation of 1 sec, a pitch count of 1, an image reconstruction of 180-degree interpolation, and a slice gap of 3 mm. Subjects were scanned in the cranial to caudal direction. Nonenhanced CT was performed first. The abdomen was then subjected to CT with bolus-tracking technology, without respiratory pause. Slices with little aortic motility were also scanned while subjects held their breath. Following the determination of regions of interest (ROIs) of the aorta, the entire volume of the contrast medium was administered at a flow rate of 3.0 ml/sec. The CT value of an aortic ROI was measured continuously. Early-phase scans were initiated 15 sec after the CT value exceeded 100 HU. Late- and delayed-phase scans were initiated 50 sec and 150 sec after the start of the early-phase scans, respectively.

ROIs were drawn on transverse tomograms of the aorta and liver. ROIs were determined without knowledge of the concentration of the contrast medium or the patient. ROIs were determined for all slices in the early-phase scan, but were determined only for three slices, namely; the upper (upper slice), portal level (middle slice), and lower regions of the liver (lower slice), in the late- and delayed-phase scans. Hepatic ROIs were arranged in normal parenchyma. Hepatic lesions and intrahepatic vessels were avoided in the ROI selection. To avoid partial volume effects, no ROI was selected for the marginal region closest to the liver surface. With the difference in CT values obtained before and after scanning set as the enhancement unit (EU), time-concentration curves were plotted for the 300 and 350 groups and body weight groups (<50 kg, ≥50 <60 kg, ≥60 kg). Time-density curves were used to determine concentration-related contrast enhancement. The areas under the time-concentration curves were calculated and analyzed by the U-test to assess the statistical significance of differences between the early-phase group, and analyzed by the Tukey-Kramer test for the late- and delayed-phases.

**Results**

1) Adverse reactions

No adverse reactions were observed in any dosage group.

2) Figures 1-8 show time-concentration curves. The statistical significance of the differences in the time-density curves between the early-phase groups was assessed using the U-test by comparing the areas under the curves, whereas the differences in the late- and delayed-phases were assessed using the Tukey-Kramer test.
i) Early-phase CT of aorta (Figs. 1, 2)

The time-concentration curve obtained using iomeprol 300 was higher in the <50 kg group than in the ≥50~<60 kg group, and higher in the ≥50~<60 kg group than in the ≥60 kg group. The contrast enhancement was greater in groups with lower body weights. The EU exceeded 300 HU in the <50 kg group during the first half of the scan and was less than 300 HU during the latter half, but the contrast enhancement in this group was greater than that in the other groups. The EU was between about 150 and 250 HU in the ≥50~<60 kg and ≥60 kg groups. The difference in EU between these groups was less than the difference between the <50 kg and ≥50~<60 kg groups. There were significant differences among the three groups as assessed by the U-test (P = 0.0004).

The time-concentration curve obtained using iomeprol 350 was higher in the <50 kg group than in the ≥50~<60 kg group. This was also true for the ≥50~<60 kg group relative to the ≥60 kg group. The contrast enhancement was greater in groups with lower body weights. The EU exceeded 300 HU in the <50 kg group during the first half of the scan, but was below 300 HU during the latter half. The EU was between 200 and 300 HU in the ≥50~<60 kg group during the first half of the scan, and below 250 HU during the latter half. The EU was between 150 and 250 HU in the ≥60 kg group. The contrast enhancement in the ≥60 kg group showed a greater stability and less pronounced declines than that in the other groups. There were significant differences among the three groups as assessed by the U-test (P = 0.0006).

Aortic Time density curves of early phase scan

![Aortic Time density curves of early phase scan](image1)

![Aortic Time density curves of early phase scan](image2)

Fig.1: Aortic time-density curves of early-phase. The time-concentration curve of iomeprol 300 was higher for the <50 kg group than for the ≥50~<60 kg group, and for the ≥50~<60 kg group than for the ≥60 kg group.

Fig.2: Aortic time-density curves of early-phase. The time-concentration curve of iomeprol 350 was higher for the <50 kg group than for the ≥50~<60 kg group, and for the ≥50~<60 kg group than for the ≥60 kg group.

ii) Early-phase CT of liver (Figs. 3, 4)

The contrast enhancement obtained using iomeprol 300 was highest in the ≥50~<60 kg group, but the differences between the groups were slight. The EU was between 0 and 10 HU in all groups during the first half of the scan. The contrast enhancement tended to gradually increase, beginning with slice 13, in all groups. No significant differences were observed among the three groups as assessed by the U-test (P = 0.6120).

The contrast enhancement obtained using iomeprol 350 approximately around 10 HU in all groups during the first half of the scan, with no appreciable differences among the three groups. The contrast enhancement tended to increase from slice 16. In subsequent slices, the contrast enhancement was greater in the <50 kg group than in the ≥50~<60 kg group, and greater in the ≥50~<60 kg group than in the ≥60 kg group. No significant differences were observed among the three groups as assessed by the U-test (P = 0.7115).
Hepatic Time density curves of early-phase scan

Fig.3: Hepatic time-density curves of early-phase. The differences among groups were slight.

iii) Late- and delayed-phase CTs of aorta

(Figs. 5, 6)

The contrast enhancement obtained using iomeprol 300 in the late-phase was greater in the <50 kg group than in the ≥50 ~ <60 kg group, and greater in the ≥50 ~ <60 kg group than in the ≥60 kg group. The EU was between 110 and 140 HU in the <50 kg group, between 90 and 120 HU in the ≥50 ~ <60 kg group, and between 80 and 100 HU in the ≥60 kg group. The EU in the delayed-phase was from 80 to 90 HU in the <50 kg group, about 70 HU in the ≥50 ~ <60 kg group, and about 60 HU in the ≥60 kg group. There were significant differences among the three groups as assessed by the Tukey-Kramer test (P < 0.01).

The contrast enhancement obtained using iomeprol 350 in the late-phase was greater in the <50 kg group than in the ≥50 ~ <60 kg group, and in the ≥50 ~ <60 kg group than in the ≥60 kg group. The EU was between 120 and 140 HU in the <50 kg group, between 100 and 130 HU in the ≥50 ~ <60 kg group, and about 90 HU in the ≥60 kg group. The EU in the delayed-phase was about 100 HU in the <50 kg group, between 80 and 90 HU in the ≥50 ~ <60 kg group, and about 70 HU in the ≥60 kg group. There were significant differences among the three groups as assessed by the Tukey-Kramer test (P < 0.01).

Aortic Time density curves of late and delayed phase scan

Fig.5: Aortic time-density curves of late- and delayed-phases. Contrast enhancement using iomeprol 300 in the late-phase was greater in the <50 kg group than in the ≥50 ~ <60 kg group, and in the ≥50 ~ <60 kg group than in the ≥60 kg group.

Fig.6: Aortic time-density curves of late and delayed-phases. Contrast enhancement using iomeprol 350 in the late-phase was greater in the <50 kg group than in the ≥50 ~ <60 kg group, and in the ≥50 ~ <60 kg group than in the ≥60 kg group.
iv) Late- and delayed-phase CTs of liver
(Figs. 7, 8)

The contrast enhancement obtained using iomeprol 300 in the late-phase was greater in the <50 kg group than in the ≥50 ~ <60 kg group, and in the ≥50 ~ <60 kg group than in the ≥60 kg group. The EU was about 50 HU in the <50 kg group, between 40 and 50 HU in the ≥50 ~ <60 kg group, and less than 40 HU in the ≥60 kg group. The EUs in the delayed-phase were approximately 35 to 45 HU in the <50 kg and ≥50 ~ <60 kg groups, and about 30 HU in the ≥60 kg group. There were significant differences among the three groups as assessed by the Tukey-Kramer test (P < 0.01).

The contrast enhancement obtained using iomeprol 350 in the late-phase was greater in the <50 kg group than in the ≥50 ~ <60 kg group, and greater in the ≥50 ~ <60 kg group than in the ≥60 kg group. The EU was approximately 55 to 65 HU in the <50 kg group, 50 to 60 HU in the ≥50 ~ <60 kg group, and less than 50 HU in the ≥60 kg group. The EU in the delayed-phase was approximately 40 to 55 HU in the <50 kg and ≥50 ~ <60 kg groups, but less than 40 HU in the ≥60 kg group. There were significant differences among the three groups as assessed by the Tukey-Kramer test (P < 0.01).

**Fig.7:** Hepatic time-density curves of late- and delayed-phases. Contrast enhancement using iomeprol 300 in the late-phase was about 50 HU for the <50 kg group, between 40 and 50 HU for the ≥50 ~ <60 kg group, and less than 40 HU for the ≥60 kg group, but the differences were slight in the delayed-phase.

**Fig.8:** Hepatic time-density curves of late and delayed-phase. Contrast enhancements using iomeprol 350 in the late-phase and delayed-phase showed a slight difference between the <50 kg group and ≥50 ~ <60 kg group, but those in the ≥60 kg group were less than those in the other groups.

**Discussion**

The purpose of contrast-enhanced CT is to localize a lesion for a qualitative diagnosis, such as the determination of the vascular component of a lesion, if a lesion is known to exist. The ideal concentration of the contrast medium for this purpose varies with the site of examination, target organ, patient body weight, body surface area, and volume of body fluid, as well as other factors. Nevertheless, in general practice, a 300 mgI preparation is commonly used in a final volume of 100 ml. The optimal degree of contrast enhancement helps locate and precisely delineate a lesion. The optimal degree of contrast enhancement varies with the type of neoplasm. Such contrast enhancement is required to detect and differentiate hepatic hemangiomas or primary hepatocellular carcinomas by allowing the visualization of a lesion, either without the visualization of the normal hepatic parenchyma as is generally observed in the early-phase, or as a clear contrast between the lesion and the normal hepatic parenchyma for images produced in the late or delayed-phase. Needless to say, the optimal contrast enhancement cannot be determined by a single parameter. However, the optimal contrast enhancement varies widely, depending not only on the concentration of the contrast medium and the body weight of the patient, but also on interindividual variations in blood circulation time and the resulting flow rate and the volume of the
contrast medium[9]. Aortic contrast was reported to improve at low contrast medium volumes and early scan start times[1]. Contrast medium volumes being equal, there is no significant difference in the contrast enhancement of the liver between groups receiving 300 mgI/ml and 320 mgI/ml preparations[7]. When a contrast medium is administered at a fixed volume while varying the flow rate between 2 and 6 ml/sec, higher flow rates reduce the time required for the maximum contrast enhancement, but the CT value of the maximum contrast enhancement remains unaffected[6]. Additionally, no difference in contrast enhancement is observed between single-phase infusion (infusion of 180 ml at a flow rate of 3 ml/sec) and two-phase infusions (infusion of 50 ml at a flow rate of 5 ml/sec followed by infusion of 130 ml at a flow rate of 2 ml/sec)[12].

Attempts were previously made to determine the optimal timing for a full scan after the administration of a small volume of the contrast medium[10]. In the current study, the interindividual variations in the timing of the activity window of the drug were negated using bolus-tracking technology, which allowed a more uniform contrast enhancement. This permitted the investigation of the relationship between body weight and drug concentration. The contrast enhancement of the liver has been shown to be greater in CT scans with bolus-tracking technology than in CT scans without this technology[2,4], and an optimal scan was obtained in the early-phase[8]. The actual contrast enhancement was generally more pronounced with the 350 mgI/ml preparation of iomeprol than with the 300 mgI/ml preparation, and tended to decrease with increasing body weight. Although the EU of the aorta tended to decrease with time, it was about 200 HU in the early-phase using the 300 mgI/ml preparation and between 60 and 100 HU in the late or delayed-phase even in the ≥60 kg group, in which the lowest imaging efficacy was observed. These values indicate that a sufficient contrast enhancement was obtained to differentiate vascular lesions from other lesions, such as lymphatic neoplasms. It should be noted that as primary hepatocellular carcinomas are supplied by the arterial system, the contrast enhancement of the abdominal aorta, common hepatic artery, and proper hepatic artery may be reduced to the detriment of hepatic lesion visualization when the early-phase contrast enhancement of the aorta is inadequate. This issue requires further research.

The EU of the liver was 10 HU or less in the early-phase, but the contrast enhancement of the hepatic parenchyma increased gradually during the last half of the early-phase. This rate of change means that portal perfusion permits the visualization of the liver during the last half of the early-phase. Kim et al. defined the early-phase as the period in which the CT value of the liver increases by 20 HU[11]. If so, the term "early-phase" is a misnomer, in the strictest sense of the term. Single-slice CT requiring a total of about 30 sec to scan the liver is difficult to perform without advancing the scan start or increasing the slice gap. Such adjustments can degrade the quality of CT images. One solution to this problem is multislice CT. The administration of a contrast medium at an injection rate of 4-5 ml/sec results in a hepatic artery angiographic image obtained using multi-detector row helical CT[5]. The late-phase EU of the liver after the administration of the 300 mgI/ml preparation was about 50 HU in the <50 kg group, between 40 and 50 HU in the ≥50 ~ <60 kg group, and a slightly less than 40 HU in the ≥60 kg group. The corresponding values obtained with the 350 mgI/ml preparation were about 60 HU, 50-60 HU, and 40-50 HU, respectively. Heiken et al. believe that a contrast enhancement of about 50 HU is required to detect hepatic lesions[3]. On the basis of this standard, hepatic lesions can be contrast-enhanced with the 300 mgI/ml preparation in patients weighing less than 60 kg, whereas the 350 mgI/ml preparation will be more effective in patients weighing 60 kg or more.

The delayed-phase EUs in all groups are between 25 and 45 HU with the 300 mgI/ml preparation, and 30 and 55 HU with the 350 mgI/ml. EUs in the delayed-phase appear to be low due to the delay of 180 sec or more after the initiation of contrast medium injection. However, as the EU of the aorta in this phase is between 60 and 100 HU, this presents little difficulty with regard to differentiating lesions from normal tissue. The required concentration of the contrast medium varied with body weight. This study showed that the 300 mgI/ml preparation is appropriate for patients weighing less than 60 kg, whereas the 350 mgI/ml preparation is more suitable for patients weighing 60 kg or more.
References


Received October 14, 2005
Accepted November 28, 2005