



Comparison of image quality of abdominopelvic CT in paediatric patients: low osmolar contrast media versus less iodine-containing iso-osmolar contrast media at different peak kilovoltages

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AIM: To evaluate the effect of iso-osmolar contrast media (IOCM) at different tube voltages on image quality for abdominal computed tomography (CT) in paediatric patients.

MATERIALS AND METHODS: The low osmolar contrast media (LOCM) group and IOCM group consisted of 101 and 102 CT examinations, respectively, in patients <18 years old. Images were reviewed retrospectively. Objective measurement of the contrast enhancement and noise were analysed and contrast-to-noise ratios (CNRs) of the abdominal aorta, portal vein, and liver were calculated. Four radiologists participated in subjective analysis using a four-point scale system to evaluate degrees of contrast enhancement, image noise, beam-hardening artefact, and overall image quality. Reader performance for correctly differentiating the two kinds of contrast media was evaluated.

RESULTS: Regarding the objective measurement, contrast enhancement was significantly higher in the LOCM group ($p < 0.05$). In subjective analysis, only CT using 120 kVp showed significantly stronger enhancement in the LOCM group ($p = 0.002$), and sensitivity to differentiate the IOCM was 80.6%. Overall sensitivity and specificity for correctly differentiating IOCM were 57.1%, and 56.9%, respectively.

CONCLUSION: The application of IOCM was found to be feasible for performing paediatric abdominopelvic CT with a low tube voltage protocol. Although objective measurements of contrast enhancement were significantly lower in the IOCM group, subjective contrast enhancement and image quality assessments were not statistically different between groups.

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Introduction

Contrast media (CM) are classified as hyperosmolar, low osmolar (LOCM), and iso-osmolar (IOCM) by their osmolality. The osmolality of hyperosmolar and LOCM are as much as five times and two or three times greater than that of plasma, respectively. IOCM, however, have an osmolality equal to that of plasma.¹ Several advantages have been suggested in using IOCM for children over LOCM in terms of physiological side effects, allergic-like reactions, complications from extravasation of contrast media, and fluid shifts.² Yet, it is not very clear if lower iodine dose in IOCM has a significant effect on image quality compared to LOCM. Some previous studies regarding the relationship of iodine concentration of the contrast media and degree of enhancement suggest that the use of a higher iodine concentration results in greater enhancement on CT images.^{3,4} Other studies have shown that there is no significant difference in the degree of enhancement between two contrast media with different iodine concentrations in certain circumstances.^{5,6} Behrendt *et al.* showed that two LOCM with iodine concentrations of 300 and 370 mg iodine/ml did not cause a significant difference in hepatic enhancement. A recent study that measured image quality between LOCM and IOCM showed no significant intergroup difference in the degree of contrast enhancement for cardiac CT angiography in paediatric patients.⁶ To the authors' knowledge, however, there are not enough studies comparing the image quality when using IOCM and LOCM for paediatric abdominopelvic CT. Therefore, the purpose of the present study was to compare the image quality of paediatric abdominopelvic CT when using IOCM and LOCM and evaluate the feasibility of LOCM for paediatric imaging in various settings of peak kilovoltage (kVp).

Materials and methods

This retrospective study was approved by the Institutional Review Board, and the requirement for informed consent was waived.

Selection of patients and study groups

Patients were selected retrospectively by searching for abdominopelvic CT in patients aged 18 years or under. For the LOCM group, 102 patients were selected who underwent contrast-enhanced abdominopelvic CT from April 2013 to January 2015. CT with routine protocols for evaluating abdominal pathology were included in this study, except for CT performed with a specific indication such as CT angiography, CT enterography, and CT for urolithiasis evaluation. Pusan National University Yangsan Hospital had used LOCM (>300 mg iodine/ml) previously, and has changed to use IOCM, Visipaque 270 (iodixanol 270 mg iodine/ml, GE Healthcare, Princeton, NJ, USA), since February 2015. IOCM became available in Pusan National University Yangsan Hospital in February 2015, and since then, in an attempt to reduce pain during injection and for economic reasons, IOCM was used for all paediatric patients

in routine abdominopelvic CT. For the IOCM group, 106 patients were selected from those who underwent contrast-enhanced abdominopelvic CT from February 2015 to September 2015 and satisfied the same inclusion criteria (Fig 1).

During the objective analysis, one examination was excluded from the LOCM group for liver left lobectomy ($n=1$), and four examinations were excluded from the IOCM group for liver segmentectomy ($n=2$), poor scan timing ($n=1$), and not having the dose report ($n=1$; Fig 1).

CT protocols

Helical CT was performed with a 64-channel multi-detector row CT system (Discovery HD 750, GE Healthcare, Milwaukee, WI, USA). Imaging parameters were as follows; 0.5 ms rotation time, 1.375:1 pitch, 64×0.625 mm beam collimation. Peak tube voltages were selected based on the patient's weight from 80 to 120 kVp; 80 kVp for body weight <30 kg, 100 kVp for body weight <70 kg, and 120 kVp for body weight ≥ 70 kg. Automatic exposure control was applied with noise index from 11 to 18 depending on the patients' weight. Single phase portovenous phase image was obtained with CM administration of 1.5 ml/kg and a maximum dose of 100 ml. CM was administered by using a mechanical injector for 30 seconds and followed by saline chaser. CM administration rate was set according to the CM injection duration. If the total amount contrast media was estimated <15 ml, to avoid insufficient enhancement, contrast media was injected with a rate of 0.5 ml/s and saline chaser was applied to prevent enhancement failure due to slow CM injection. CT was started 55–60 seconds after injection of the CM and CT was performed in the craniocaudal direction from the dome of the diaphragm and upper margin of the symphysis pubis.

The reconstructed section thickness of axial images was 2.5 mm with no interval. Adaptive statistical iterative reconstruction with a blending ratio of 50% was applied and the soft-tissue kernel was used in reconstructing images.

Regarding the radiation dose, volume CT dose index and dose–length product was recorded from the CT dose report. A reference phantom size of 32 cm was used in this study. The effective dose was calculated by multiplying the dose–length product by the previously published conversion factors.⁷

Objective image quality analysis

CT images were reviewed retrospectively by two radiologists (one with 8 years of experience in the interpretation of paediatric CT, and another with 3 years of CT image analysis experience). Contrast enhancement was evaluated at the level of main portal vein bifurcation, by drawing regions of interest on six different locations: liver right anterior segment, right posterior segment, left medial segment, and left lateral segment, abdominal aorta, and main portal vein (MPV). Mean attenuation (HU) was used as the degree of contrast enhancement, and standard

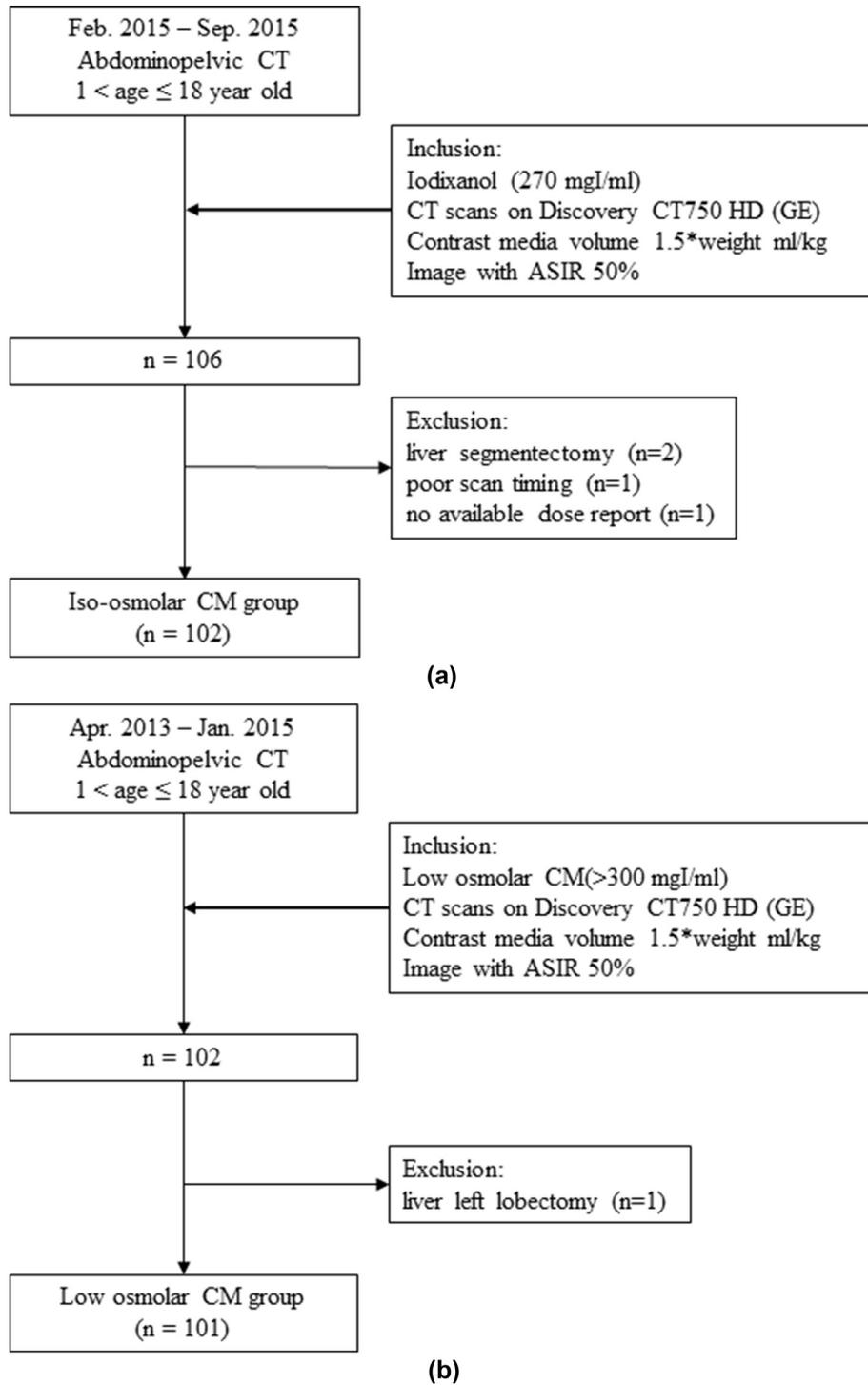


Figure 1 Inclusion and exclusion criteria for IOCM group (a) and LOCM group (b).

deviation was used as noise. Measurements of liver right anterior segment, right posterior segment, left medial segment, and left lateral segment were averaged and used as the value to represent contrast enhancement of the liver.

The cross-sectional areas of regions of interest were 30 mm² for the abdominal aorta, MPV, and 100 mm² for liver. When the calibre of the vessels was too small, regions of interest were adjusted so as not to cross the boundary.

Additionally, attenuation at the right and left erector spinae muscles were measured with regions of interest of 100 mm² to calculate the contrast-to-noise ratio. Contrast-to-noise ratios for abdominal aorta, MPV, and liver were calculated as (attenuation of the abdominal aorta – mean attenuation of both erector spinae muscles)/standard deviation of the abdominal aorta, (attenuation of the MPV – mean attenuation of both erector spinae muscles)/standard

deviation of the MPV, and (mean attenuation of the liver – mean attenuation of both erector spinae muscles)/mean standard deviation of the liver, respectively. The figure of merit was also calculated as (contrast-to-noise ratio)²/(total iodine amount × effective dose).⁸

Subjective image quality analysis

Subjective visual analysis was performed by evaluating the degrees of contrast enhancement, beam-hardening artefact, image noise, and overall image quality, using four-point scale systems. Four-point scale for contrast enhancement, overall image quality, and image noise is as follows: 1, unacceptable; 2, substandard; 3, acceptable; 4, excellent; and for beam-hardening artefact: 1, streak artefact present and unacceptable; 2, streak artefacts present and interfering; 3, streak artefact not interfering with depiction of adjacent structure; 4, no streak artefacts.⁹

A consensus reading session for reader training was held prior to the independent subjective image analysis, performed by three board-certified radiologists and one training radiologist (two radiologists mentioned above, another radiologist with 15 years of interpretation of paediatric thoracic CT, and one other with 6 years of interpretation of abdominopelvic CT) on dedicated diagnostic workstations. Reader performance to correctly differentiate the two groups by visual assessment was evaluated; readers were requested to determine whether the CT images were performed using LOCM or IOCM.⁶

Statistical analysis

Comparison between the groups regarding the age, body weight, CM volume injected, total iodine dose, volume CT dose index, and dose–length product was performed using the Student *t*-test. Comparison of the attenuation, standard deviation, contrast-to-noise ratio, dose–length product, and subjective analysis was done by using two-way analysis of variance in subsets of peak tube voltage (80 kVp, 100 kVp, 120 kVp). Reader performance to correctly distinguish the two groups by visual assessment was evaluated by calculating sensitivity, specificity, positive predictive value, and negative predictive value using two-by-two cross table.

Statistical analysis was performed using IBM SPSS Statistics for Windows (version 21.0, IBM, Armonk, NY, USA), and R version 3.2.3. A *p*-value of <0.05 was considered statistically significant.

Results

Patient characteristics, amount of CM, and total iodine dose

The IOCM group consisted of 102 patients (mean age 8.93±4.79 years, mean body weight 35.85±19.75 kg) and the LOCM group consisted of 101 patients (mean age 9.77±4.89 years, mean body weight 40.83±21.41 kg). There was no statistically significant difference in body weight

Table 1
Objective analysis of image quality.

Peak tube voltage	Anatomical structures			MPV			Liver					
	Measurements	Abdominal aorta		Enhancement	Image noise	CNR	FOM	Enhancement	Image noise	CNR	FOM	
80 kVp	IOCM group (n=51)	198.3 (19.9)	14.5 (4.0)	10.2 (3.1)	16.3 (1.2)	205.6 (22.7)	17.4 (4.8)	8.9 (2.6)	11.4 (0.7)	122.3 (11.0)	12.6 (3.3)	5.1 (1.3)
	LOCM group (n=28)	248.3 (47.0)	16.2 (4.4)	11.8 (2.9)	20.3 (1.7)	236.8 (31.9)	18.8 (6.6)	10.0 (3.1)	13.8 (0.7)	132.7 (14.8)	12.7 (3.4)	5.6 (1.2)
100 kVp	<i>p</i> -Value	<0.001*	0.07	0.03*	0.22	<0.001*	0.33	0.08	0.14	0.002*	0.89	0.06
	IOCM group (n=42)	172.8 (19.3)	17.7 (4.3)	6.4 (1.6)	2.3 (1.4)	185.2 (23.4)	17.5 (4.3)	7.0 (1.8)	2.9 (0.8)	112.1 (16.6)	15.5 (3.1)	3.2 (1.3)
120 kVp	LOCM group (n=48)	205.3 (40.2)	18.4 (4.5)	7.8 (2.3)	3.7 (1.3)	198.6 (25.8)	18.3 (5.4)	7.8 (2.4)	3.9 (0.7)	121.3 (17.2)	16.2 (4.5)	3.6 (1.3)
	<i>p</i> -Value	<0.001*	0.46	0.002*	0.002*	0.01*	0.47	0.12	0.14	0.01*	0.41	0.21
120 kVp	IOCM group (n=9)	138.8 (14.9)	21 (4.8)	3.5 (1.0)	0.5 (2.9)	157.6 (18.7)	19.8 (7.1)	5.0 (1.5)	0.9 (1.6)	101.5 (11.1)	17.2 (3.3)	2.0 (0.5)
	LOCM group (n=25)	178.4 (31)	21.4 (3.1)	5.1 (1.6)	0.8 (1.8)	181 (19.3)	22.1 (3.9)	5.1 (1.2)	0.8 (1.0)	113 (15.2)	19.5 (5.7)	2.3 (0.9)
	<i>p</i> -Value	<0.001*	0.8	0.01*	0.11	0.004*	0.25	0.8	0.54	0.04*	0.28	0.48

Data are mean (standard deviation).

IOCM, iso-osmolar contrast media; LOCM, low osmolar contrast media; ASIR, adaptive statistical iterative reconstruction; MPV, main portal vein; CNR, contrast to noise ratio; FOM, figure of merit.

* *p*-value of <0.05.

($p=0.09$), age ($p=0.22$), and sex ($p=0.2$) of patients between the groups.

Mean volumes of injected CM were not significantly different between the IOCM, and LOCM groups (53.8 ± 29.6 ml and 62.4 ± 31.9 ml, respectively; $p=0.39$); however, the total iodine dose was significantly different between the two groups (14.5 ± 8 versus 20.2 ± 10.4 g, respectively; $p<0.001$).

Objective image analysis

In all three peak tube voltages (80, 100, and 120 kVp), contrast enhancement at the abdominal aorta, MPV, and liver, and contrast-to-noise ratio of the abdominal aorta was significantly lower in the IOCM group; however, image noise, contrast-to-noise ratio of the MPV, and contrast-to-noise ratio of the liver was not significantly different between the two groups (Table 1). The degree of enhancement was lower, and the degree of image noise was higher when the peak tube voltage was higher. At 120 kVp, the mean

attenuation of the abdominal aorta, MPV, and liver enhancement in the IOCM group was 138.8, 157.6, and 101.5 HU, respectively. The figure of merit was not significantly different between the two groups, except for the abdominal aorta in 100 kVp (0.64 versus 1.04, $p=0.002$; Table 1, Fig 2).

Subjective image analysis

There was no significant difference between the two groups regarding beam-hardening artefact, image noise, and overall image quality; however, contrast enhancement was significantly stronger in the LOCM group overall ($p<0.001$). In three subgroups of different peak tube voltages, contrast enhancement was significantly stronger in the LOCM group only in 120 kVp ($p=0.002$; Table 2).

There were images evaluated as “substandard” in both groups (two in the LOCM group, four in IOCM group); however, none were evaluated as “unacceptable” by any readers.

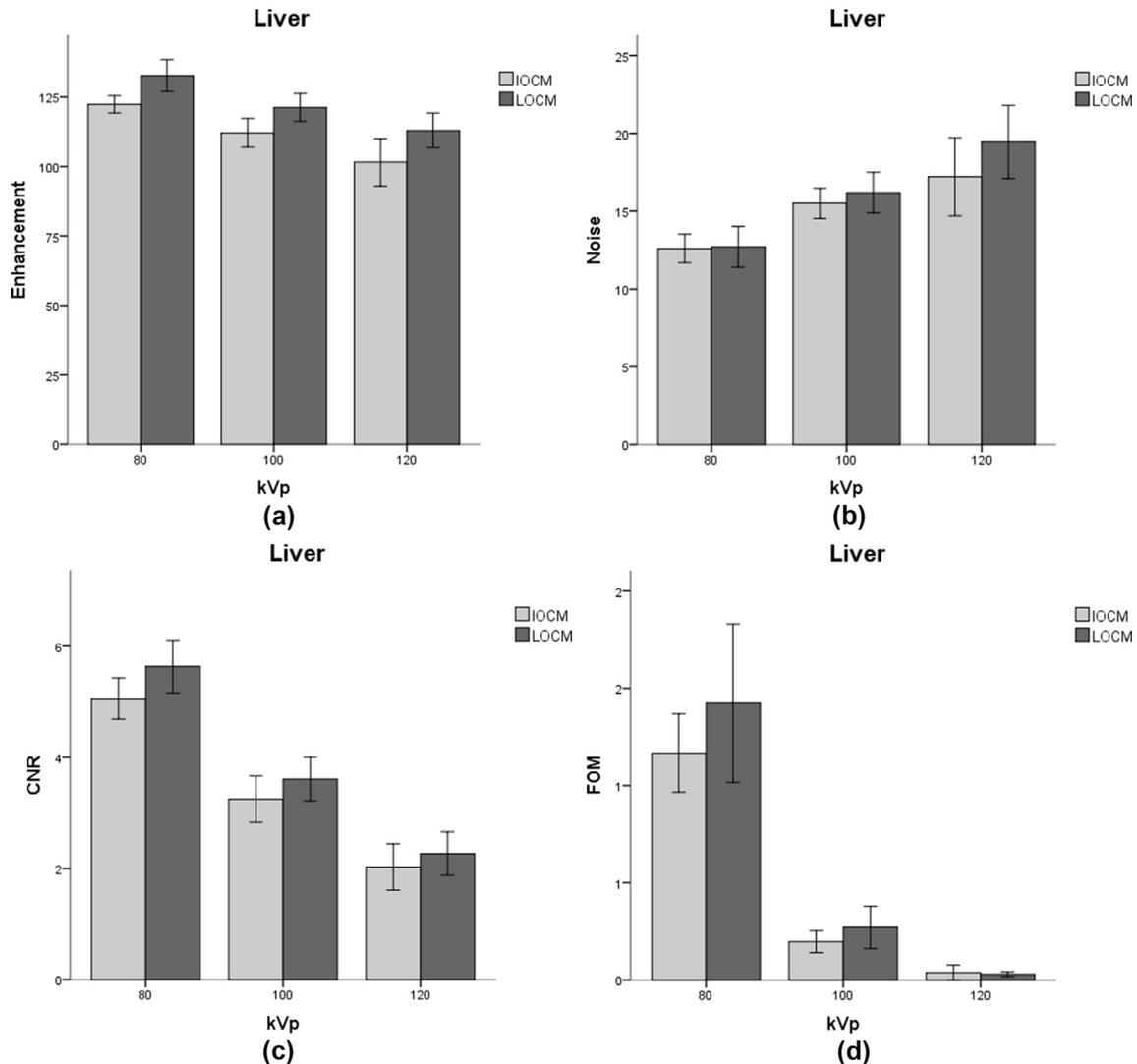


Figure 2 Objective analysis of image quality of the liver enhancement (a), noise (b), contrast-to-noise ratio (c), and figure-of-merit (d) in three peak tube voltages.

Table 2
Subjective analysis of image quality.

Peak tube voltage		Contrast enhancement	Beam-hardening artefact	Noise	Overall image quality
80 kVp	IOCM group (n=51)	3.55 (0.04)	3.29 (0.03)	3.26 (0.06)	3.24 (0.05)
	LOCM group (n=28)	3.68 (0.06)	3.34 (0.04)	3.26 (0.08)	3.26 (0.06)
	p-Value	0.07	0.26	0.95	0.81
100 kVp	IOCM group (n=42)	3.57 (0.05)	3.42 (0.04)	3.33 (0.05)	3.45 (0.06)
	LOCM group (n=48)	3.62 (0.05)	3.44 (0.04)	3.19 (0.05)	3.34 (0.05)
	p-Value	0.46	0.63	0.06	0.20
120 kVp	IOCM group (n=9)	3.08 (0.10)	3.61 (0.07)	3.33 (0.12)	3.25 (0.10)
	LOCM group (n=25)	3.48 (0.06)	3.52 (0.04)	3.20 (0.07)	3.38 (0.06)
	p-Value	0.002*	0.25	0.36	0.29
Overall	IOCM group (n=102)	3.51 (0.54)	3.37 (0.50)	3.30 (0.62)	3.33 (0.56)
	LOCM group (n=101)	3.60 (0.50)	3.43 (0.51)	3.21 (0.59)	3.33 (0.56)
	p-Value	<0.001*	0.90	0.07	0.74

Data are mean (standard deviation).

IOCM, iso-osmolar contrast media; LOCM, low osmolar contrast media.

Reader performance to differentiate IOCM from LOCM is summarised in Tables 3 and 4. Overall sensitivity, specificity, positive predictive value, negative predictive value was 57.1%, 56.9%, 57.2%, and 56.8%, respectively. In the group with 120 kVp, the sensitivity was measured as 80.6% (95% confidence interval: 64%–91.8%), and it was significantly higher than other tube voltages.

Discussion

In the present study, the IOCM showed significantly less enhancement compared with LOCM at abdominal aorta, MPV, and liver in all three peak tube voltages in the objective analysis. Nevertheless, the CT images using IOCM showed >50 HU of enhancement, which can be considered as optimal enhancement for the liver.^{10–12} In addition, the contrast-to-noise ratio of the abdominal aorta was significantly lower in the IOCM group; however, the contrast-to-noise ratios of the MPV and the liver, which are more important in abdominal CT, showed no significant difference between the two CMs, and can be considered sufficient enough to maintain diagnostic quality images. The figure of merit showed no intergroup difference except for abdominal aorta when using 100 kVp.

The degree of enhancement was decreased as the tube voltage was increased in the present study, and it corresponds well with previous studies.¹³ Interestingly, image noise was increased as the peak tube voltage was increased; an outcome not clearly explained by previous studies

Table 4
Reader performance by different peak tube voltages.

	80 kVp	100 kVp	120 kVp	Overall
Sensitivity	54.9%	54.8%	80.6%	57.1%
95% CI	47.8–61.9%	46.9–62.4%	64–91.8%	52.2–62%
Specificity	67.9%	55.2%	48%	56.9%
95% CI	58.4–76.4%	47.9–62.4%	37.9–58.2%	51.9–61.8%
PPV	75.7%	51.7%	35.8%	57.2%
95% CI	69.8–80.7%	46.5–56.9%	30.3–41.7%	53.8–60.6%
NPV	45.2%	58.2%	87.3%	56.8%
95% CI	40.4–50.2%	53.1–63.2%	77.4–93.2%	53.3–60.2%

CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

showing image noise level increases with less tube voltage when using the same phantom.^{13,14} Considering the fact that we used higher tube voltage for larger-sized patients, and the fact that image noise also increased as the phantom size increased in a previous study can explain why the image noise increased with more tube voltage in the present study¹³ (Fig 2). As the tube current was limited, a lack of photons can also cause this discrepancy between the image noise and peak voltage.¹⁴

The subjective analysis showed no significant difference in the degree of enhancement between the two contrast media except for 120 kVp groups in which the degree of enhancement was significantly lower in the IOCM group (Fig 3). This suggests that in lower peak tube voltage images, the difference in the extent of enhancement is

Table 3
Reader performance: by reader.

	Reader 1	Reader 2	Reader 3	Reader 4	Overall
Sensitivity	64.7%	52%	55.9%	55.9%	57.1%
95% CI	54.6–73.9%	41.8–62%	45.7–65.7%	45.7–65.7%	52.2–62%
Specificity	56.4%	62.4%	49.5%	59.4%	56.9%
95% CI	46.2–66.3%	52.2–71.8%	39.4–59.6%	49.2–69.1%	51.9–61.8%
PPV	60%	58.2%	52.8%	58.2%	57.2%
95% CI	53.5–66.1%	50.5–65.6%	46.3–59.2%	50.9–65.1%	53.8–60.6%
NPV	61.3%	56.3%	52.6%	57.1%	56.8%
95% CI	53.6–68.4%	50–62.3%	45.3–59.9%	50.4–63.6%	53.3–60.2%

CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

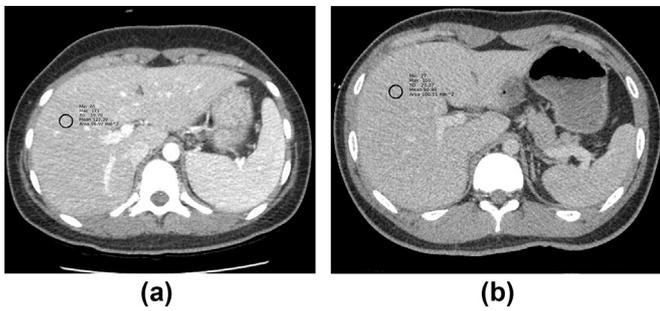


Figure 3 (a) Contrast enhancement of the liver in a 15-year-old female patient, who underwent abdominopelvic CT at 120 kVp using LOCM. Subjective analysis showed an average score of enhancement of 3.5. (b) A 16-year-old male patient, who underwent abdominopelvic CT at 120 kVp using IOCM. Subjective analysis showed an average score of enhancement of 2.25.

visually unrecognisable, and supports the fact that the IOCM group has sufficient enhancement for diagnostic quality images in a low peak tube voltage protocol in paediatric abdominopelvic CT even though there were significant intergroup differences in the attenuation in the objective analysis (Fig 4).

In addition, sensitivity to differentiate IOCM from LOCM was <65% in all readers without significant difference between them, suggesting difficulty in differentiating the two groups by visual assessment. In the 120 kVp group, however, the sensitivity was significantly higher compared to other tube voltages and was as high as 80.6% (95% confidence interval: 64%–91.8%), which suggests it might be possible to distinguish the two CM when using this peak tube voltage. This correlates with the result that the subjective degree of enhancement was significantly different at 120 kVp.

This study showed that even though the degree of enhancement was objectively lower when used iodixanol 270, there are possibly more advantages than disadvantages, especially for smaller children, because subjectively there was no significant difference regarding the degree of enhancement and image quality. In addition, objectively, the images still showed optimal diagnostic.

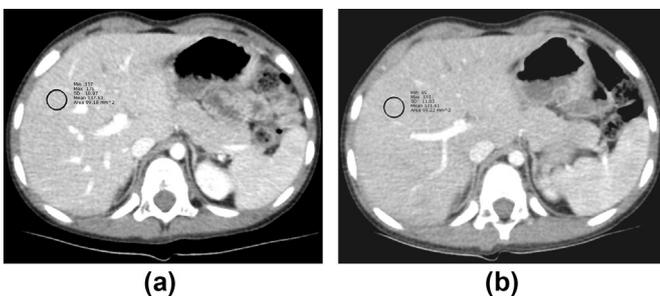


Figure 4 (a) Contrast enhancement of the liver in a 5-year-old male patient, who underwent abdominopelvic CT at 80 kVp using LOCM. Subjective analysis showed an average score of enhancement of 3.75. (b) Subjective analysis of abdominopelvic CT at 80 kVp using IOCM in the same patient 5 months later, showed an average score of enhancement of 3.75.

Neonates and small children are more susceptible to fluid shifts and vulnerable to intravascular osmotic loads compared to adults.² The iso-osmolarity of iodixanol 270 has several advantages over LOCM when used for paediatric patients: it minimises blood volume expansion and is thought to reduce injection-related pain, which can potentially cause children to be agitated and as a result increase motion artefacts.¹⁵ Several studies suggested that lowering the iodine dose by using IOCM instead of LOCM also reduces the risk for contrast-induced nephropathy.^{16–18}

There are conflicting results, however, in some other studies comparing contrast-induced nephrotoxicity when using IOCM and LOCM. Zo'o *et al.* showed that LOCM was not inferior to IOCM in children with normal renal function in terms of relative variation of the creatinine clearance.¹⁹ In addition, some LOCM have the advantage of lower viscosity, which is also an important physical property of CM, especially for children.² Therefore, additional prospective studies are needed to investigate the optimal CM for paediatrics, including observation for adverse effects.

The present study has several limitations. First, its retrospective design is an inherent limitation; for example, adverse effects, such as nephrotoxicity or allergic reactions, were not monitored. Second, the two CM were not compared in the same patients. CT contrast enhancement depends on various interacting factors, not only volume and concentration of the CM, but the injection technique, tissue characteristics, and patient characteristics such as sex, age, weight, height, cardiovascular status and renal function.³ Finally, there is a significant difference in dose–length product and effective dose between the two groups. During the study period, CT protocols regarding the radiation dose were periodically audited and optimised by the clinical dose optimisation team at Pusan National University Yangsan Hospital. As this study was retrospective, this confounding factor could not be controlled.

In conclusion, the present study indicates that paediatric abdominopelvic CT using an IOCM containing 270 mg iodine/ml is feasible especially for 80 and 100 kVp. Objective assessment of contrast enhancement was significantly lower than LOCM, but sufficient enough for diagnostic quality, and subjective contrast enhancement was not significantly different at 80 and 100 kVp.

Conflict of interest

The authors declare no conflict of interest.

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