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320-row multidetector CT angiography for hepatocellular carcinoma using CO2 gas instead of iodinated contrast agents: Experiment and preliminary clinical study

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Purpose

#Patients develop allergic or nephrotoxic reactions to iodinated media # carbon dioxide (CO_2) gas angiography can be used.

#For effective transarterial chemoembolization (TACE), the position of the tumor and its feeding arteries must be known.

#Unlike iodinated contrast media, intravascularly-injected CO_2 does not mix with blood and flows away in an instant.

CO_2 gas angiography can not detect neither a tumor nor its feeding artery well.

#The usefulness of CO_2 gas as a contrast agent at CTA for the detection of liver tumor has not been evaluated.

#320-detector-row CT (320-MDCT) (Toshiba Medical Systems Corp., Tochigi, Japan) makes it possible to scan the whole liver within 0.35 sec.(Figure.1)

#We performed clinical studies to examine the feasibility of using CO_2 CTA combined with 320-MDCT for the detection of malignant liver tumor.

Images for this section:

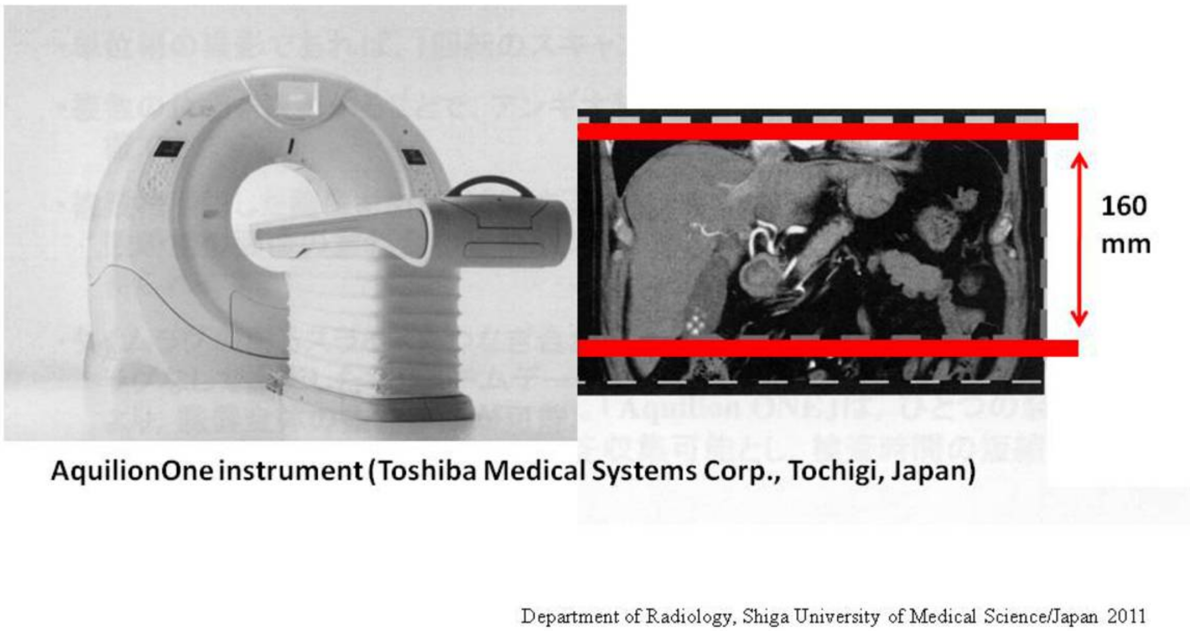


Fig. 1: 320-detector-row CT. AquilionOne instrument (Toshiba Medical Systems Corp., Tochigi, Japan) makes it possible to scan the whole liver within 0.35 sec.

Methods and Materials

Animal for pre clinical study

#Rabbits (two Japanese white rabbits 2.5-3.0Kg)

(SLC, Tokyo, Japan)

#All rabbit studies were approved by the Research Center for Animal Life Science of our institution.

#General anesthesia : Subcutaneously injection

medetomidine hydrochloride (0.1 mg/kg, Meiji

Seika Co. Ltd., Tokyo, Japan) and ketamine

hydrochloride (25 mg/kg, Sankyo Yell Yakuhin

Co. Ltd., Tokyo, Japan)

Clinical study

#Patients(six, with malignant liver tumors ,

manifested allergic reactions to iodinated

contrast media or renal failure)

#Prior written informed consent was obtained.

#This study was approved by the Ethics

Committee of our institution

A CO_2 gas delivery system#Figure 1)

#Autoenhancer A60 (Nemoto, Co. Ltd., Tokyo, Japan)

#A 100-ml disposable syringe (Nemoto)

#A 1.8-ml extension tube (CT-L1000CH; Hakko, Tokyo, Japan) was filled with normal saline.

CT scanning parameters

#AquilionOne instrument (Toshiba Medical

Systems Corp., Tochigi, Japan).

#Scan mode, dynamic volume; 120 kV, 150mA.

#D-FOV: 320.0, scan speed, 0.35 sec;

total scan time, 5 sec;

slice thickness, 0.5 mm;

scan area, 160.0 mm.

The investigation of relationship between Syringe volume, CO2 injection volume and injection rate

#A 7m microcatheter (MSP2.8F-110-ST, TERUMO, Tokyo, Japan) was connected to the delivery system.

#Injection protocols (injection rate 1-, 3-, and 6 ml/sec, injection volume 8-, 16-, and 32 ml, syringe volume 8-, 16-, 32-, and 100 ml)

#The start-time of CO2 blowout and its duration were recorded 5 times from the microcatheter.

The investigation of relationship of CO2 catheter and lumen capacity

#microcatheters (m7; MSP2.8F-110-ST; Sniper2 revo

Selective, MSR2.9F-110-ST; Sniper2 Highflow,

MHX2.9F-110#ST#was connected to the delivery

system.

#The start-time of CO2 blowout and its duration were recorded 5 times using an injection rate of 1 ml/sec and injection- and syringe volumes of 8 ml.

The investigation of imaging timing

#Under fluoroscopic guidance using the cut-down method, a 4-Fr sheath was inserted

#A m7 microcatheter (MSP2.8F-110-ST) was introduced into the trunk of the abdominal- and the celiac artery.

#CO2 was injected 3 times (1 ml/sec, injection and syringe volume 8 ml)

#The start-time of each CO2 blowout was recorded.

Clinical studies

#A 4-Fr sheath was inserted into the right femoral artery.

#A 7m microcatheter (MSP2.8F-110-ST) was introduced into the trunk of the common hepatic artery.

#CO2 gas (injection rate 1 ml/sec, injection- and syringe volume 8 ml)

#CT scan was acquired 12 sec after the start of injection.

#The branch from a segmental artery as the subsegmental artery and the branch from a subsegmental artery as the feeding artery was defined.

#Based on previously-acquired CT and/or MR images Two radiologist judged whether it was possible to detect the vascular tumor area and flow into the tumor on images acquired after the delivery of CO2

Data analysis

#Dr. SPSS II for Windows (SPSS Japan Inc., Tokyo, Japan).

one-way analysis of variance (ANOVA) and Tukey's post-hoc test #assessed the start-time and duration of CO2 blowout

#Cramer's V statistic #the relationship between the vascular tumor area and the tumor size or the tumor location in the lobe of the liver.

#Differences of $p<0.05$ were considered statistically significant.

Images for this section:

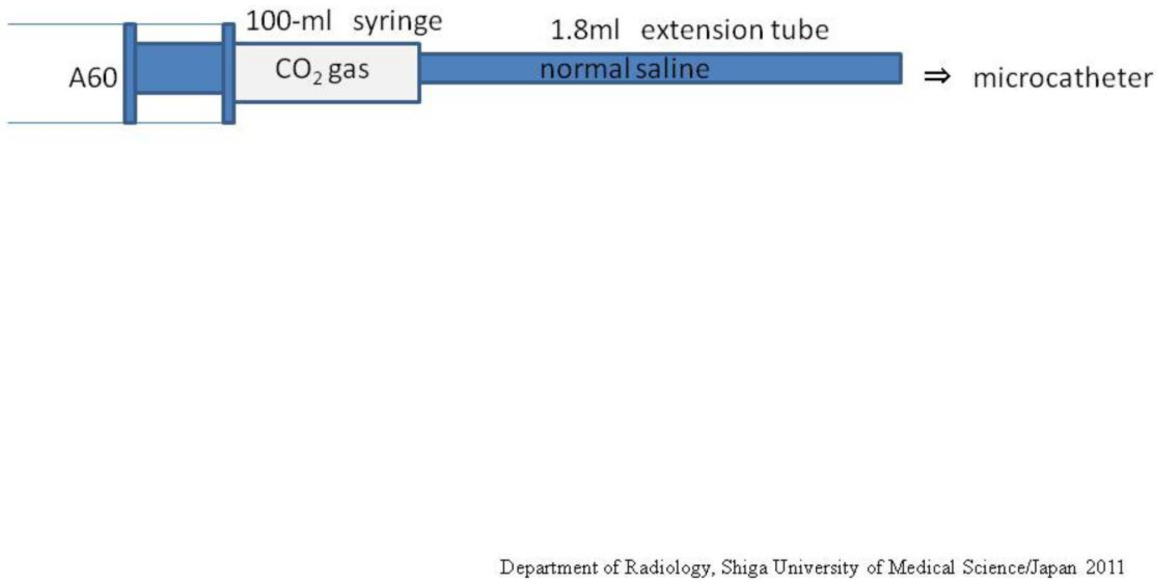


Fig. 1: Figure 2. A CO2 gas delivery system. A CO2 gas delivery system was constructed by linking a contrast medium injector, a 100-ml disposable syringe , and a 1.8-ml extension tube. The extension tube was filled with normal saline.

Results

Syringe volume and CO2 injection volume and -

rate

#As the injection rate increased, the start-time of

CO2 infusion tended to decrease.

the start-time tended to become shorter when

the syringe- and injection volume were nearly

equivalent.

#The injection rate had little effect on the

duration of blowout

#The duration of blowout

was longer when the syringe volume was larger

(Figure. 1).

CO2 catheter and lumen capacity

#The start-time of CO2 blowout tended to be

shorter when the lumen capacity of the

catheter was larger.

#The duration of CO2 blowout tended to be

longer when the catheter lumen was larger

(Figure. 2).

Imaging timing and identification of liver function changes

#The start-time of CO2 blowout produced no noticeable changes in the aorta and celiac artery.

#Some gas dispersion for about 0.35 sec, the start-time was almost constant (Figure 3).

#No vessel breakdown

Clinical Study-1

#6 patients (26 nodules); 4 had primary HCC ,

one each presented with hepatic metastasis from

gastric cancer or gastrinoma.

#CO2-CTA detected the subsegmental- or the

feeding artery in 17 of the 26 hepatic tumors

(65.4%).

Clinical Study-2

#There was a correlation between the detection of the vascular tumor area and the site of the hepatic lesion in the lobe ($p<0.05$) (Figure 4)

#The feeding arteries could be identified in 9 of the 26 tumors (34.6%).

These imaging studies were necessary for the detection of the vascular tumor area on CO2-MDCT scans (Figure 6) because without reference to these images, neither the tumors nor their shapes could be detected.

Images for this section:

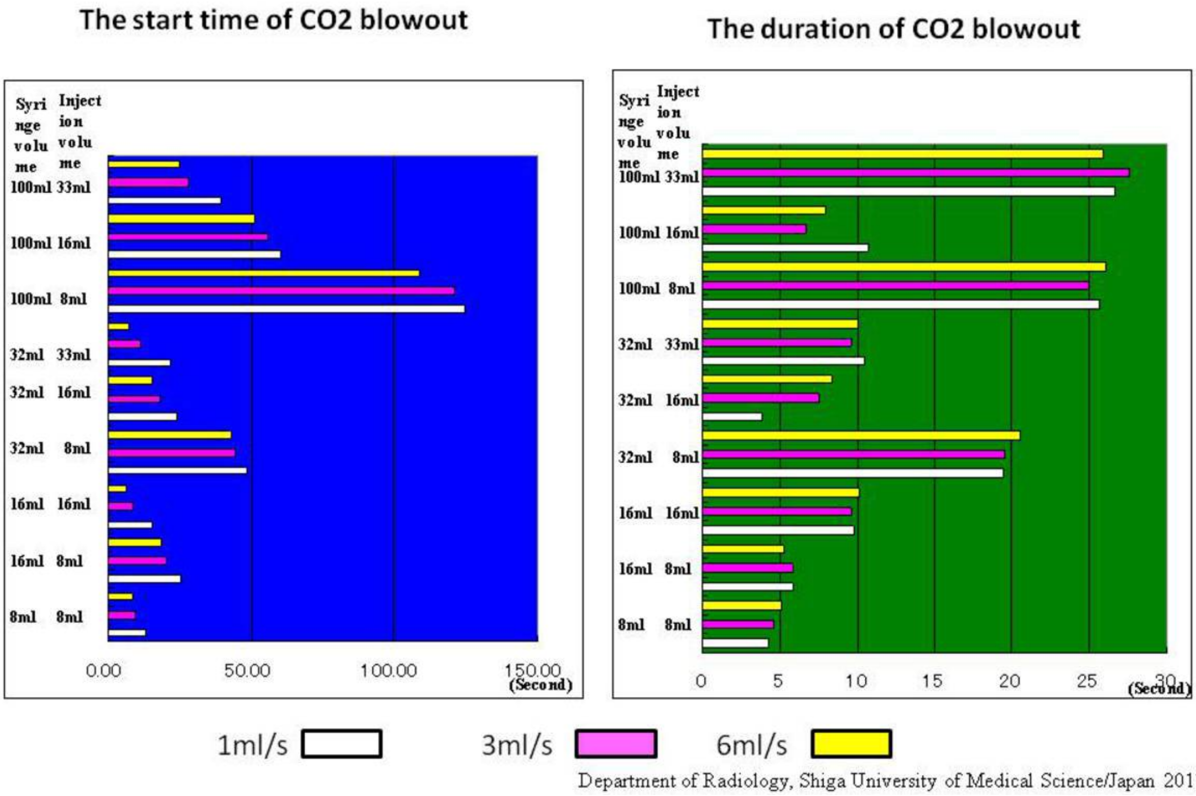
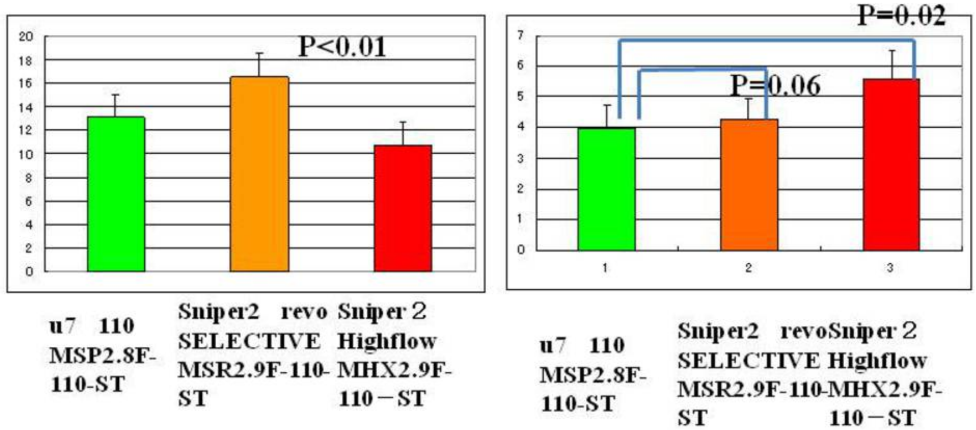


Fig. 1: Syringe volume and CO2 injection volume and rate. As the injection rate increased, the start-time of CO2 infusion tended to decrease; it tended to become shorter when the syringe- and injection volume were nearly equivalent. The injection rate had little effect on the duration of blowout; it was longer when the syringe volume was larger



	The start time of CO2 blowout			The duration of CO2 blowout		
Distal diamiter(mm)	0.67	0.67	0.9	0.67	0.67	0.9
Proximal diamiter(mm)	0.92	0.95	0.95	0.92	0.95	0.95
Volume(ml)	0.41	0.38	0.59	0.41	0.38	0.59

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Fig. 2: The start-time of CO2 blowout and the duration of CO2 blowout. The start-time of CO2 blowout tended to be shorter when the lumen capacity of the catheter was larger. The duration of CO2 blowout tended to be longer when the catheter lumen was larger

Start time of CO_2 blowout into the abdominal aorta and celiac artery

	Aorta (Second)	Celiac A. (Second)
Rabbit1 1st.	13.45	13.12
Rabbit1 2st.	12.57	12.45
Rabbit1 3st.	13.37	13.53
Rabbit2 1st.	13.11	12.91
Rabbit2 2st.	12.98	12.97
Rabbit2 3st.	13.13	13.11
Average (S.D.)	13.1(0.31)	13.02(0.35)

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Fig. 3: The Start time of CO2 blowout into the abdominal aorta and celiac artery

Relationship between tumor area and the vascular area of the tumor

Tumor area	Arterial identification			
	Unclear	Segmental	Subsegmental	Feeding
S1	2	—	—	—
S2	—	—	1	—
S3	—	—	2	—
S4	1	—	1	1
S5	—	1	—	—
S6	3	1	3	5
S7	—	1	—	—
S8	—	—	1	3

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Fig. 4: Relationship between tumor area and the vascular area of the tumor

Conclusion

We found that while this technique under CO_2 CTA using 320-detector-row CT made it possible to visualize hepatic tumors and their feeding arteries, it had some limitations.

#in vitro and in vivo experiments showed that the start-time of CO_2 gas blowout and its duration could be controlled.

we encountered a difference of about 1 sec in the blowout start-time and its duration.

#We used a 100-ml syringe because 8- or 32-ml syringes are not available for auto-injector use at CT.

#The precise calibration of such small volumes in 100-ml syringes is difficult.

#We filled an extension tube with normal saline and injected the CO_2 gas via this tube tens of seconds later

#Small residual amounts of saline may have altered the volume of the injected gas.

#in vitro experiments showed that the start-

time of CO_2 gas blowout tended to become

shorter as the injection rate increased

The start-time of CO_2 gas tended to be

shorter when the syringe- and injection

volume were nearly equivalent.

#The injection rate had little effect on the

duration of CO_2 blowout.

The duration of CO_2 blowout tended to

increase with larger syringe volumes.

#At larger catheter lumen volumes the start-time of CO_2 blowout became shorter and its

duration became longer.

#Based on these in vitro and in vivo experimental ,the detection by CO_2 CTA of human hepatic tumors and vessels could be improved by increasing the gas injection rate and by using syringes of larger volume and injection volumes equal to the syringe volume.

As the injection of large amounts of CO_2 at high speeds raises the risk of vascular injury, catheters with a smaller lumen are desirable for the selective treatment of tumors after CTA.

#We injected CO_2 at a rate of 1 ml/sec and

used an injection- and syringe volume of 8 ml.

These parameters are similar to conventional

clinical techniques performed manually.

In our clinical study

#The vascular area of the tumor was shown clearly at a high probability rate

#Our sample size (n=6) is too small to

permit meaningful extrapolations.

#Nonetheless, it appears possible to identify the vascular area of the tumor in the S4-, S6-, and S8 area

#The gas tends to accumulate on the side opposite that directly affected by gravity.

#In the supine position, the depiction of vessels in areas S4 and S8, which are located on the anterior abdominal wall, is excellent.

In area S6.

After branching from the right hepatic artery, the course of the vessel is relatively horizontal.

However, in many instances it features 2 or more branches and gas may enter these branches and become dispersed.

Additional studies on larger populations are necessary to address this issue

#Intratumoral gas in 7 of 26 tumors (26.9%).

#Our sample size was too small to allow conclusions regarding the relationship between intratumoral gas and the tumor size and location.

#Detected intratumoral gas in areas S3, S4, S5, and S6; they tend to be on the side of the common hepatic artery that is opposite the side affected by gravity in the supine position.

#The use of CO2-320-MDCT scans that identify the hepatic tumor vessels may facilitate the performance of selective TACE.

CTA with CO2 gas and area-detector CT may facilitate the detection of liver tumors and their feeding arteries on TACE.

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