

Carbon Dioxide Contrast Enhancement for C-Arm CT Utility for Treatment Planning during Hepatic Embolization Procedures

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ABSTRACT

A pilot study was performed to evaluate the use of carbon dioxide (CO₂) as a contrast medium for C-arm computed tomography (CT). C-arm CT using CO₂ was performed during embolization procedures in 12 patients with hepatic malignancies and severe iodine allergy or high risk for nephrotoxicity. C-arm CT using gadolinium or iodinated contrast medium was performed for comparison. Of segmental arteries identified by conventional contrast enhancement, 96% were also seen with CO₂ enhancement, but subsegmental arteries were not reliably depicted. CO₂ enhancement identified 60% of tumors. Small, hypovascular, and infiltrative tumors were difficult to detect. CO₂ is a promising alternative intraarterial contrast agent for C-arm CT.

ABBREVIATIONS

MinIP = minimum intensity projection, MIP = maximum intensity projection

The boundaries between cross-sectional imaging and angiography are disappearing (1). The advent of cone-beam C-arm computed tomography (CT) allows interventionalists to obtain cross-sectional volumetric images using angiographic equipment (2). C-arm CT has the advantage of allowing selective catheter-directed contrast enhancement, rendering it especially useful for arterial interventional oncologic applications (3,4). However, some patients have severe renal insufficiency or allergy to contrast media, or both.

Carbon dioxide (CO₂) has been used as an intravascular contrast medium since the 1970s (5–7) and is a safe and useful alternative in patients with renal insufficiency or contrast medium allergies. We investigated the feasibility of using CO₂ as an intraarterial contrast medium for C-

arm CT for arterial mapping and tumor visualization during oncologic embolization procedures.

MATERIALS AND METHODS

This retrospective study was granted exemption from obtaining patient consent by the institutional review board. Data were handled in compliance with the Health Insurance Portability and Accountability Act. From March 2007 to March 2012, 12 patients with unresectable hepatocellular carcinoma or hepatic metastases underwent 15 procedures using C-arm CT for treatment planning with intraarterial CO₂ as contrast agent (Table 1). These patients either had severe iodinated contrast medium allergy, defined as a history of airway compromise or anaphylaxis or both, or were at high risk of nephrotoxicity, based on preexisting azotemia, history of contrast medium-induced acute renal failure, or the presence of a solitary kidney. During this 5-year period, approximately 1,500 hepatic arterial oncologic procedures were performed, of which only these 15 (1%) involved the use of CO₂.

Procedures were performed on a single-plane angiography system capable of C-arm CT (Axiom Artis dTA; Siemens Medical Solutions, Forchheim, Germany) with a 30-cm × 40-cm flat-panel detector. Acquisition parameters have been previously described (8,9). Briefly, images were acquired every 0.5 degree over a 200-degree

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Table 1. Patient Demographics and Tumor Characteristics

Patient No.	Age/Sex	eGFR (mL/min/m ²)	Iodinated Contrast	Tumor	Largest Tumor	Hyper-vascular	Tumor Visible	Tumor Visible
			Medium	Cell	Size, Axial		by CO ₂ -enhanced	by Conventional
			Allergy	Type	Cross-section (cm)		C-Arm CT	C-Arm CT
1	84/M	32	No	HCC	1.7 × 1.7	Yes	No [†]	Yes
2*	64/F	68 [†]	Yes	mNEC	4.1 × 3.3	Yes	Yes	Yes
3	67/M	34	No	mRCC	2.1 × 2.2	Yes	Yes	Yes
4	63/M	31	No	mRCC	1.0 × 1.0 diffuse	Yes	No	No
5	62/M	43	No	HCC	0.5 × 0.5	Yes	No	Yes
6	74/M	20	No	Carcinoid	4.4 × 3.6	No	No	No
7	66/M	23	No	HCC	6.3 × 6.7	Yes	Yes	Yes
8	69/F	19	No	HCC	13.1 × 9.7	Yes	Yes	Yes
9	55/F	42	No	HCC	1.8 × 1.7	Yes	No	Yes
10	54/M	76	Yes	mCRC	2.6 × 3.5	No	No	Yes
11	51/M	57	No	mRCC	4.8 × 4.7	Yes	Yes	Yes
12	70/F	17	No	HCC	2.1 × 2.6	Yes	Yes	Yes

CO₂ = carbon dioxide; CT = computed tomography; eGFR = estimated glomerular filtration rate; F = female; HCC = hepatocellular carcinoma; M = male; mCRC = metastatic colorectal carcinoma; mNEC = metastatic neuroendocrine carcinoma; mRCC = metastatic renal cell carcinoma.

*Two separate study dates.

[†]Mean of two study dates.

[‡]Differences between CO₂ and conventional contrast tumor visibility highlighted in bold text.

rotation in 8 seconds. Data were transferred to a workstation (syngo X-Workplace; Siemens Medical Solutions) for three-dimensional reconstruction and postprocessing. A 512 × 512 pixel matrix was used. Correction algorithms for scatter, beam hardening, ring artifact, and truncation were applied.

Filtered United States Pharmacopeia–grade CO₂ was loaded at ambient pressure into a 60-mL syringe, which was first purged five times using airtight tubing. After clearing the microcatheter of saline, CO₂ was injected by hand at a rate of up to 5 mL/s for 12 seconds, and imaging was initiated after the first 4 seconds. The maximum injection rate was first determined by performing digital subtraction angiography using CO₂ to evaluate for reflux into nontarget arterial beds. Because of the uncertainty of the adequacy of the CO₂-enhanced images, a comparison C-arm CT scan using conventional intraarterial contrast medium was performed, generally immediately following and without repositioning of the patient or catheter. Gadolinium was used for the patients with contrast medium allergy (n = 3), gadodiamide 0.5 mmol/mL (Omniscan; GE Healthcare, Waukesha, Wisconsin), and dilute iodinated contrast medium was used for the patients at risk for nephrotoxicity (n = 12), iodixanol 320 mg I/mL diluted 1:1 with saline (Visipaque; GE Healthcare).

Images were viewed during procedures as multiplanar reconstructions and minimum intensity projections (MinIP) for CO₂-enhanced studies and maximum intensity projections (MIP) for gadolinium-enhanced and iodine-enhanced studies. For this retrospective review, new reconstructions were performed using AquariusNET

(TeraRecon, Inc, Foster City, California). Images were blindly reviewed by all four authors independently, and discrepancies were adjudicated as a group until consensus was reached.

CO₂-enhanced images were evaluated using the iodine-enhanced or gadolinium-enhanced images as benchmarks, and all were compared with diagnostic imaging obtained before procedures for reference. In a few cases in which a discrepancy between catheter positioning was present between the CO₂ and conventional contrast medium images, only territories enhanced by the more distally positioned catheter were compared. Criteria to evaluate CO₂-enhanced images included spatial and contrast resolution, branch artery identification, and tumor conspicuity. The smallest enhanced vessels were measured with electronic calipers to determine the limit of spatial resolution in millimeters and pixels. The numbers of visualized lobar, segmental, and subsegmental arteries enhanced were tallied. Tumor visibility and characteristics, including size and vascularity, were recorded.

RESULTS

CO₂-enhanced images were successfully obtained in all patients. As a result of selective injection or prior resections, or both, only 97 Couinaud segments were downstream from contrast medium administration. Of the 97 segmental arteries enhanced by gadolinium or iodine-containing contrast media, CO₂ contrast agent successfully enhanced 93 (96%) (**Fig 1a–c**).

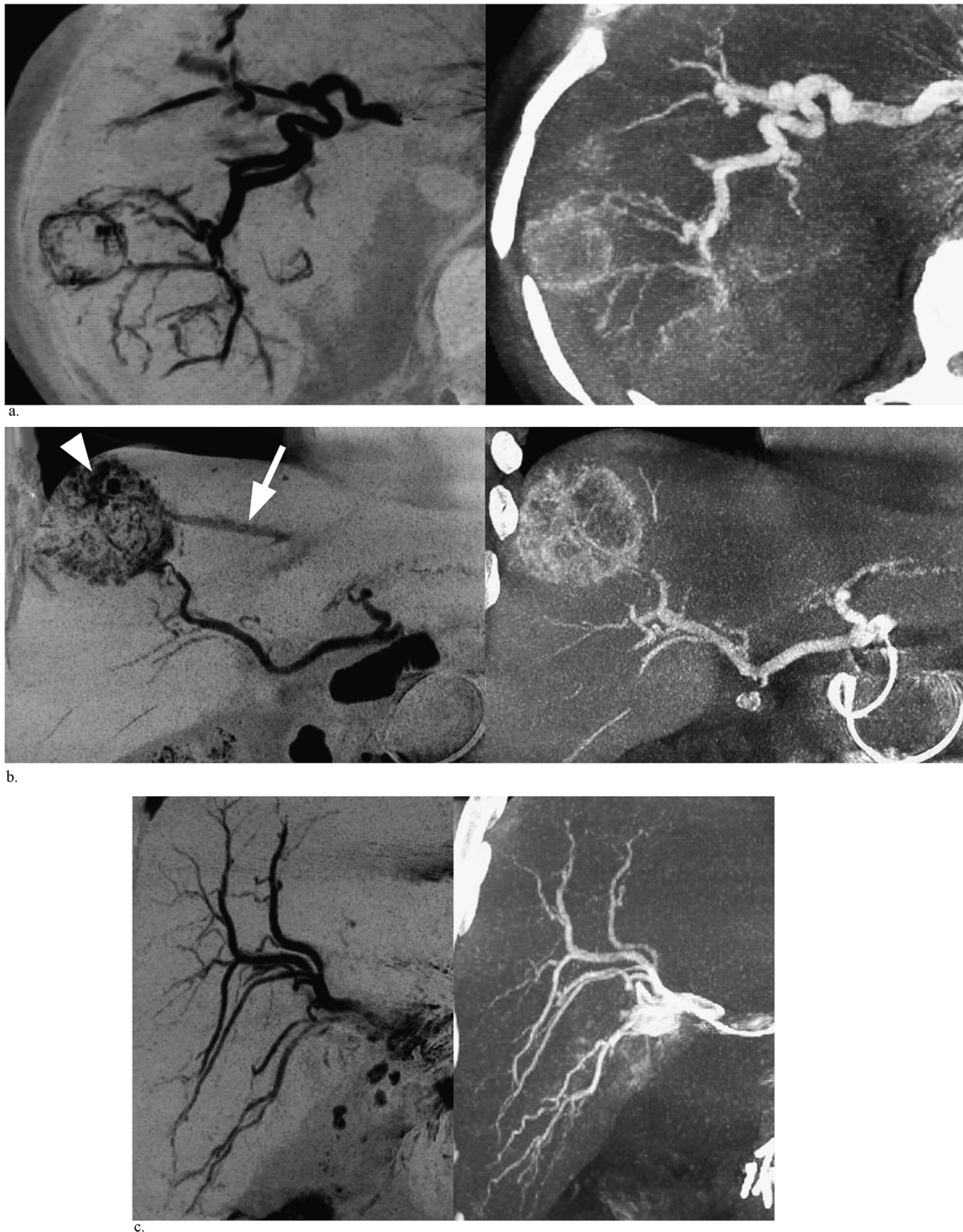


Figure 1. Cone-beam C-arm CT images obtained from three different patients created using thin-slab MinIP and MIP reformats. The patient depicted in (a) had a metastatic neuroendocrine tumor, and the patients in (b) and (c) had metastatic renal cell carcinoma. (a) Intraarterial CO₂-enhanced (left) and gadolinium-enhanced (right) axial images obtained after injection in the right hepatic artery both show adequate delineation of lobar, segmental, and subsegmental arteries as well as tumor hypervascularity. (b) Intraarterial CO₂-enhanced (with depiction of a draining vein [arrow]) (left) and iodinated contrast medium-enhanced (right) coronal reconstructions obtained after injection in the common hepatic artery both show subsegmental arterial anatomy and a dominant mass containing venous lakes (arrowhead). (c) Intraarterial CO₂-enhanced (left) and iodine contrast-enhanced (right) coronal reconstructions after injection in the common hepatic artery both show subsegmental hepatic arterial anatomy, but fine detail in parts of the CO₂-enhanced image appears subjectively inferior, possibly because of bolus fragmentation artifact.

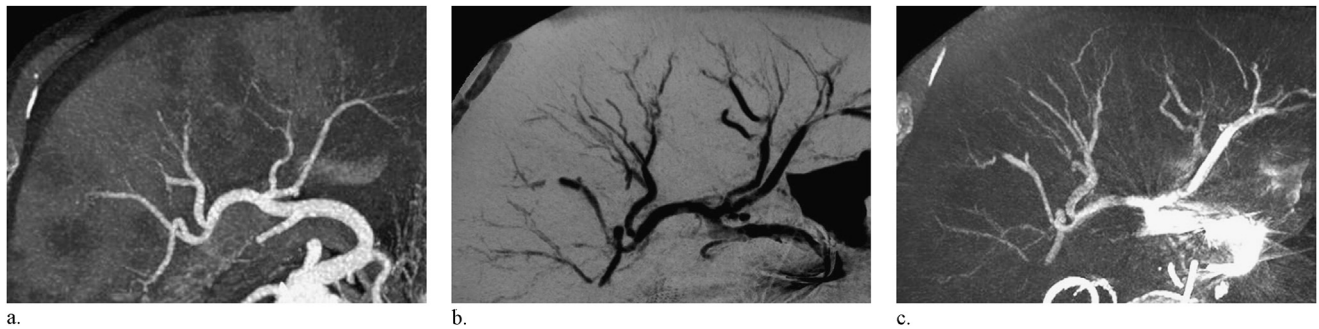


Figure 2. Conventional CT and C-arm CT images obtained from a patient with diffuse hypovascular metastatic carcinoid tumor created using thin-slab MinIP and MIP reformats. **(a)** Arterial phase of intravenous iodinated contrast medium–enhanced conventional CT image of the liver portrayed parenchymal heterogeneity owing to the hypovascular masses. **(b)** Intraarterial CO₂–enhanced and **(c)** iodinated contrast medium–enhanced axial images obtained after injection in the common hepatic artery showed superior depiction of subsegmental arterial anatomy, but the tumors were inconspicuous.

Table 2. Spatial Resolution, Measured as Diameter of Smallest Artery Resolved on Axial Reconstruction

Contrast Medium	Pixels*	Arterial Diameter (mm)
CO ₂ (n = 15)		
Mean ± SD	2.4 ± 0.45	1.1 ± 0.17
Median	2.1	1.01
Range	2.05–3.57	0.86–1.5
Iodine (n = 12)		
Mean ± SD	2.2 ± 0.06	0.93 ± 0.03
Median	2.2	0.93
Range	2.05–2.30	0.86–0.93
Gadolinium (n = 3)		
Mean ± SD	2.1 ± 0.11	0.87 ± 0.05
Median	2.0	0.84
Range	1.98–2.21	0.83–0.93

CO₂ = carbon dioxide.

*1 pixel = 0.42 mm × 0.42 mm using the described imaging protocol.

The spatial resolution of CO₂–enhanced C-arm CT was comparable to the spatial resolution afforded by gadolinium-enhanced and iodine-enhanced images (Fig 2a–c). The smallest enhanced vessels identifiable using each of the contrast media measured approximately 1 mm in diameter (Table 2). The average differences in Hounsfield units between the enhanced artery and the adjacent liver parenchyma were similar between iodinated contrast medium and CO₂, both of which were superior to gadolinium (Table 3).

The targeted tumors were enhanced and identifiable in 10 of 12 iodinated contrast medium–enhanced studies, 3 of 3 gadolinium-enhanced studies, and 9 of 15 CO₂–enhanced studies. Hypovascular tumors, infiltrative tumors, and some tumors < 1.8 cm in diameter were not visualized using CO₂ (Fig 2a–c). Tumors that were most conspicuous by CO₂ enhancement were markedly hypervascular with venous lake abnormalities. All tumors identifiable by CO₂ were also enhanced by iodinated and gadolinium contrast media.

Table 3. Contrast Enhancement by Different Contrast Media

	Contrast enhancement* (HU)	
	Mean ± SD	Range
CO ₂ (n = 15)	505 ± 118	328–774
Iodine (n = 12)	635 ± 514	217–2,012
Gadolinium (n = 3)	201 ± 39	165–243

CO₂ = carbon dioxide; HU = Hounsfield units.

*Contrast enhancement was measured as the difference between attenuation of arteries vs attenuation of adjacent hepatic parenchyma in HU.

Two patients showed incomplete enhancement of segmental arterial anatomy by CO₂. One patient underwent coil embolization of the gastroduodenal, right gastric, and segment 2 arteries between iodinated contrast medium–enhanced and CO₂–enhanced imaging, affecting flow dynamics and resulting in nonenhancement of arteries to segments 1 and 2. In a second patient, enhancement of segments 1 and 7 by CO₂ was absent but also poor by iodinated contrast medium, probably owing to sclerotic vessels from previous treatments including embolotherapy (Fig 3). Poor flow may have been accentuated further by dependent location of the unenhanced segments. In addition, in all patients, fewer subsegmental arteries were adequately enhanced by CO₂ than by iodine or gadolinium agents, likely owing to incomplete columns of CO₂ disturbing the continuous enhancement of smaller vessels. This observation was qualitative, however, and not quantifiable.

One CO₂–related adverse event occurred. After aortic injection of CO₂ for digital subtraction angiography, a patient developed hypotension, bradycardia, and nausea. The patient was placed in the left lateral decubitus position to treat suspected mesenteric arterial vapor lock and to dislodge possible trapped gas (10,11). The vasovagal symptoms resolved completely within 1 minute. No adverse events related to C-arm CT were encountered.

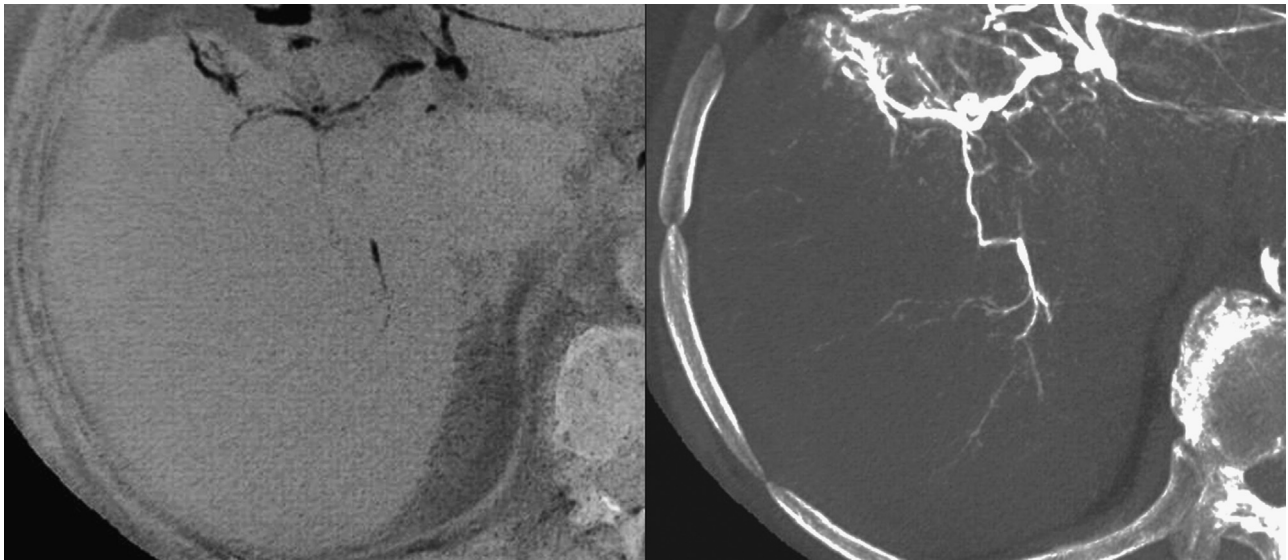


Figure 3. Axial thin-slab MinIP and MIP reconstructions of C-arm CT images illustrate the insufficient arterial opacification of segment 7 using CO₂ (left) and iodinated contrast medium (right). This insufficient opacification was likely due to sclerotic arteries from prior hepatic interventions, including chemoembolization and bland embolization.

DISCUSSION

Intravascular negative contrast enhancement using CO₂ has been in clinical use for decades for arteriography and venography (5–7,12). We also found intraarterially administered CO₂ to be useful for contrast enhancement of C-arm CT. This technique is feasible and relatively safe, yielding images of sufficient spatial and contrast resolution to provide the interventionalist with clinically useful three-dimensional arterial mapping for embolization procedures. All vessels amenable to microcatheterization were adequately depicted. However, enhancement of tumors was achieved in only about 60% of the tumors. Spatial resolution was not substantially affected by the use of negative rather than positive contrast enhancement using conventional reconstruction and artifact correction algorithms. Although this pilot study compared each CO₂-enhanced scan with an iodine-enhanced or gadolinium-enhanced scan, the use of conventional contrast media could be completely avoided in patients with severe renal insufficiency or contrast medium allergy.

CO₂ is not useful for conventional CT imaging because intravenous administration does not result in systemic arterial enhancement. Imaging of CO₂ by conventional CT was shown to be feasible after nonselective aortic injection in an animal model (13). However, CO₂ as a contrast medium for C-arm CT has similar limitations as CO₂ with catheter angiography. In contrast to liquid contrast media, CO₂ is buoyant and does not mix with blood, resulting in bolus fragmentation and incomplete displacement of intravascular blood, leading to artifacts such as missing branches and underestimation of vessel diameters (6,7,12). In addition, buoyancy can result in preferential enhancement of nondependent vessels. The gaseous nature of CO₂ can also result in adverse events,

such as the vasovagal response we encountered from vapor lock occlusion of mesenteric flow (10,11).

Limitations of this study include the small sample size, retrospective analysis of the data, and lack of validated criteria for evaluation of image utility. Only a small number of patients met the study criteria and were treated by a physician investigating the CO₂ contrast technique.

In conclusion, we have demonstrated the feasibility and relative safety as well as some limitations of using CO₂ for arterial enhancement of C-arm CT. Mapping and navigation of segmental hepatic arteries for oncologic interventions can be reliably achieved, but enhancement of tumors is limited.

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