

## CURRENT STATUS OF CARBON DIOXIDE ANGIOGRAPHY

Scott R. Kerns, MD, Irvin F. Hawkins, Jr, MD,  
and Frank W. Sabatelli, MD

Vascular and endovascular surgery have progressed significantly in the past decade with more aggressive revascularization procedures being performed to increase limb salvage rates as well as preserve quality of life and level of function. Paralleling this trend has been the need to provide accurate, detailed preoperative angiographic evaluation of the patient's anatomy. More demands have been placed upon the angiographer to demonstrate not only the condition of the aortoiliac and proximal leg vessels but also the distal runoff down to and including the plantar arch. Only this detailed evaluation will allow the more aggressive revascularization procedures. With the development and ongoing improvement of sophisticated imaging systems such as digital subtraction angiography, technology has attempted to keep up with these demands.

Increasingly revascularization procedures are a joint effort between the vascular surgeon and the interventional radiologist. For example, a common iliac artery angioplasty or stent placement may be performed prior to a femoral to popliteal surgical bypass graft. Alternatively, the patient may be treated solely by the radiologist with percutaneous endovascular procedures. This may become even more prevalent with the current research into percutaneously placed grafts for

abdominal aortic aneurysms or superficial femoral artery occlusion.<sup>1,4</sup> Radiologists must now provide themselves with the most accurate "preoperative" imaging evaluation possible prior to any percutaneous intervention.

Although several methods exist for the imaging or visual evaluation of blood vessels including angioscopy, Doppler and intravascular ultrasound, 3-D helical computed tomography (CT), and magnetic resonance angiography, the most commonly used method to evaluate the arterial and venous anatomy remains the intravascular injection of contrast during cut film or digital subtraction imaging. This is particularly true if percutaneous intervention is a possibility as direct access to the abnormality is needed. Because in many instances a major advantage to percutaneous intervention is less morbidity and mortality with results equivalent to those obtained by surgical repair, many of the patients who present for angiographic evaluation and intervention are those who would have a higher operative morbidity and mortality owing to their cardiopulmonary disease, renal insufficiency, diabetes mellitus, and so forth. Other patients may tolerate an operative procedure but are at risk for the necessary preoperative imaging evaluation and its use of iodinated contrast because of renal insufficiency or a history of reaction to iodinated

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From the Division of Vascular/Interventional Radiology, Department of Radiology, University of Florida College of Medicine, Gainesville, Florida

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contrast media. Some patients have such extensive atherosclerotic disease that access for angiography may be dangerous due to luminal obliteration by catheters necessarily large enough to deliver relatively viscous iodinated contrast. All of these patients place special demands on the interventional radiologist to obtain high quality images with the least possible risk to the patient.

It is with these factors in mind that we have developed carbon dioxide (CO<sub>2</sub>) as an intravascular contrast agent not only for diagnostic imaging but also as a guide for percutaneous interventional therapy. Special equipment has been developed to overcome the particular problems posed by the use of gas as a contrast agent. Dedicated postprocessing software has greatly increased the reliability and usability of this method. This article presents the current status of CO<sub>2</sub> angiography for diagnosis and intervention, the nature of intravascular gas behavior, the principles of successful imaging using CO<sub>2</sub>, specific limitations and disadvantages of this technique, and future directions for this very promising technique.

## BACKGROUND

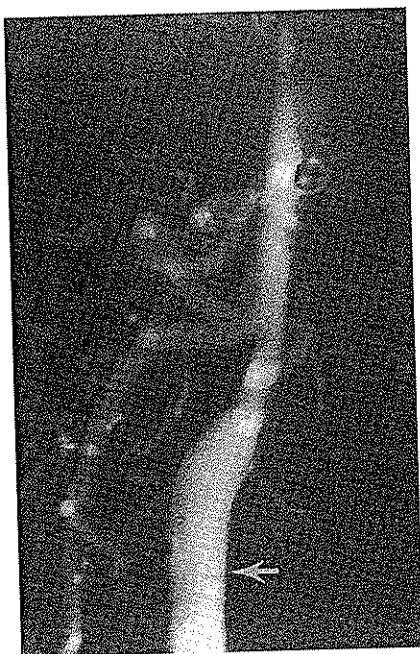
The concept of using gas as a contrast agent is not new to radiology. Many examples exist showing the usefulness of a negative contrast agent. In 1914 Rautenberg<sup>20</sup> first described the insufflation of gas into the peritoneal cavity for the radiographic evaluation of intraabdominal abnormalities. Seven years later several investigators reported using room air, CO<sub>2</sub>, or oxygen to visualize retroperitoneal masses.<sup>2, 21</sup> The intravascular use of CO<sub>2</sub> came later with the introduction of gas into the right atrium to detect pericardial effusions.<sup>19, 22, 27</sup> The physiologic effects of intravascularly injected CO<sub>2</sub> have been studied and there seems to be no significant change in blood gas parameters or hemodynamics even with relatively large injection volumes.<sup>16, 17</sup>

Peripheral vascular imaging using CO<sub>2</sub> as an intravascular contrast agent was pioneered by Hawkins in 1971.<sup>7</sup> He originally used cut film subtraction techniques with promising results. The introduction of digital subtraction angiographic capabilities vastly improved the visibility of intravascular gas thereby extending the range of uses of this technique as well as improving the accuracy of interpretation. Originally, the gas was hand-injected

with subsequent use of standard contrast injectors. CO<sub>2</sub> subsequently has been used for a large variety of procedures, diagnostic and therapeutic, in both the arterial and venous systems. New injection equipment, smaller catheter delivery systems, modified examination tables, and the use of intraarterial vasodilators and postprocessing software have all helped make CO<sub>2</sub> angiography a safe, reliable, and accurate method of vascular imaging. Effective use of this technique, however, requires a thorough understanding of the behavior of intravascular CO<sub>2</sub> and how this affects imaging.

## BEHAVIOR OF INTRAVASCULAR CO<sub>2</sub>

When CO<sub>2</sub> is injected into a blood vessel it interacts with blood in a significantly different manner than does iodinated contrast material. Iodinated contrast material mixes with blood with the composite increase in density depending on how much contrast has been injected into any given volume of blood per unit time. The more iodinated contrast that is injected per unit time the larger the increase in density. CO<sub>2</sub> initially maintains an interface with blood. When injected into a vessel the gas displaces the blood rather than mixes with it. Initially the gas will rise to the most nondependent position within the vessel due to the buoyancy of the gas. Therefore, if small volumes of gas are injected only nondependent branches or organs will be imaged. The gas "floats" on the blood and is carried distally. If imaged in this manner the vessel may appear narrower than its true diameter. These effects can be overcome by completely displacing all of the blood within the target vessel. Because the gas/liquid interface is maintained, the entire vessel and its branches will be imaged until the gas bolus is propelled distally by flowing blood behind it. We and others have found that there is an upper limit to the injection volume after which no further improvement in imaging occurs.<sup>23</sup> Increasing the volume simply displaces more blood without affecting the density difference between the gas-filled vessel and the surrounding soft tissues. We have found both in laboratory work and in clinical practice that the injection rate is relatively more important than the total volume. Because the gas will be propelled out of the area of interest by the flowing blood behind it, a quick total



**Figure 1.** Cross-table lateral aortogram shows incomplete filling of an infrarenal abdominal aortic aneurysm with formation of a gas-blood level (arrow).

displacement of blood in the target area is a more effective method than injection of the same volume over a longer period in which case the gas tends to "float" on the flowing blood rather than completely displacing it. In abdominal aortic aneurysms, complete displacement may not be possible because of the large volume of blood and turbulent flow within the aneurysm (Fig. 1). These problems are less relevant if the target vessel or organ, such as the origins of the mesenteric arteries, are in a nondependent position or if the target is elevated so that it is in a relatively nondependent position. This buoyancy can actually be used advantageously in imaging as discussed below.

The fate of intravascular  $\text{CO}_2$  depends in part on the volume injected. If a small amount of gas is injected it may dissolve in the blood as it is carried downstream before reaching the arteriole or capillary level. We have seen this occur in clinical practice when too small an amount is injected and/or the native blood flow is slow. These conditions allow the gas to maintain contact with blood on the arterial side of the circulation long enough for the solubility of  $\text{CO}_2$  to become a factor.  $\text{CO}_2$  is approximately 20 times more soluble than oxygen in serum.<sup>17</sup> Dissolution on the arterial side of the circulation becomes less of a factor

as the volume of gas injected is increased. The bolus instead tends to break up into a series of bubbles that are still large enough to reach the precapillary or capillary level. A lower limit to the injection volume exists when the bolus breaks up in the area of imaging rather than downstream.<sup>23</sup> In this situation any given image may then be a series of discontinuous bubbles. This could seriously degrade the usefulness of these images; however, postprocessing software can be used to summate or "stack" the images to create a continuous image (Fig. 2). This allows accurate depiction of the arterial anatomy with smaller injection volumes.

During the original development of  $\text{CO}_2$  angiography concern existed about the possibility of acute right ventricular failure due to gas embolism. We performed studies on dogs in which large quantities of  $\text{CO}_2$  were injected into the abdominal aorta. Eight to 10 seconds after injection gas was seen in the inferior vena cava, thus indicating that the gas traversed capillaries or possibly shunted via precapillary pathways. Imaging over the heart and lungs showed that the gas was cleared by the lungs in one pass. If only moderate total amounts of gas (several hundred milliliters) were used, transient tachypnea would occur as the animals hyperventilated to expire the gas. Nonetheless, death occurred if several thousand milliliters were injected because of flooding of the right ventricle with gas. The heart could not deliver the gas to the lungs for expiration because of a "vapor lock." The key to avoiding this situation in clinical practice is the temporal spacing of injections, which allows gas dissolution and ventilation. We have performed vena cavagraphy in humans using up to 70 mL of  $\text{CO}_2$  per injection without adverse effects. The gas pools in the right atrium, pulmonary outflow tract, and central pulmonary arteries forming numerous bubbles that gradually dissolve or pass into the distal pulmonary circulation.  $\text{CO}_2$  in both the dissolved and gaseous state is then cleared by the lungs. A large number of injections may be made if separated by 1 to 2 minutes, especially if each injection is as small a volume as possible for adequate imaging.<sup>15, 26, 29</sup> We do recommend, however, that no more than 200 mL of  $\text{CO}_2$  be used in any one injection. Under usual conditions, diagnostic images are obtained with volumes substantially lower than this limit.

The viscosity of  $\text{CO}_2$  is much lower than that of iodinated contrast material. This easily



**Figure 2.** A and B, Single images of popliteal artery and tibial trifurcation. C, Composite image using summation software.

can be demonstrated by comparing the effort needed to hand-inject iodinated contrast through a small-gauge needle as compared with that needed for room air.  $\text{CO}_2$  can be injected through very small catheters, even as small as 1.5 F. In clinical practice we routinely use 3-F catheters, which reflects the low viscosity of the gas. In patients with hepatic and renal neoplasms, arteriovenous shunting is seen more commonly with  $\text{CO}_2$  than with conventional contrast material (Fig. 3).<sup>28</sup> Similarly, improved detection of gastrointestinal or pelvic bleeding may be seen with  $\text{CO}_2$  (Fig. 4). This is probably due to the low viscosity of the gas, which allows it to travel through small arteriovenous shunts or breaches in vessels more easily. Reconstitution via collateral vessels is more easily demonstrated for the same reason (Fig. 5).

### IMAGING PRINCIPLES

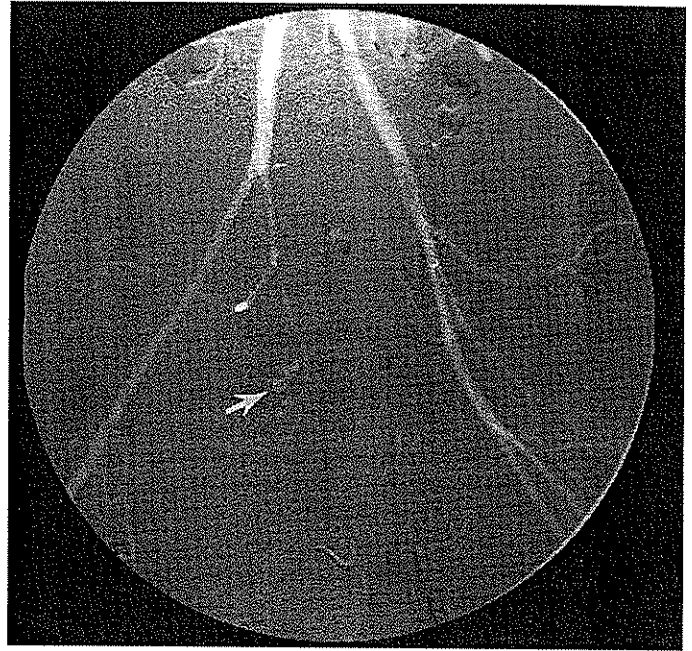
The use of  $\text{CO}_2$  as an intravascular contrast agent introduces many concepts that are new or unusual to most radiologists. Unlike conventional contrast agents,  $\text{CO}_2$  is a colorless, odorless, compressible gas. It is available in varying degrees of purity. We use highly pure gas available in disposable cylinders (AngioDynamics, Glens Falls, NY) because we have discovered that reusable cylinders retain water vapor, which over time, results

in the formation of carbonic acid and corrosion of the interior of the metal cylinders.

Several different methods may be used to deliver the gas. Originally Hawkins injected 35 to 60 mL by hand during which the gas



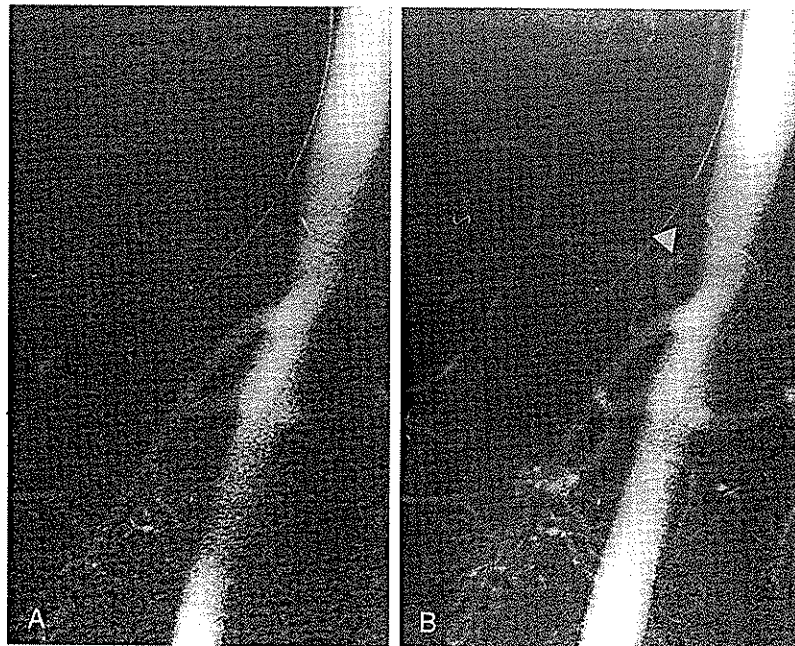
**Figure 3.** Rapid arteriovenous shunting in a renal cell carcinoma (arrowheads).  $\text{CO}_2$  appeared in the renal vein and inferior vena cava 1 second after selective arterial injection.



**Figure 4.** Right posterior oblique pelvic arteriogram shows extravasation (*arrow*) caused by active arterial hemorrhage in a patient with pelvic fractures. Iodinated contrast-enhanced imaging failed to show bleeding.

would compress within the syringe making for a difficult and unpredictable delivery. The majority of the gas left the syringe in the last half-second in a rather explosive manner. This problem can be solved partially by using a 3-mL syringe of CO<sub>2</sub> to clear the catheter of

fluid. The plunger of the small syringe is easier to push forward by hand because of the greater pressure generated. It is then easy to deliver the main volume of gas through the cleared line. Nonetheless, this method is somewhat cumbersome as several stopcocks



**Figure 5.** A, Right posterior oblique abdominal aortogram shows occluded celiac axis with a patent superior mesenteric artery. B, Later in the run there is reconstitution of the celiac axis and its branches (*arrowhead*).

must be turned quickly in the correct sequence for successful imaging. A standard contrast mechanical injector may be used with some improvement in the reliability of injection although the danger of room air contamination exists. Because CO<sub>2</sub> is heavier than room air, when a standard injector is loaded, the tip must be kept up and the injector syringe purged of room air with CO<sub>2</sub> before loading the volume that actually will be injected. The injector nozzle should be open to the atmosphere when the final desired injection volume is loaded. If it is not, more than the desired volume may be inadvertently loaded and subsequently injected because of the compressibility of the gas.

Many of these difficulties have been solved with the development of a dedicated CO<sub>2</sub> injector (AngioDynamics, Glens Falls, NY). This injector can be gated to both the electrocardiogram and blood pressure so that more gas is injected during systole and less during diastole to give a constant delivery over the entire cardiac cycle. Multiple transducers and high speed valves ensure against inadvertent injection of large volumes. For added safety, the current model cannot be programmed above 200 mL for a single injection. Flow volumes and rates are programmed as are catheter size and length. Injected volume is recorded as is time since the last injection. Submicron filters ensure gas sterility. A sterile connecting tubing system allows constant flushing of the catheter through one port while intermittent gas injections are performed through a second port. The entire system is sealed to protect against room air contamination.

Modern CO<sub>2</sub> angiography is based upon the concept of digital subtraction angiography. Although the low density gas can be seen on cut films, digital subtraction angiography greatly amplifies the information present on the image. Current 1024 × 1024 matrix digital subtraction angiography units in general practice will suffice for CO<sub>2</sub> angiography. To maximize the accuracy of the images while keeping the volume of each injection and total volume as low as possible all motion during the accumulation of images must be kept to a minimum. We lightly restrain the lower extremities for a runoff study; 0.5 mg glucagon IV may be given to halt bowel peristalsis for evaluation of the abdomen and pelvis. In addition, the patient is carefully instructed to hold their breath during the injection. Although we routinely provide systemic seda-

tion and analgesia for these studies, we have found that less medication is required for studies performed with CO<sub>2</sub> because of less discomfort. The patient is more responsive to commands with less medication and can cooperate better with breathholding. Any motion artifact that cannot be prevented by these measures can be eliminated in most cases by using postprocessing functions such as pixel shifting, remasking, and edge enhancement.

Injection volumes and rates depend on the area of interest and the blood flow in the area being imaged. In general, smaller volumes are needed the closer the catheter is to the target. Smaller volumes cause less sensation and therefore less motion artifact. Bubble formation is no longer a problem with image summation postprocessing capabilities. Exact injection parameters will also depend on the method of injection used. The dedicated CO<sub>2</sub> injector allows the precise delivery of smaller volumes over short injection times, which is difficult to perform reproducibly by other methods.

Extremely small catheters can be used because of the very low viscosity of gas. Catheters as small as 3 F result in decreased vessel trauma and less luminal obliteration and carry a smaller risk of bleeding. CO<sub>2</sub> also can be easily injected through sheaths or guiding catheters around instruments such as atherectomy devices, angioplasty balloons, and angioscopes. These instruments need not be removed for angiography, which results in faster and more convenient percutaneous intervention.

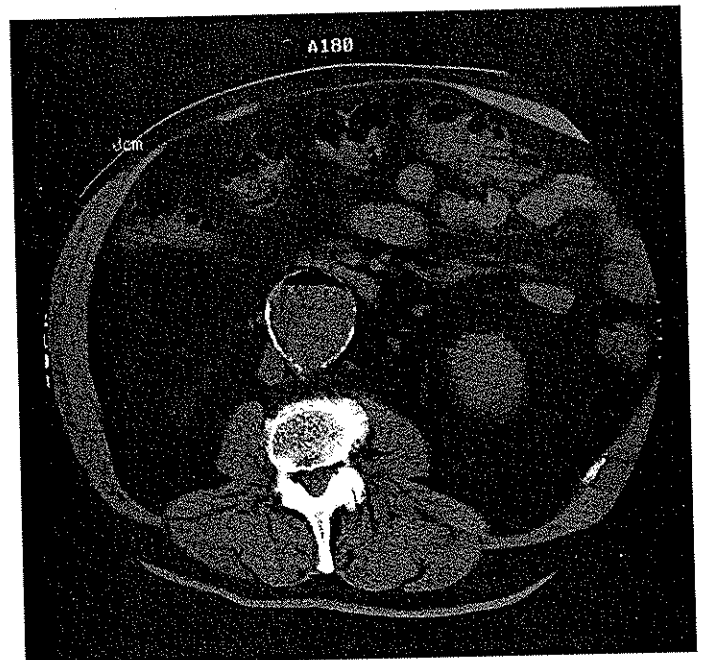
The buoyancy of CO<sub>2</sub> may be used to advantage during imaging. During examination of the lower extremities the legs are raised 15 to 20 degrees on a rigid platform device. This accelerates gas movement distally which is particularly important when blood flow is slow and the runoff is poor, both of which can cause gas dissolution proximal to the level of imaging.<sup>14</sup> We prospectively compared filling of the tibial trifurcation vessels in 20 patients with legs flat and elevated 15 to 20 degrees. Overall, elevation resulted in marked improvement in visualization.<sup>10</sup> Intraarterial nitroglycerin can help improve gas delivery distally although the effects are variable. Similarly, the posteriorly located renal arteries are visualized better if the side of interest is elevated, especially if selective injections are made after the intraarterial injection of nitroglycerin.



**Figure 6.** Gas trapped in an abdominal aortic aneurysm 30 seconds after completion of an anteroposterior aortogram.

Although elevating the area of interest aids in visualization, it may also potentially cause ischemia, especially in low flow situations. The only complication that we have had in more than 800 patients has been transient left colon ischemia when greater than 2000 mL of CO<sub>2</sub> was injected into an abdominal aortic aneurysm in less than 1 hour. The inferior mesenteric artery was patent and probably

was exposed to gas for an excessive period. We also have noticed that gas will become trapped in large abdominal aortic aneurysms (Fig. 6). Nonenhanced abdominal CT scans performed up to 24 hours after CO<sub>2</sub> aortography have shown residual gas within aneurysms (Fig. 7). This may be due to replacement of CO<sub>2</sub> with oxygen and nitrogen, both of which have higher partial pressures and



**Figure 7.** Abdominal CT scan 24 hours after arteriography shows retained trapped gas in an abdominal aortic aneurysm.

lower solubilities than CO<sub>2</sub>. If trapping occurs these patients should be rolled onto their side for 1 to 2 minutes after injection to release the gas into the legs for dissolution. Likewise, we routinely lower the legs to the supine position after several injections. If the buoyant force of the gas is greater than the kinetic energy of the blood flow behind it, the gas may become trapped in the elevated or nondependent body part. Lack of continuing exposure to nonsaturated blood may slow or stop dissolution of free gas and result in ischemia caused by gas embolism. Lowering the body part avoids this situation.

## CLINICAL USES AND RESULTS

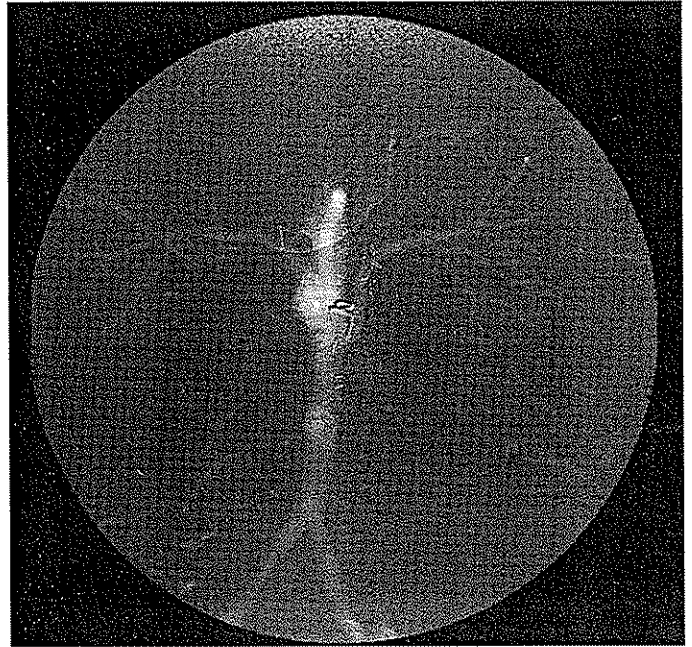
At the University of Florida, CO<sub>2</sub> angiography currently is being used primarily in high-risk patients who have renal failure or have had a previous documented or suspected reaction to iodinated contrast agents. It could potentially be used, however, in any patient that might require angiography. Because it is a normal constituent of the body there is no possibility of an adverse reaction. In our large clinical experience we have noticed neither intravascular nor catheter thrombosis during CO<sub>2</sub> angiography. Iodinated contrast agents may induce thrombosis and have a finite reaction rate even with pretreatment regimens and the use of nonionic contrast medium.<sup>5, 11, 13</sup> CO<sub>2</sub> is neither nephrotoxic nor hyperosmolar and therefore can be used safely in patients who have renal or cardiovascular disease. Unlimited volumes may be used, even in patients with pulmonary disease, as long as there is a thorough understanding of its behavior and the aforementioned precautions are observed. All commonly used medications may be injected through the same catheter unlike with iodinated contrast agents.<sup>12, 18</sup>

If CO<sub>2</sub> is injected distal to the renal arteries there is no chance it will come in contact with the kidneys as the gas is eliminated by the lungs in one pass. This is not the case with iodinated contrast material which is distributed throughout the vascular and extravascular spaces and is ultimately eliminated by the kidneys. We have investigated the possibility of nephrotoxicity when CO<sub>2</sub> is injected directly into the renal arteries. Renal blood flow and function were measured using technetium-99m dimethyl succinic acid (DMSA) and iodine-131 hippuran scans before, immedi-

ately after, and 24 hours after selective injection into canine kidneys.<sup>9</sup> Light and electron microscopy of the excised kidneys were performed 36 hours after injection as well. Flow decreased immediately after injection by 5% but returned to normal within 24 hours. Electron microscopy showed no significant changes, but light microscopy in one of nine kidneys showed some signs of acute tubular necrosis although the nuclear studies were normal. This was one of three kidneys that were placed directly above the catheter to deliberately cause arterial gas trapping. These changes were not seen with the dogs that were supine.

We have followed the renal function of patients in whom we have performed either selective renal artery injection or aortography using CO<sub>2</sub> and have found no significant change in renal function.<sup>6</sup> As long as the injections are kept to the lowest volume needed for imaging and they are spaced apart by 1 to 2 minutes to allow dissolution, the potential problems of gas trapping and ischemia do not occur. Therefore, CO<sub>2</sub> has become the contrast agent of choice at the University of Florida for evaluating suspected renovascular hypertension or renal insufficiency. Renal transplants and aortorenal bypass grafts, performed either for renal artery stenosis or in conjunction with abdominal aortic aneurysm repair, are usually well-imaged, because they are anteriorly located and the gas rises into the graft (Figs. 8 and 9).<sup>6</sup> The reverse is true in native renal arteries, although positioning the side of interest up, occasionally supplemented with the use of selective catheterization and intraarterial nitroglycerin immediately before injection, can overcome this problem (Fig. 10). The main renal arteries and their major branches are seen well, but small intrarenal branches are frequently not filled;<sup>23, 29</sup> however, enough information usually can be gained without the toxic effects of circulating iodinated contrast material to allow percutaneous intervention such as transluminal angioplasty (Fig. 11).

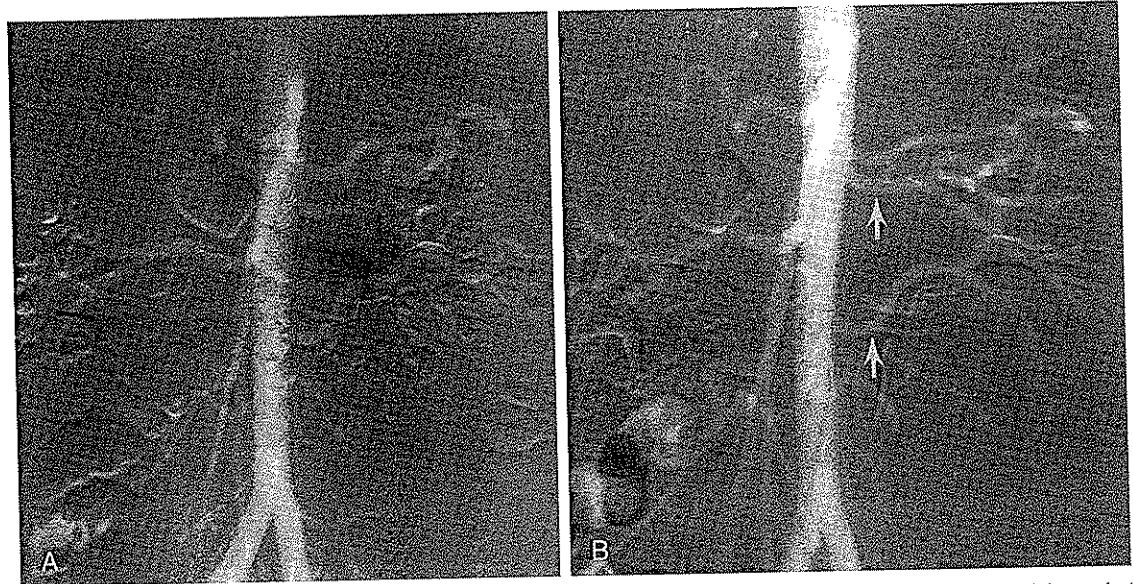
Another important clinical use of CO<sub>2</sub> angiography is the evaluation of peripheral vascular disease in patients who have coexistent renal insufficiency or a history of reaction to iodinated contrast agents. A retrospective study of 128 CO<sub>2</sub> lower extremity arteriograms in 115 patients showed excellent or good imaging results in 91%. Accurate surgical therapeutic plans were possible on the basis of the CO<sub>2</sub> studies alone in 92% of these



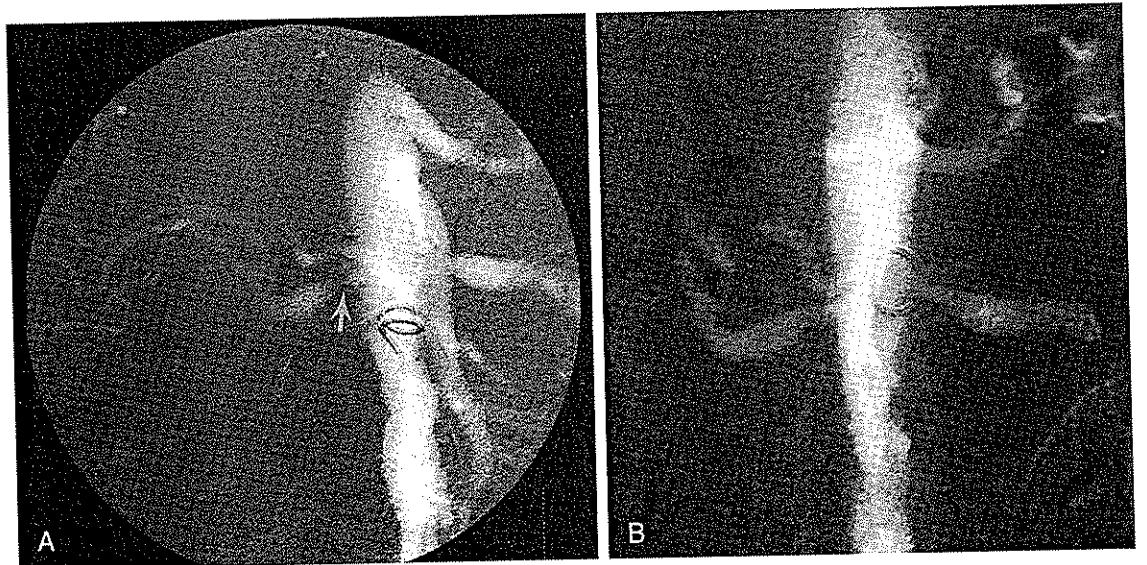
**Figure 8.** Anteroposterior abdominal aortogram after bilateral aortorenal bypasses for renal artery stenosis shows widely patent grafts.



**Figure 9.** Renal transplant patient with recurrent hypertension and azotemia. The transplant artery is widely patent (*arrowhead*), but a common iliac artery stenosis (*arrow*) is present, which is limiting flow to the transplant.



**Figure 10.** A, Abdominal aortogram of renal donor in the supine position inadequately demonstrates arterial supply to the left kidney. B, Repeat study with the patient's left side elevated 15 degrees clearly shows two renal arteries (arrows).



**Figure 11.** A, Left posterior oblique abdominal aortogram demonstrates high grade proximal stenosis of the right renal artery (arrow). B, Anteroposterior abdominal aortogram after renal artery CO<sub>2</sub>-guided angioplasty. Luminal caliber is greater, and the patient's hypertension improved.



**Figure 12.** A, Arteriogram of left superficial femoral and popliteal arteries in a patient with claudication shows two high grade stenoses (arrows). B, Repeat study after CO<sub>2</sub>-guided angioplasty shows improvement in vessel caliber (arrows). The patient's symptoms resolved.

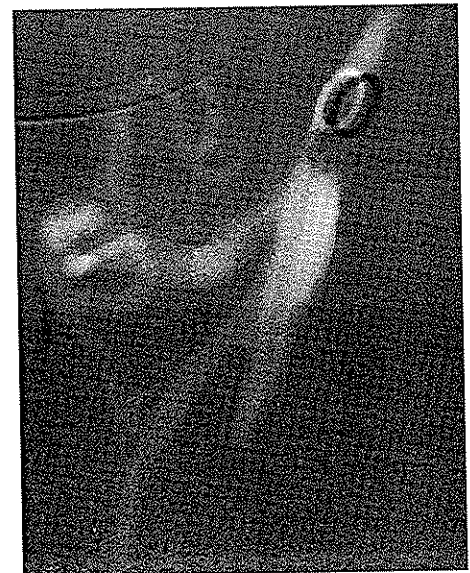
patients. Comparison of CO<sub>2</sub> arteriograms with iodinated contrast studies in the same patients showed agreement between the two in 95%.<sup>24</sup> Similarly, this technique may be used to guide peripheral interventional procedures such as angioplasty, atherectomy, embolization, and transluminal angioplasty (Fig. 12).

The buoyancy of CO<sub>2</sub> makes it the perfect contrast agent to evaluate anteriorly located vessels such as the celiac axis and superior mesenteric artery. Excellent visualization can be obtained with as little as 10 mL (Fig. 13). Selective catheterization further improves imaging of branch vessels. As with iodinated contrast, the closer the catheter is to the target organ the better the images. With iodinated contrast agents this is to overcome dilutional effects, whereas with CO<sub>2</sub>, close proximity allows smaller injection volumes, which in turn produces less discomfort, less motion artifact, and less chance of gas trapping.

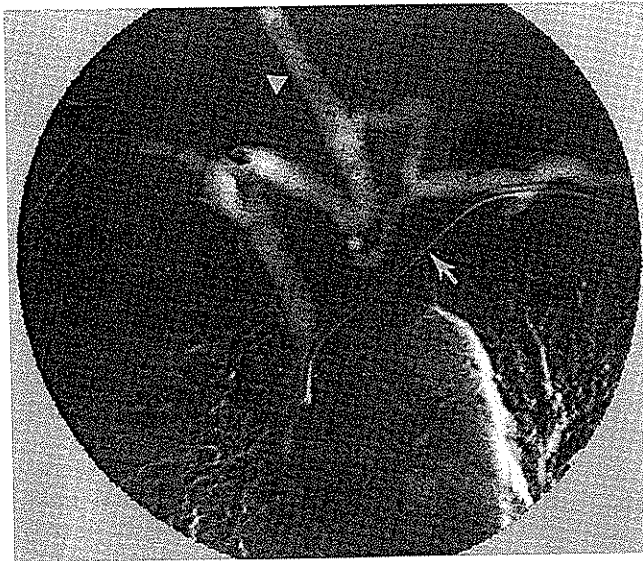
Other uses for intravascular CO<sub>2</sub> are emerging. Angioscopy is frequently used by vascular surgeons in the operating room, for example, to evaluate native arteries after thromboembolectomy, to monitor valvulotomy during an in situ bypass graft, and to evaluate flow-limiting lesions seen on angio-

graphy. Saline usually is infused to provide a bloodless field. In the operating room proximal arterial occlusion can decrease the volume of saline needed, but volume overload and cardiovascular compromise may still occur. Inflow occlusion is clearly not possible if angioscopy is performed percutaneously. Larger volumes of saline are needed although inadequate visualization frequently still occurs. Because it displaces blood, rather than mixes with it as does saline, CO<sub>2</sub> represents the perfect angioscopic viewing medium. Intravascular volume is unchanged, unlimited quantities may be used, and improved visualization for a longer viewing time is possible. CO<sub>2</sub> provides a higher percentage of bloodless fields, less time to a clear visual field, and a longer duration of a clear field once it is reached.<sup>26</sup> There is also a subjective improvement in the visual field and the depth of field when using CO<sub>2</sub> as compared to saline.<sup>15</sup> Smaller scopes may be used as the low viscosity of CO<sub>2</sub> allows it to be injected at adequate rates through the smallest channels.

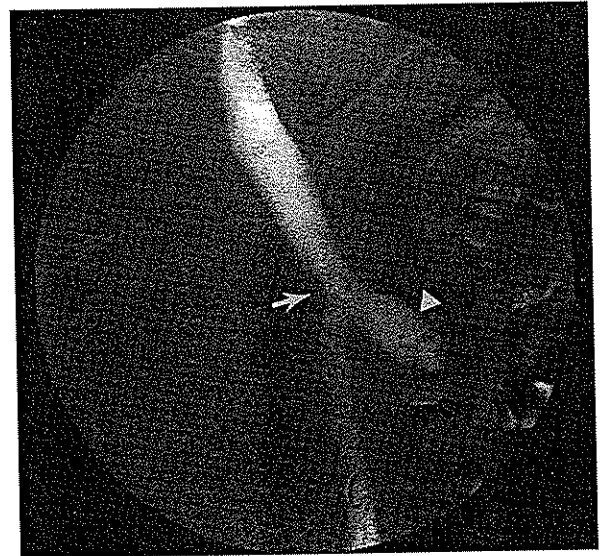
Carbon dioxide venography currently is being investigated for a variety of uses. Extremity venography as well as the evaluation of the central veins of the chest and abdomen are possible (Figs. 14 and 15). The basic principles of imaging remain the same, but even more strict attention must be paid to injection volumes and intervals to avoid flooding of the right ventricle due to the greater proximity of the catheter to the heart. We routinely



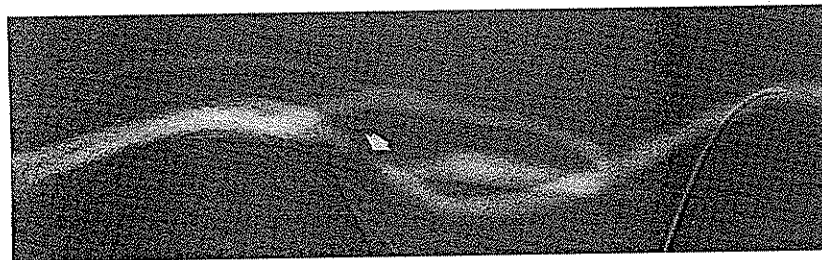
**Figure 13.** Cross-table lateral aortogram using 10 mL of CO<sub>2</sub> demonstrates normal mesenteric artery origins.



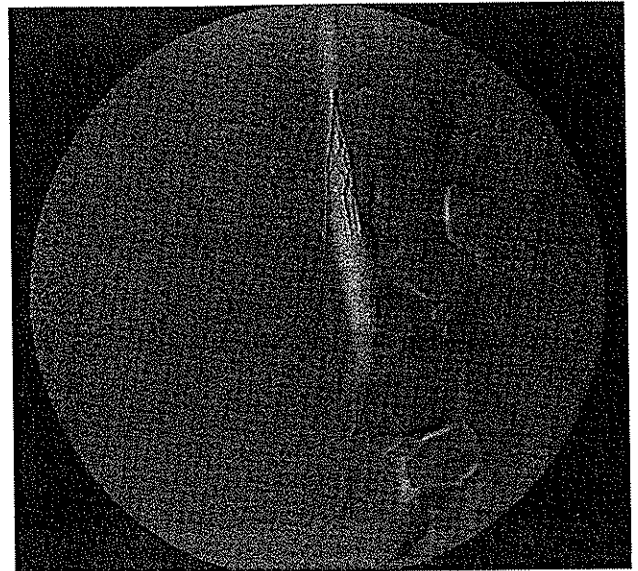
**Figure 14.** Left arm venogram in a patient who presented with left arm swelling. The brachiocephalic vein in which a Hickman catheter is located is thrombosed (*arrow*). Collateral vessels are present, and there is transient retrograde filling of the right internal jugular vein (*arrowhead*).



**Figure 15.** Inferior vena cavagram in a patient with a 15-cm right renal cell carcinoma shows displacement of the inferior vena cava and tumor thrombus extending from the right renal vein. The left renal vein fills transiently (*arrowhead*).



**Figure 16.** Brachial vein stenosis (*arrow*) in a patient who has an arteriovenous fistula and high venous pressures. This was later successfully dilated under CO<sub>2</sub> guidance.



**Figure 17.** Cross-table lateral inferior vena cava-gram after placement of a titanium Greenfield inferior vena cava filter. The inferior vena cava was sized with intravascular ultrasound.

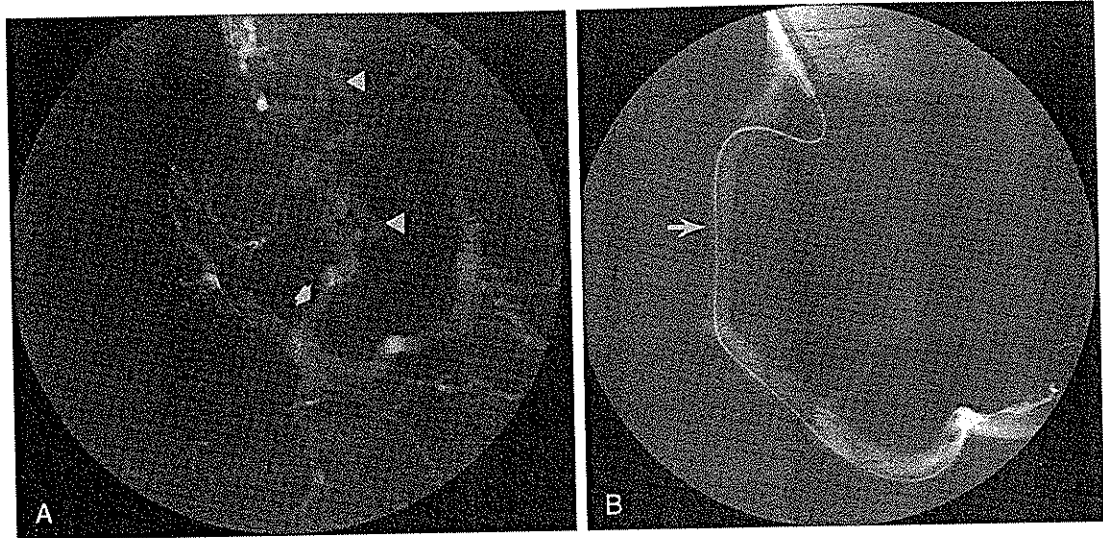
examine the heart fluoroscopically after each injection to be sure all  $\text{CO}_2$  has been expired. Volumes up to 70 mL per injection are well-tolerated with dissolution of the gas within seconds. Nondependent branches may be filled transiently in a retrograde fashion because of the buoyancy of  $\text{CO}_2$ .

As on the arterial side of circulation,  $\text{CO}_2$  may be used to guide percutaneous venous intervention such as thrombolysis, angioplasty, dialysis fistula evaluation and therapy, and placement of inferior vena cava filters (Figs. 16 and 17). Vessel size may be ascertained by using either intravascular ultrasound or by placing a calibrated catheter or guide wire in the vessel during imaging against which the vessel diameter may be measured. Another use for  $\text{CO}_2$  is in the performance of transjugular intrahepatic portosystemic shunts (TIPS) for the treatment of portal hypertension. Prior to shunt placement, wedged hepatic venography may be performed or  $\text{CO}_2$  can be injected through a small needle (e.g., 22 gauge) into the liver parenchyma. In both instances the low viscosity of the gas enables visualization of the portal system, which in turn helps to direct puncture into the portal venous system. No parenchymal staining occurs, and unlimited amounts may be used. After the portal venous system is entered,  $\text{CO}_2$  portography may be used to define the anatomy and the direction of flow, although the left portal vein may

fill preferentially if the injection volume is small. After formation of the shunt the gas is carried to the right atrium by brisk flow through the shunt (Fig. 18).

#### LIMITATIONS

The primary limitation to the use of  $\text{CO}_2$  angiography is the possibility of neurotoxicity. Only a few animal studies have been performed, and these show contradictory results. Studies performed on rats in which  $\text{CO}_2$  was injected directly into the carotid artery showed damage to the endothelial cell membrane on microscopic examination and multifocal ischemic infarction on gross examination. Although the cause of these changes was not determined exactly, it was thought to be due to gas embolism with the degree of infarction being roughly proportional to the volume of gas injected.<sup>3</sup> What effect pressure of injection had on these results is uncertain. Conversely,  $\text{CO}_2$  thoracic aortography and selective carotid arteriography have been performed on canines with no detectable changes on neurologic examination, electroencephalographic monitoring, or at gross pathology.<sup>8, 25</sup> Gas was clearly detected in cerebral veins, thus indicating passage through the capillary bed. Until more animal research is performed on the neurologic response to intracranial  $\text{CO}_2$  we do not recommend its use above the



**Figure 18.** A, Pre-TIPS portogram in a patient who has cirrhosis and recurrent variceal hemorrhage shows reversed flow in the coronary vein (*arrow*) and esophageal varices (*arrowheads*). B, The portal system is decompressed on the post-TIPS portogram with brisk flow through the shunt (*arrow*).

diaphragm. We have injected CO<sub>2</sub> into the abdominal aorta of dogs in the prone position without subsequent neurologic changes on physical examination. In our clinical practice there have been no cases of neurotoxicity resulting from injections into the abdominal aorta. The use of CO<sub>2</sub> in examinations below the diaphragm seems to cause no inadvertent effects on the spinal circulation. If its safe use in the cerebral vasculature can be documented clearly in primates, the role of CO<sub>2</sub> angiography would be extended greatly.

### CONCLUSIONS

Digital subtraction CO<sub>2</sub> arteriography and venography have become a viable alternative to angiography using iodinated contrast agents. A thorough understanding of the behavior of CO<sub>2</sub> is necessary to perform this technique safely and to optimize imaging. The diagnostic quality is equivalent to that obtained by conventional methods, and in certain instances it may be superior. Risks are fewer although the question of neurotoxicity currently precludes the use of CO<sub>2</sub> cerebral arteriography. Percutaneous interventional procedures guided by CO<sub>2</sub> angiography may be performed without altering therapeutic techniques or equipment. The use of CO<sub>2</sub> as an intravascular contrast agent promises to expand with ongoing research into new uses in both the arterial and venous circulations.

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*Address reprint requests to*

Scott R. Kerns, MD  
 Department of Radiology  
 University of Florida  
 1600 SW Archer Road  
 Gainesville, FL 32610-0374