# CARBON DIOXIDE DIGITAL SUBTRACTION ANGIOGRAPHY

The use of $CO_2$ as an imaging agent dates back to 1914 when it was originally used for the visualization of the abdominal viscera (1). It was subsequently utilized in the evaluation of the retroperitoneum and hepatic veins, and in the diagnosis of pericardial effusion (2, 3, 4). In the 1970's, the intraarterial use of $CO_2$ was pioneered by Hawkins (5). With the development of digital subtraction angiography, stacking software, tilting tables and reliable delivery systems, it became viable as an angiographic imaging agent.

## Unique Properties of $CO_2$:

$CO_2$ is a nontoxic, invisible gas that is highly compressible, non viscous and buoyant. Most importantly, $CO_2$, as an intravascular imaging agent, lacks both allergic potential and renal toxicity. It is 20 times more soluble than $O_2$ and is rapidly dissolved in the blood.

Unlike iodinated contrast, $CO_2$ does not mix with blood but must displace it to render an image. Also the buoyancy of $CO_2$ causes it to rise to the anterior, nondependent portion of the vessel. Therefore in larger vessels (aorta and iliac arteries), if an insufficient volume is injected, there will be incomplete displacement of blood resulting in diminished contrast and potentially, a spurious image. Normal vessels may appear smaller than their true caliber. To overcome this phenomenon, either a larger amount of $CO_2$ must be administered or, using the buoyancy principle, the area of interest should be placed in the nondependent position.

## Indications:

$CO_2$ can be injected as a contrast agent in any luminal structure (arterial, venous, biliary tree, urinary tract, abscess cavity, fistula). We previously used $CO_2$ primarily in patients with iodinated contrast allergy and renal failure. However, its gaseous characteristics can occasionally provide additional information otherwise unattainable. Its very low viscosity permits detection of arterial bleeding, visualization of the portal system by hepatic parenchymal injection for TIPS

procedures, visualization of small collaterals in ischemic disease and AV shunting in tumors. The lack of viscosity also allows delivery via very small catheters and injections between the guidewire and the needle or catheter, making it ideal for interventional procedures such as angioplasty and stent placement. Furthermore, there is no maximum dose if less than 100 cc are injected every 2-4 min. since we believe $CO_2$ is eliminated by the lungs in a single pass. This is of great benefit in complex interventional procedures where $CO_2$ can be used in combination with iodinated contrast to minimize the risk of renal compromise.

## Contraindications:

Our studies with rats (6) suggest that the safety of cerebral $CO_2$ is questionable. We therefore avoid any arterial injections above the diaphragm and never administer $CO_2$ with the patient's head in an elevated position.

$CO_2$ DSA has not been a problem in patients with chronic obstructive airway disease COPD. However, in these patients, we do attempt to reduce the volume and allow more time between each injection. A recent evaluation by our laboratory using swine included the direct IVC administration of $CO_2$ at different volumes. This resulted in no significant change in either $PO_2$ or pulmonary artery, central venous or systemic arterial pressure at an injection of 1.6 ml/kg. This is well below the individual dose required for diagnostic purposes.

## Potential Complications and Precautions:

Because $CO_2$ is invisible, it is subject to contamination without detection. Our initial studies revealed water, rust and particulate matter within reusable sources. Therefore, a pure medical-grade source and disposable cylinder (CMD, Gainesville, FL) are mandatory. Furthermore, a closed delivery system is imperative to eliminate the additional possibility of room air contamination. Because of diffusivity, an open syringe containing $CO_2$ can be replaced with less soluble room air in approximately 72 minutes (.2cc/sec.). In addition, a system employing stopcocks can be easily contaminated if they are inadvertently malpositioned or loose. In a closed system, one-way "check" valves and glued stopcocks can be utilized to reduce this possibility.

Another rare, yet potential, complication is "trapping." This occurs when an excessive volume of $CO_2$ is delivered or the blood-gas interface is reduced and interferes with normal dissolution. Because of buoyancy, it usually occurs in the nondependent portion of a vessel. As a result, a bolus of gas can cause a vapor lock which can restrict blood flow and potentially cause ischemia. Abdominal aortic

aneurysms, pulmonary outflow tract, celiac, superior mesenteric and inferior mesenteric arteries are most susceptible because of their nondependent location.

If trapping does occur, it can be reduced by positional maneuvers. For example, if trapping during an inadvertent excessive, large volume injection occurs in the pulmonary artery, bradycardia hypotension and coronary ischemia (elevated ST segments) can result. By placing the patient in the left lateral decubitus position, $CO_2$ migrates to the nondependent portion of both the pulmonary artery and the right atrium. This allows blood flow to be reestablished beneath the residual $CO_2$. Similarly, trapping in an AAA can be reduced by rolling the patient, first to one decubitus position and then to the other. As a precaution for trapping, fluoroscopy of susceptible sites can be performed between $CO_2$ injections. If persistent gas is visualized, positional changes can be instituted. For venous injections, fluoroscopy of the pulmonary artery will demonstrate dissolution of the gas within 10-30 sec. If the gas remains longer, the possibility of room air contamination must be considered.

Injection of excessive volumes (> 400 cc) is the most dangerous potential complication. Excessive doses are first and foremost avoided by ensuring that the $CO_2$ cylinder is never connected directly to the catheter. A $CO_2$ cylinder usually contains 3,000,000 cc of pressurized gas and can flood the low resistance circulatory system if a stopcock is inadvertently malpositioned. Also, because it is compressible, a syringe loaded under pressure will have an indeterminate volume of $CO_2$ and potentially result in an excessive dose. It is suggested that a non compressed, known volume (usually 100 cc, or less, depending on the site of evaluation) be administered via a dedicated injector or closed plastic bag system. Purging the catheter of saline or blood with a small volume of $CO_2$ should be performed prior to injection to eliminate compressed $CO_2$ and explosive delivery. We have also found that the elimination of explosive delivery reduces the subjective discomfort of pain, nausea and the urge to defecate. Moreover, if using $CO_2$ to evaluate permanent dialysis access, great care should be taken to avoid explosive delivery and reflux into the cerebral circulation (7).

$CO_2$ should be used cautiously with nitrous oxide anesthesia. In theory, nitrous oxide may diffuse from the soft tissue into the $CO_2$ "gas bubble" and cause a five-to-six fold increase in volume (8). An innocuous 100 cc $CO_2$ injection may become 500-600 cc of gas and result in a "vapor lock" condition.

## Delivery:

Currently, there are two safe delivery mechanisms: dedicated injectors and the closed plastic bag hand delivery system (9). Since a dedicated $CO_2$ injector is not currently available in the United States, the closed bag system can be utilized (Fig. 1). It consists of a plastic bag reservoir, extension tubing, one-way check valves with

glued fittings, and delivery and purge syringes. Using a pure source, the bag is filled with $CO_2$ and flushed three times to purge any residual air. Following this, the bag should be left flaccid to avoid any $CO_2$ compression. Next the bag is connected to the delivery fitting with a one-way stopcock. Now the delivery system is similarly flushed to eliminate room air prior to injection. It is then connected to the angiographic catheter which is subsequently relieved of any residual blood or saline by forcefully injecting three cc of $CO_2$ via the purge syringe. A controlled, nonexplosive delivery of known volume can then be performed. The check valves primarily prevent reflux of blood into the catheter and permit rapid injections without stopcock manipulation. No additional connecting tubes or stopcocks should be added to the system. All ports should be occupied and syringes attached to prevent any possibility of air contamination.

## General Delivery Principles:

1. Use a closed system, i.e., the plastic bag or a dedicated $CO_2$ injector.
   a. Never connect the catheter directly to the $CO_2$ cylinder. This avoids the potential inadvertent delivery of excessive and possibly lethal volumes.
   b. Malpositioned stopcocks can result in room air contamination and air embolus.
2. Avoid explosive delivery. Purging fluid (blood or saline) from the angiographic catheter results in a more consistent delivery with less discomfort.
3. Initially, inject small volumes of $CO_2$. Increase volume as required for specific anatomy.
4. Wait 2-3 min. between injections to allow any potentially trapped $CO_2$ to dissolve.
5. Elevate area of interest in poor flow conditions (feet, 10-15°; renal artery, 30-45°).
6. Vasodilators (nitroglycerin 100-150 ug IA) can be used to improve filling.
7. Delivery catheter
   a. Use radiopaque-tipped catheter.
   b. At least one sidehole is recommended for safety.
   c. Any flush catheter is acceptable.
8. DSA imaging
   a. Three-to-four frames/sec. using a 60 ms pulse width with adequate penetration.
   b. When the $CO_2$ bolus is "broken up" (fragmented), use image stacking, if available.
   c. If imaging is consistently poor, consult an equipment applications specialist to optimize acquisition.

## Specific Procedure:

1. Runoff
   a. Initially, obtain both leg runoffs with the catheter in the distal aorta. Perform aortogram after the runoff.
   b. Inject 20-40 cc in □ second.
      c. Elevate the feet 10-15° for optimal filling and obtain images of pelvis, thigh, knee, lower legs and feet.
      d. If there is no stacking program, a longer injection (~ 60 cc over 2-3 sec.) is necessary.
      e. Problem - poor filling of the lower leg and feet.
         - Perform a selective (antegrade is preferable) injection of the common femoral or more distal arteries. Positioning can be either "over the hill" or antegrade placement of a 3-F catheter in the contralateral extremity. For ipsilateral vessels, retract the catheter to the distal external iliac.
         - With stacking, inject 20 cc in two sec. If filling remains poor, inject 20-40 cc over 3-4 sec.
         - Without stacking, begin with 20-40 cc over 3-4 sec.
         - Intraarterial nitroglycerine, 100-150 ug prior to injection.
         - When large volumes are required, discomfort may occur, precipitating patient motion and distorting images. We have found the use of intraarterial lidocaine helpful.
3. Aortogram
   a. Usually performed after the runoff. We believe this allows the patient to become acclimated to $CO_2$ and, as a result, less discomfort and nausea are experienced with larger aortic injections.
   b. Attempt to obtain the aortogram without glucagon. Our experience is that $CO_2$ and glucagon may cause nausea.
   c. High-flow rates are necessary (60 cc in □ sec.).
   d. The left renal is more difficult to image and may be better visualized by elevating that side. If necessary, a selective injection with a shepherd hook catheter (10-30 cc $CO_2$ in □-1 second) can be performed. The ostium is usually apparent secondary to $CO_2$ reflux.
   e. Selective injections of the visceral arteries commonly require 10-30 cc in □-2 seconds.
4. Venous - always image the pulmonary artery after the first injection to rule out air contamination (persistent gas). Normally, $CO_2$ should disappear after 10-30 sec.
   a. SVC and IVC - 20-60 cc in □-2 sec.
   b. Subclavian - 20-40 cc in 1-2 sec.
   c. Peripheral veins - 20-40 cc, 4-8 sec.

5. Interventional Procedures
   a. Using a Touhey-Borst fitting, $CO_2$ can be injected between the guidewire and needle or catheter. Wires without coil wrap are better (glidewire, .018 torque wire).
   b. Use a 20-40 cc Luer-locked syringe. With a smaller syringe, $CO_2$ will simply compress without injecting.
   c. Wait 20-30 sec. for $CO_2$ to exit the catheter. $CO_2$ will compress, purge fluid from the catheter and inject.
   d. After purging, subsequent injections require less pressure and delay.
6. TIPS
   a. Using any needle, inject 20 cc of $CO_2$ into the hepatic parenchyma for visualization of the portal vein.
   b. With the guidewire in place, $CO_2$ can be used to verify the needle entry site and determine stent positioning.

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Figures

Figure 1: Closed Plastic Bag Delivery System