

ANGIOGRAPHY WITH CARBON DIOXIDE

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INTRODUCTION

Optimal planning of surgical and endovascular arterial reconstruction requires detailed visualization of the involved arterial system. Contrast arteriography using currently available digital subtraction imaging systems provides accurate images of the lower extremity arterial tree in most patients with peripheral vascular disease. However, current contrast agents used for arteriographic imaging have significant associated risks including hypersensitivity reactions and nephrotoxicity. Furthermore, many revascularization candidates are elderly and have co-existing renal, cardiac and other medical illnesses that increase the risk of contrast-related complications. Therefore, not infrequently, the risks associated with arteriography surpass those associated with revascularization. In such patients, revascularization procedures must be deferred or based upon alternative arterial imaging techniques such as magnetic resonance angiography, transcutaneous duplex or intravascular ultrasonography, and angiography that do not produce the luminal detail and dimensional accuracy afforded by contrast arteriography.

Intravenous injection of carbon dioxide (CO₂) gas was first used clinically to delineate hepatic veins [1] and to diagnose pericardial disease [2-4] in the 1950's and 1960's. Visualization of caval, portal and cardiac structures using CO₂ gas without complications was reported in over 1600 patients [5] and this experience fueled interest in use of CO₂ gas as a contrast agent for other vascular structures. Hawkins described the initial use of intraarterial CO₂ gas for diagnostic peripheral arteriography in 20 patients in 1982 [6]. Subsequently, development of digital subtraction angiography (DSA) systems, stacking software, tilting examination tables, and reliable CO₂ delivery systems has made CO₂ angiography a viable alternative to iodinated contrast studies. Furthermore, CO₂ gas used as an arterial contrast agent has been demonstrated to have no allergic potential, to produce no renal toxicity (with appropriate use), and to be extremely inexpensive.

UNIQUE PROPERTIES OF CO₂ GAS AS AN ARTERIAL CONTRAST AGENT

Currently used iodinated contrast agents are ^{non}incompressible liquids (like blood) which produce an image of the lumen of the arterial tree because they are radiopaque. When delivered in adequate volumes, these liquid contrast agents mix with blood to fill the vascular system being imaged. Improvements in the quality of the arterial image are obtained by increasing either the injection rate or the concentration of the contrast agent. In contrast, CO₂ is a highly compressible gas (density 1000 times less than iodinated contrast at body temperature) which is radiolucent. An arterial image is produced by displacing flowing blood within the vessel with the CO₂ and detecting the small differences in radiographic density between the gas and that of the surrounding soft tissue using digital subtraction and electronic enhancement. Image quality of CO₂ arteriography is dependent on the degree of blood displacement by CO₂ gas within vessels of interest. Although heavier than air, CO₂ gas is extremely buoyant and this buoyancy produces preferential filling of non dependent portions of vessels unless adequate columns of CO₂ gas are used to completely displace flowing blood. Thus, incomplete blood displacement is common in aneurysmal or large diameter vessels such as the aorta. In addition, posteriorly located renal and lumbar branches may not be filled with CO₂ and therefore not visualized with the patient in the usual supine position while anterior arteries such as the celiac axis and superior mesenteric artery are easily imaged. CO₂ gas is also 400 times less viscous than iodinated contrast and this low viscosity facilitates filling of collateral channels and stenotic vessels increasing the likelihood of imaging distal vessels in patients with severe arterial occlusive disease (Fig. 1). Identification of arteriovenous shunting within malignant tumors and vascular malformations is aided by the low viscosity of CO₂ as well [7]. Finally, the low viscosity of CO₂ allows delivery through small diameter catheters (2-3 French) and through the narrow space between guide wires, various endovascular devices, and the inner walls of introducer catheters which greatly facilitates intraprocedural imaging.

SAFETY AND POTENTIAL ADVERSE CONSEQUENCES

A. SAFETY OF INTRAVASCULAR INJECTION OF CO₂

In theory, intravenous injection of CO₂ gas could lead to “vapor lock” in the right heart outflow tract leading to decreased cardiac output as is seen with air embolism. However, differences in the pathophysiologic response to intravenous injection of CO₂ gas and air have been demonstrated in animal experiments [8, 9]. The volume of CO₂ gas causing death of anaesthetized cats after rapid injection into the pulmonary veins was approximately 6 times that of air (CO₂ 6.6 ml/kg vs air 1.1 ml/kg) [8] while the volume of CO₂ delivered by continuous intravenous infusion (100-150 ml/min) which caused death in dogs was approximately 2.5 times the volume of air (CO₂ ≥ 500 ml vs air ≥ 200 ml) [9]. Rapid intravenous and intraarterial injections of up to 7.5 ml/kg of CO₂ given repetitively (every 15 minutes for 2 hours total) and continuous infusion (100 ml/min IV) of up to 10 L of CO₂ also produced minimal hemodynamic and blood gas derangements in dogs [10-12]. These results were obtained despite use of significantly larger amounts of CO₂ in these animal experiments than that used clinically for imaging of cardiac structures (50-200 ml). Tolerance of larger volumes of intravascular CO₂ compared to room air or oxygen is likely due to the greater solubility of CO₂ (20 times that of O₂) in blood. As a result, dissolution of CO₂ bubbles in blood will occur more rapidly than with air bubbles and trapped right atrial CO₂ gas bubbles have been seen to disappear within 15-30 seconds [10]. The transport capacity of blood for CO₂ is also greatly facilitated by formation of bicarbonate in red blood cells by carbonic anhydrase and by binding of CO₂ with carbamino compounds (e.g. hemoglobin). Furthermore, CO₂ rapidly diffuses into alveoli across pulmonary capillary membranes owing to its high tissue solubility following which it is efficiently cleared from the lungs during normal ventilation.

Peripheral arterial injections of CO₂ gas should be safer than intravenous injections because CO₂ bubbles would have to pass through at least one capillary bed before potentially being trapped within the right heart, pulmonary microvasculature or coronary and cerebral circulations. However, intraarterial

injection of CO₂ gas could lead to ischemic injury to peripheral organs by trapping of gas bubbles within small arteries or the microvasculature. Although small CO₂ bubbles will likely pass through capillary beds, the buoyancy of larger bubbles could lead to gas trapping within larger vessels in nondependent portions of organs or in any non-horizontal vessels where the buoyant force of bubbles equals the momentum force of antegrade blood flow. Furthermore, large bubbles may dissolve more slowly than small bubbles because of a lower surface area to volume ratio and thereby a proportionally smaller surface area over which gas transport to blood can occur. Large CO₂ bubbles are also difficult to dislodge because of their buoyancy and trapping of significant amounts of CO₂ gas within an organ for significant periods of time could lead to ischemic injury.

The potential of ischemic injury due to microvasculature occlusion by CO₂ bubbles after intraarterial injection has been evaluated in several organ systems. Injections of 100 - 800 ml of CO₂ gas into the abdominal aorta of dogs at the University of Florida resulted in rapid opacification of the renal veins and inferior vena cava indicating some degree of bubble transport through renal capillary beds or through precapillary shunts [13]. However, injection of 7 ml/kg (~ 10 times the normal human dose) of CO₂ gas directly into canine renal arteries resulted in no decrease in renal blood flow or renal function as measured by technetium-99 dimercaptosuccinic acid and iodine -131 sodium iodohippurate scans done within 24 hours after CO₂ injections [13]. Furthermore, no microscopic changes in the endothelium of major renal arteries or in the glomeruli were seen by scanning or transmission electron microscopy when CO₂ injections were done with the animal supine. Only when the kidney was vertically positioned above the injection site were changes compatible with minimal acute tubular necrosis seen by transmission electron microscopy. This minimal injury appears to be due to prolonged CO₂ trapping within the kidney based upon a preliminary ultrasound study demonstrating clearance of injected CO₂ from the renal cortex of kidneys positioned vertically within approximately 2 minutes compared to 30 seconds when the kidney is in a horizontal position. Thus, renal injection of CO₂ is well tolerated despite transport of CO₂

gas through the renal microvasculature.

In contrast, the effects of CO₂ gas in the cerebral circulation are unresolved. Direct injection of CO₂ into the carotid arteries of rats at the University of Florida resulted in significant neurologic deficits [14]. Histologic examination of brain tissue revealed multi focal ischemic infarction and disruption of the blood-brain barrier. The quantity of infarcted cerebral tissue was related to the volume of CO₂ delivered. In contrast, Shifrin reported no immediate electroencephalographic changes or any neurologic deficits occurring after aortic arch and carotid injections of 3 - 5 ml/kg CO₂ in dogs [15]. Further animal studies are needed to fully determine the neurotoxic risk of cerebrovascular CO₂ exposure but at present we avoid injection of CO₂ gas into regions where it can reach the cerebral circulation.

B. CONTROL OF CO₂ DELIVERY

The compressibility of CO₂ gas results in considerable difficulty in the operator knowing the exact volume of CO₂ gas that is being injected. CO₂ gas cylinders for medical applications contain over 3 million ml of gas at high pressure and, if a direct connection between a CO₂ cylinder and an angiographic catheter occurred or the cylinder regulator malfunctioned, the vascular system could be flooded with CO₂ gas. Additionally, because the volume of a perfect gas varies inversely with pressure (Boyle's Law), small volumes of gas delivered from pressurized CO₂ cylinders assume large volumes when exposed to atmospheric pressure or pressures within the arterial tree. Therefore, syringes loaded under pressure from a CO₂ cylinder will contain an indeterminate volume of CO₂ gas which can potentially result in an excessive dose of CO₂ being delivered into the patient. In addition, "explosive" delivery can result when standard syringes are used to inject CO₂. In vitro testing of hand and mechanically-driven syringes connected to fluid-filled angiographic catheters of various diameters have demonstrated that 95% of the volume of the CO₂ within the syringe is delivered in the last 0.5 seconds of a 4 second controlled injection (Fig. 2). This results in extremely high flow rates of CO₂ which could cause intimal injury at injection sites. The initial delay in CO₂ delivery from the syringe occurs due to

$$PV = nRT$$

$$V = \frac{1}{P}$$

resistance in the fluid-filled catheter causing compression of CO₂ gas. When the pressure generated in the syringe overcomes the fluid resistance in the catheter, the injected CO₂ expands rapidly resulting in “explosive” delivery.

These problems have been circumvented with development of a dedicated CO₂ injector and a closed plastic bag delivery system [16] that deliver noncompressed, controlled volumes of CO₂. Dedicated CO₂ injectors are not currently available in the U.S., but one device developed by Angio Dynamics (Queensbury, NY) has multiple transducers that continually monitor pressure in the system. If pressure becomes excessive, computer-controlled mechanisms terminate the injection. Injections are gated to the electrocardiogram and delivery rates and volumes of CO₂ can be programmed. The closed plastic bag delivery system consists of a 1500 ml plastic bag reservoir that is kept flaccid, extension tubing, one-way check valves, and delivery and purge syringes (Fig. 3). After filling the plastic bag reservoir with CO₂ gas, the delivery syringe can be filled with noncompressed CO₂ so that a known volume of can be CO₂ injected. The purge syringe (3 ml) is used to completely fill the angiographic catheter with CO₂ and remove residual blood or saline. A controlled, nonexplosive delivery of a noncompressed, known volume of CO₂ can then be performed. Check valves prevent reflux of blood into the catheter and permit rapid injections without stopcock manipulation.

Because CO₂ gas is invisible, it is subject to contamination which is difficult to detect. We examined reusable CO₂ cylinders acquired from hospital stores early in our experience and found that many contained water, rust and particulate matter. Subsequently, pure medical-grade CO₂ gas stored in a disposable cylinder (CMD, Gainesville, FL) has been used for CO₂ angiography. Proper positioning of stopcocks and function of check valves to maintain a closed system are also necessary to limit room air contamination prior to delivery. Because of its high diffusivity in air (0.18 ml/sec) and the large differences in partial pressures of CO₂ between a delivery syringe (100%) and surrounding room air (0.03%), the time required to completely replace CO₂ with air in a 20 ml syringe open to air is only

approximately 14 minutes.

C. ARTERIOGRAPHIC TECHNIQUE

The low density of CO₂ requires subtraction and electronic enhancement, available in DSA equipment, to produce adequate CO₂ arteriography. We currently use a 1024 x 1024 pixel digital subtraction angiography (DSA) system acquiring 3 - 4 frames/sec with a 60 msec pulse width. Images are post-processed if needed by compiling multiple digital images into a single composite image using a "stacking" software program (Toshiba America, Tustin, CA). The stacking software is used to overcome fragmentation of CO₂ by flowing blood particularly in the distal extremity vessels, and adequate visualization of the ankle and foot arteries can be provided after injection of as little as 10 ml of CO₂ gas. Bowel gas motion, motion from arterial pulsation in the abdomen, and patient movement can degrade the resolution of stacked images but bowel gas motion can be diminished by intravenous glucagon (0.5 mg) administration.

Lower extremity arteriography is performed with the patient initially supine on a standard or newer tilting angiographic table. Four French (Fr) arteriographic catheters are inserted following common femoral or axillary artery puncture. With the catheter positioned in the distal aorta, leg runoff studies are generally done before the aortogram to allow patient acclimation to any discomfort occurring after CO₂ injection. Twenty to 40 ml of CO₂ at 40 ml/sec are used initially for runoff imaging. For adequate filling of tibial and distal arteries elevation of the feet by 10 to 20° is necessary. Repeated injections of 20 - 40 ml over 2 - 4 seconds can be performed if filling remains poor and intraarterial nitroglycerin (100 - 150 mg) given before CO₂ injection may provide additional vasodilatation to augment distal vessel filling. Injections of CO₂ gas are spaced 3 - 5 minutes apart and the extremities returned to a horizontal position between injections to optimize clearing of CO₂ from the extremity. Fifty to 70 ml of CO₂ gas are delivered at a rate of 140 ml/sec for aortic and renal artery studies. The left renal artery is typically more difficult to image and may be better visualized by elevating the patient's

left side. Selective injections (10 - 30 ml over 0.5 - 1.0 sec) can also be performed using a shepherd hook catheter into the renal artery ostium. Visceral artery imaging can be done by selective injection of 10 - 30 ml of CO₂ delivered over 0.5 - 2.0 seconds.

CLINICAL EXPERIENCE

A. DIAGNOSTIC APPLICATIONS

Over twelve hundred patients have undergone angiography using CO₂ gas and DSA techniques at the University of Florida since 1981. Over 700 aortogram and lower extremity runoff studies have been done using CO₂ as a contrast agent, primarily in patients with underlying renal insufficiency (serum > 1.5 mg/dL) or known hypersensitivity reactions to iodinated contrast agents. Additionally, carbon dioxide angiography has been used to demonstrate feeding vessels and arteriovenous shunting within bone and soft tissue neoplasms in over 180 patients and during transjugular intrahepatic portosystemic shunt (TIPS) procedures in over 50 patients [17]. Forty-four percent of suspected arterial bleeding sites in the gastrointestinal tract have been detected with CO₂ in 27 patients compared to only 14% detected using iodinated contrast. Finally, peripheral artery angioplasty and stenting, embolization, vena caval filter placement, permanent central venous access, and percutaneous nephrostomy have been performed with CO₂ contrast in over 120 patients at the University of Florida and use of CO₂ contrast has allowed such procedures to be done in multiple patients with severe renal insufficiency (Fig. 4).

1) ACCURACY

Early experience with CO₂ arteriography during the development of DSA techniques was hampered by poor quality images. In the initial report describing use of CO₂ gas as an arteriographic contrast agent, Hawkins [6] found that relatively large volumes of CO₂ were required to produce only fair images of the aorta and proximal femoral arteries. Poor visualization of more distal vessels was noted. Similarly, Miller [18] described 9 patients receiving 50 mL of CO₂ for aortography and runoff

study and concluded that CO₂ images of the common femoral through popliteal levels were adequate but that visualization of the aorta, iliac, distal profunda femoris, and tibial arteries was inadequate compared to studies done with iodinated contrast. More recently, Weaver et al reported experience with CO₂ arteriography in 33 patients [19, 20] and found incomplete imaging of distal aortoiliac segments in 3 patients with infrarenal abdominal aortic aneurysms as well as occasional suboptimal images distal to occlusions or high grade stenoses, primarily in the infrapopliteal arteries. Comparative studies with iodinated contrast agents were not performed in these patients due to underlying renal insufficiency (mean serum = 2.7 mg/dL), congestive heart failure or contrast hypersensitivity, but supplemental dilute nonionic contrast (10 - 60 mL) was required for adequate imaging of selected arterial segments in one-quarter of the studies. However, diagnostic information obtained from CO₂/DSA studies was adequate to guide operative procedures or balloon angioplasties in two-thirds of cases (with the remaining patients being treated non-operatively) and operative findings correlated well with predictions from CO₂ arteriography.

In 1993, Seeger [21] reviewed 115 patients undergoing renal, visceral, aortic and lower extremity arteriograms done with CO₂ at the University of Florida including 98 patients in whom arteriograms using standard iodinated contrast agents were also done. Ninety-one percent of the CO₂ studies were of good or excellent quality and agreement between findings of CO₂ and contrast arteriograms was present in 95% of cases. One-third of the studies were done using CO₂ gas alone while two-thirds of the CO₂ studies required small volumes (mean 39.5 mL) of dilute iodinated contrast for optimal imaging. Standard contrast arteriograms required an average of 196.5 mL of contrast for imaging by comparison. CO₂ image quality was best in the aorta, iliac, renal and mesenteric arteries (Fig. 5), and was judged to be of good or excellent quality in 90% of femoral arteries as well (Fig. 6). Use of stacking programs also provided adequate imaging of infrapopliteal vasculature in 70% of CO₂ arteriograms (Fig. 7). Accurate therapeutic plans could be developed based on CO₂ studies alone in 92% of cases with inadequate

visualization of infrapopliteal arteries being the major limitation in 7 cases. No allergic reactions were reported and only a single patient who received CO₂ and supplemental contrast experienced a rise in serum creatinine. Because 79% of patients had a history of contrast allergy or pre-existing renal insufficiency, use of CO₂ markedly decreased the risks associated with arteriography in that study.

B. ANGIOSCOPY

CO₂ also has potential advantages over conventional saline infusion used to clear the viewing field during angiography. By virtue of its low viscosity, CO₂ injection can be easily done through the small channels found in angioscopes, and because of its rapid clearance by the lungs, large volumes of CO₂ can be used if sufficient time is allowed for CO₂ expiration. The feasibility of CO₂ gas as an angiographic medium has been demonstrated in canine and porcine lower extremity arteries [22 - 24]. Without inflow occlusion, CO₂ gas successfully displaced flowing blood and allowed angiographic inspection in 80% of canine iliac arteries in the study of Silverman [22] and 60% of similar arteries in the study of Smits [24]. In contrast, only 14% and 3%, respectively, of the same arteries could be inspected using an infusion of saline solution to clear the flowing blood. In addition, the use of CO₂ gas was associated with a shorter interval from onset of infusion to total visual field clearance, a longer duration of a clear visual field once blood was displaced compared to saline infusion [22], and the clarity of images was better [23] (Fig. 8). Preliminary clinical experience with CO₂ gas during lower extremity arterial angiography at our institution has also been favorable. Injection of 200 mL of CO₂ over 20 seconds provided clear visual fields for 20 to 60 seconds in several patients. Elevation of the extremity assisted trapping of CO₂ in the segment of interest and improved intraluminal visualization.

C. COMPLICATIONS

Adverse events associated with diagnostic and therapeutic vascular imaging using CO₂ have been rare in our experience with over 1200 patients. Trapping of CO₂ gas and subsequent vapor lock phenomena have complicated only 4 angiographic cases. One patient with a large infrarenal aortic

aneurysm required large volumes of CO₂ (2000 ml over 30 minutes) for imaging of the runoff vasculature and developed transient diarrhea likely due to CO₂ trapping anteriorly in the aneurysm and vapor lock within a patent inferior mesenteric artery [21]. Immediate sigmoidoscopy suggested ischemic changes but a mucosal biopsy performed at the time was normal. No gross colonic abnormalities were noted 3 weeks later during aortobifemoral graft construction. Two patients developed transient manifestations of vapor lock in the right ventricular outflow tract during TIPS procedures [25]. Stopcock malpositioning caused large volume (1200 - 3000 mL) delivery of CO₂ in one case and room air embolization in another. Hemodynamic compromise, EKG changes and symptoms resolved within 1 minute after left lateral decubitus positioning in each case. Finally, transient neurologic changes possibly due to cerebral embolization of CO₂ developed during evaluation of an axillofemoral bypass graft when a patient inadvertently raised his head during CO₂ injection.

D. CONTRAINDICATIONS

Although we have not seen untoward effects in patients with chronic obstructive pulmonary disease (COPD), severe COPD with evidence of CO₂ retention by blood gas analysis is a relative contraindication to CO₂ angiography. Similar to Weaver [20] and Frankhouse [26], when patients with COPD undergo CO₂ arteriography, we increase the time between CO₂ injections to greater than 2 minutes. However, both Weaver [20] and Bettman [27] have demonstrated no increase in the partial pressure of CO₂ in arterial blood gas samples after CO₂ arteriography and 5 patients in Weaver's series had significant COPD. We also do not use CO₂ angiography in evaluation of cerebral or upper extremity vasculature because of the risk of neurotoxicity. The potential for retrograde embolization of CO₂ gas bubbles into cerebral arteries exists if the patient's upper torso is in a nondependent position. In addition to the one patient experiencing transient neurologic symptoms at our institution (described above), another report of a similar event occurring during CO₂ angiographic evaluation of an arm dialysis shunt [28] has prompted use of CO₂ arteriography exclusively below the level of the diaphragm at the

University of Florida.

E. BENEFITS OF CO₂ ARTERIOGRAPHY

Use of CO₂ as an arterial contrast agent appears beneficial in a significant number of patients requiring arteriography for evaluation and treatment of peripheral vascular disease. The risk of hypersensitivity reactions approaches 25% when ionic contrast agents are used in patients with a history of contrast allergy [29]. Nonionic contrast agents and pre-treatment of patients with steroids have reduced but not eliminated this risk [29, 30]. In contrast, no hypersensitivity reactions to CO₂ injection have been observed during CO₂ arteriography in the over 1200 patients done at the University of Florida, despite this being one of the primary indications for use of CO₂ as a contrast agent in these patients.

Acute renal dysfunction after arteriography performed with iodinated contrast has also been reported to occur in 11% of patients with peripheral vascular disease and in 42% of patients with preexisting elevation of serum creatinine above 1.8 mg/dL [31]. Additional risk factors associated with contrast-induced renal insufficiency include the presence of diabetes mellitus, the volume of contrast used, and the severity of baseline elevation of serum creatinine [31 - 33]. Although animal studies have shown nonionic contrast agents to be less nephrotoxic [34], a randomized, controlled clinical trial comparing nonionic and ionic media during cardiac catheterization failed to demonstrate such a benefit [35]. Use of CO₂, on the other hand, appears to essentially eliminate the nephrotoxic risk of arteriography. Despite pre-existing renal dysfunction in 70 of 115 patients in the series of Seeger [21] and 22 of 33 patients in the series of Weaver [20], transient increases in serum creatinine were noted in only 1 and 3 patients in each series, respectively, and each of these patients required small supplemental doses of iodinated contrast to optimize arteriographic imaging with CO₂. Furthermore, approximately 70 of our patients have undergone CO₂ arteriography of renal transplants, surgically reimplanted kidneys and recently constructed renal artery bypass grafts [36] without evidence of worsening renal function.

SUMMARY

CO₂ possesses many advantages when compared to conventional iodinated contrast agents used for arteriography. It is nonallergic and lacks renal toxicity. Its unique properties permit use of smaller catheters in diagnostic and therapeutic angiographic procedures and allows optimal vascular imaging of various neoplasms and occult gastrointestinal bleeding and during TIPS procedures. With digital subtraction techniques and stacking programs, CO₂ arteriography is as accurate as iodinated contrast studies in most patients and thus is the preferred arterial imaging technique in patients with contrast allergy and renal insufficiency. CO₂ is also extremely inexpensive compared to available contrast agents [25]. Understanding of the effects of buoyancy and compressibility are necessary for safe, controlled delivery of CO₂ during arteriography but only rare complications have occurred in our large experience with CO₂ angiography. Thus, use of CO₂ as an arterial contrast agent significantly expands the safety and utility of arterial imaging in patients with peripheral vascular disease.

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FIGURE LEGENDS

Fig. 1. Left : Distal popliteal and infrapopliteal arteriogram done using iodinated contrast showing apparent occlusion of a popliteal to posterior tibial artery bypass. Right : Repeat study done with CO₂ gas as the contrast agent and elevation of the feet by 15 degrees showing a patent graft. Flow into the graft was diminished due to a distal graft stenosis which prevented opacification of the graft using standard iodinated contrast.(Reprinted with permission [21]).

Fig. 2. Time dependent CO₂ delivery through 1.5 - 4.1 Fr angiographic catheters using hand-held and mechanically driven syringes as measured experimentally. Approximately 90% of the CO₂ in the syringe is delivered in the last 0.5 seconds during a 4 second injection. The delay in CO₂ injection is greater in smaller diameter catheters.

Fig. 3. Schematic of the plastic bag delivery system for CO₂ contrast angiography. A 1500 ml plastic bag is connected to a three-port fitting with two one-way check valves. Any size Luer-Lok delivery syringe can be used. Three-port fitting is connected via 100 cm of connecting tubing to a second three-port fitting with two in-line check valves and a 3 ml purge syringe. A standard three-way stopcock is interposed between this fitting and the angiographic catheter.

Fig. 4. Left : CO₂ arteriogram of a severe, focal superficial femoral artery stenosis (arrow) and significant disease in the remainder of the vessel. Second and third order branches of the artery and fine luminal detail are demonstrated. Right : Repeat CO₂ study after successful balloon angioplasty of the focal stenosis.(Reprinted with permission [21]).

Fig. 5. CO₂ contrast study of the aorto-iliac system after injection of 60 ml of CO₂ at 100 ml/sec through angiographic catheter positioned at renal arteries. An approximately 50% stenosis is noted in the proximal right common iliac artery with minimal occlusive disease present in the left iliac and renal arteries and the distal aorta.

Fig. 6. Percent of CO₂ arteriographic images by location which were graded as either excellent / good or poor / inadequate on blinded review. Results are from 115 patients reviewed at the University of Florida.(Reprinted with permission [21]).

Fig. 7. Example of improved image quality using stacking software. Left : Poor initial image of distal infrapopliteal arteries due to breakup of the gas column. Right : Composite image generated with the stacking program. An excellent image of all three infrapopliteal arteries at the ankle is obtained with minimal occlusive disease present.(Reprinted with permission [21]).

Fig. 8. Angioscopic imaging in the superficial femoral artery of dogs. Left : The hand-injected saline image is hazy and lacks depth of field. A small side branch is poorly visualized. Right : Injection of CO₂ as the angioscopic medium provides a sharp image with excellent depth of field.