The History of CT Angiography

After gradual progress for several decades, this modality has advanced rapidly over the last several years.

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For decades, only catheter-based angiography could display accurate anatomic detail of blood vessels for diagnosis and therapy. Today, computerized tomography (CT), magnetic resonance imaging, and various sonographic techniques often serve as definitive angiographic studies, replacing invasive catheterization. Recent improvements in CT scanning and image postprocessing include development of slip-ring gantry technology, multirow detector arrays, high-load x-ray tubes, and fast, inexpensive computers. This article is a review of the contemporary application of CT scanning and CT angiography (CTA) to visualize the circulatory system.

HISTORY

The earliest CT scanner, developed by Sir Godfrey Hounsfield, and independently developed by Allen Cormack, was first used for brain imaging in 1972. Each single tomographic slice required hours of scan time and days of computation to render what was a truly revolutionary image of skull, brain, and cerebrospinal fluid. These early CT images were remarkable because for the first time, the soft tissues within the skull could be visualized with both contrast and spatial resolution that was not possible with other tomographic techniques. Advances during the next 2 decades led to scanners that were faster and could achieve even better contrast and spatial resolution. Nevertheless, by the mid-1980s, CT scanners still worked the same way, obtaining each image slice-by-slice, with incremental table movement followed by circular revolution of the x-ray tube/detector array gantry once around the patient for each image. CT scanning was slow and provided a series of relatively thick and discontinuous slices through the body.

The early 1990s saw the introduction of the first helical CT scanners into clinical practice, using a slip-ring mechanism that allowed the x-ray tube/detector array gantry to rotate continuously while the patient was moved smoothly into the scanner. The image data set was therefore a continuous spiral through the patient. Because scanning was continuous, study times were much shorter than comparable studies obtained with nonhelical scanners. Still, early helical scanners were not fast enough for many CTA applications. Limitations to faster speed and thinner slice collimation included single-row detector technology (that allowed only one image per gantry rotation), x-ray tubes that were not designed to handle the intense heat generated during continuous scanning, and computers that were not able to

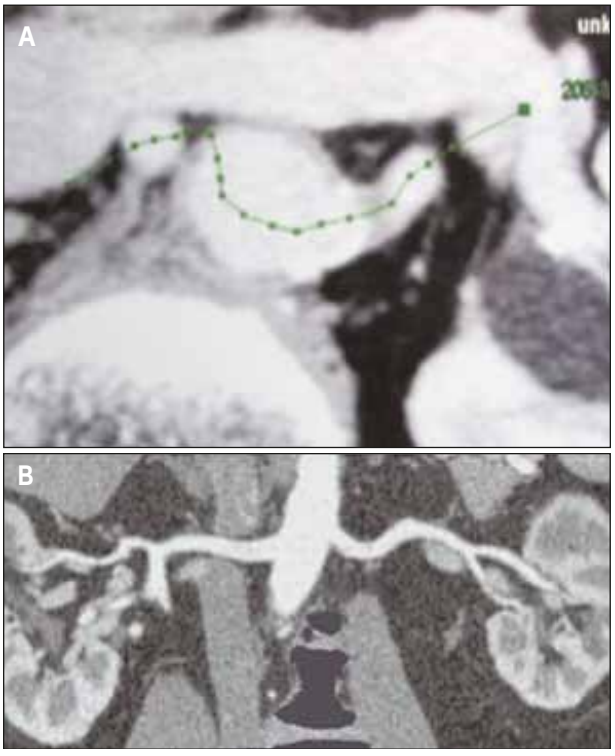

Figure 1. Curved planar reformations (CPRs) of the renal arteries. Plotting the curved coronal plane (A). Curved coronal (B).

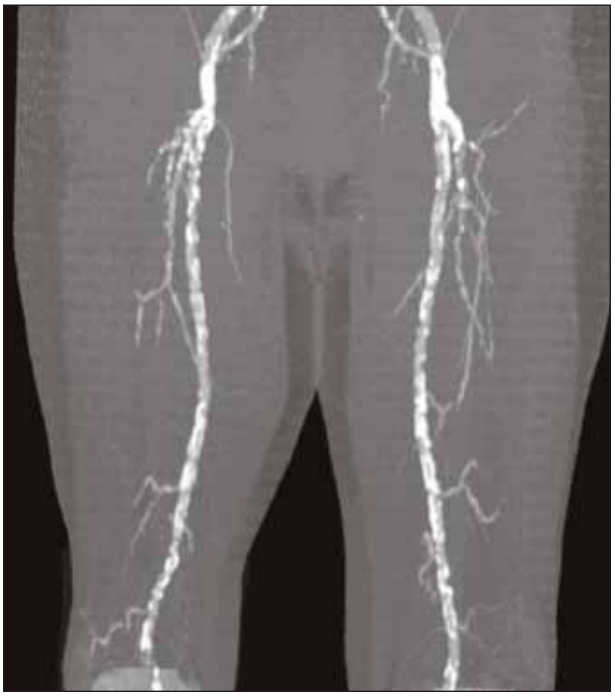

Figure 2. Maximum intensity projection CTA of calcified femoral arteries.

process image data quickly. CT angiography had arrived, but only in very limited applications.

Toward the mid-1990s, computers had advanced to the point that large image data sets could be reconstructed into a CTA image using a dedicated workstation. X-ray tube technology had also advanced, with the production of tubes that could withstand the amount of heat loading that was generated during continuous x-ray production. However, scanners were still too slow for most angiographic studies because only one image was obtained during gantry rotation, and most gantry spin times had reached a lower threshold of .5 second to 1 second. The only way to scan quickly with a single-detector CT was to use unacceptably thick collimation, or "slice thickness," that reduced the number of images obtained during the study. Thickly collimated images, however, gave poor spatial resolution in the cranial-caudal or Z-axis (Figure 1A).

This problem was solved in the late 1990s with the advent of multiple rows of detectors so that many images could be acquired during a single helical revolution. Simultaneous acquisition of multiple slices not only led the way to improved Z-axis resolution, but also reduced the scan time and finally allowed scanning through long segments of the body using acceptable volumes of rapidly delivered intravenous contrast. CTA scanning had finally become a reality, although manipulation of the huge image data sets that resulted from these extensive, thin-collimated studies was relatively slow and required purchase of an expensive workstation that was dedicated to the sole task of three-dimensional (3-D) image manipulation. With ongoing workstation advances during the past 5 years (faster computers, increased random access memory, and improved 3-D software) and high-speed data transfer networks in most imaging environments, affordable and clinically useful CTA has finally been realized (Figure 1B). In fact, today most CT scanners are sold with some form of workstation that can be used for 3-D image postprocessing. In the near future, it is likely that 3-D software and computational power currently located in a dedicated 3-D workstation will reside somewhere within the imaging picture archiving and communication system network so that any volumetric angiographic imaging study (CT, magnetic resonance imaging, rotational angiography) can be reconstructed into an 3-D angiogram simply by retrieving that study from the data archive. Distribution of 3-D images, still a problem today, will likely be solved through advances in both PACS and Web-based technology.

As scanners and computers continue to improve, most single-detector array helical CT scanners in the US have been replaced with multirow detector units. It was predicted in 1998 that by 2003 at least half of the CT scanners in the US would use multirow detector technology,[1] and this has been realized. What was not predicted, however, was the extremely rapid technological development that led to scanners beyond our 1998 imagination. In 2000, a 4-row detector CT scanner was state of the art. By 2001, 8-row scanners were introduced. By 2003, 16-row scanners entered clinical use. Today, 32- and 40-row scanners are common, while 64-row detector scanners are being installed at many sites. Certainly, one of the driving forces for this burst of CT development and purchase has been the capability of CT

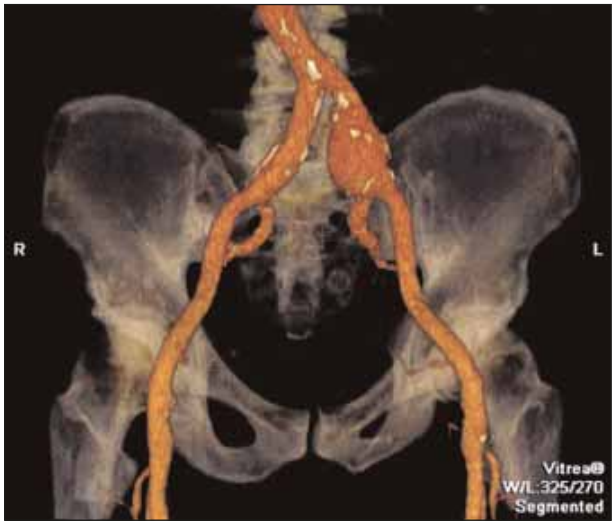

Figure 3. Volume-rendered CTA of the iliac arteries.

scanners to perform CTA of both peripheral and coronary arteries. Scanning peripheral arteries from the skull base to the common femoral arteries with collimation of 0.5 mm to 1 mm takes no longer than 12 seconds to 15 seconds on a 64-row detector CT scanner, and the CTA images are typically superior to those obtained using invasive angiography.

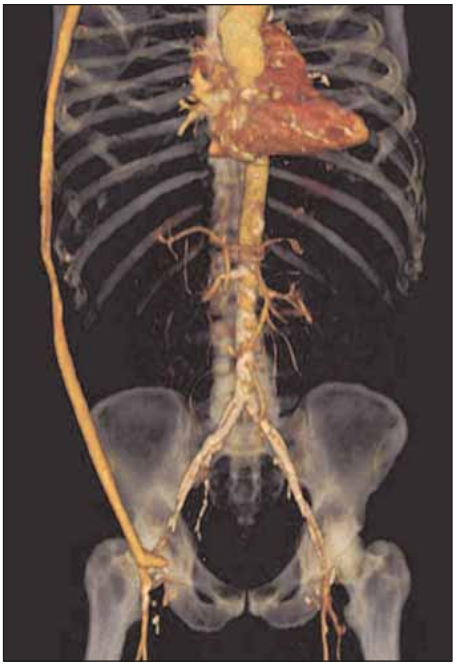

Figure 4. Volume-rendered image of an axillofemoral bypass graft with an occluded cross-femoral bypass graft.

CLINICAL BENEFITS

The power of contemporary CTA is seen in many ways. For the patient, a comprehensive angiographic study requires only intravenous contrast injection and 10 minutes to 15 minutes in the scanner. Scan times for even the most comprehensive study (brain-to-toes) is under 1 minute. When scanning is finished, the intravenous line is removed, and the patient can leave without observation. Of course, all risks related to invasive angiography are avoided, with the exception of intravenous contrast administration and radiation exposure.

For the referring physician, angiographic studies can now be reviewed and therapeutic options considered, allowing the referring physician to participate in the management of the patient before they learn that stenting or bypass grafting has been performed. Because there is little risk for most patients who undergo CTA, there will likely be greater referral for early diagnosis of vascular conditions compared to timing of invasive angiography with its incumbent procedure-related risks.

There are a number of advantages for the angiographer. There is no need for extensive preprocedure patient work-up, consent, review of coagulation parameters, or modification of anticoagulation or antiplatelet medications. Catheter-related risks are entirely avoided, and there is neither a puncture site to compress nor time needed to monitor the patient in a recovery area. Scan protocols are easy to standardize, and most technologists are able to achieve excellent studies with limited physician input. Physician time is further economized because most CTAs require 15 minutes to 45 minutes of total physician time (mostly for interpretation), whereas catheter angiography consumes at least an hour or more of the physician's time from the point when the patient arrives until the catheter is removed and the study interpreted. CTAs also provide an understanding of the entire vascular disease process far beyond an invasive angiogram because they are volumetric and can show vascular anatomy from any orientation (including true cranial-caudal projection that is technically impossible with catheter angiography). Furthermore, CTA demonstrates vascular anatomy far beyond the contrast column, showing both calcified and soft plaque, thrombus, inflammatory changes, and extravascular hemorrhage. Finally, sizing of vascular stenoses and occlusions permits the interventionist to plan treatment and select appropriately sized balloons, stents, and endografts.

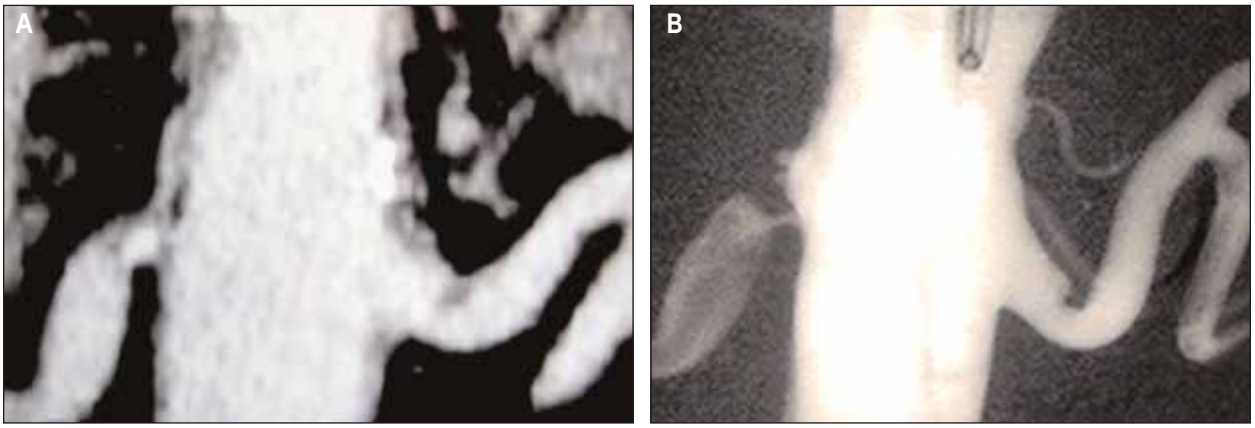

Figure 5. CTA showing calcified high-grade right renal artery stenosis and 40% to 50% soft plaque stenosis of the proximal left renal artery stenosis (A). The DSA shows only the lumen of the renal arteries (B).

There are considerations for the hospital as well. It is not difficult for most centers to add several CTA studies to the daily workload of a multidetector CT scanner and improve scanner use without the need for expanding recovery facilities or adding the extra nursing and technologist staff that would be required for additional invasive angiography. When diagnostic angiography is shifted from the high-cost angiography lab environment to the CT scanner, the angiography lab is more available for interventional procedures that require these resources and also afford higher reimbursement to the hospital compared to diagnostic angiography.

TECHNIQUES

Conceptually, CTA is performed via acquisition of images when the blood vessels are optimally enhanced with radiodense contrast material (administered intravenously). These images represent information within a volume of tissue, and once transferred to a workstation, processing of this information yields a 3-D angiographic study. The best rendering of blood vessels will be achieved when iodinated contrast is infused at a rate between 3 mL/s to 6 mL/s, waiting to scan until these blood vessels are maximally contrast-enhanced. Most CTA scanning is started once the density of blood (measured in Hounsfield units [HU]) within the blood vessel of interest reaches at least 150 HU, although a target range of at least 180 HU to 200 HU is desirable.

There is debate regarding both contrast administration protocols and techniques for determining the optimal delay from the time that the intravenous infusion is started until the scan is started (scan delay). There are three approaches used to determine scan delay; (1) empiric delay based on experience; (2) preliminary timing bolus to determine how long it takes for contrast to reach the target vessel followed by the definitive contrast infusion; and (3) administration of the definitive contrast infusion with bolus-triggered scanning once intravascular density reaches the desired threshold. Each of these techniques has its champions, although it seems that bolus triggering is emerging as the most widely accepted method.

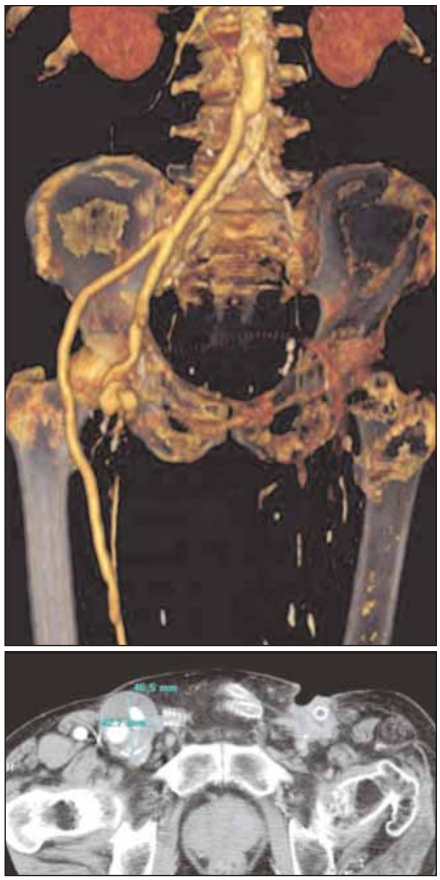

Figure 6. CTA for evaluation of infected bypass grafts of the pelvis (top) and legs (bottom).

Collimation is selected on the basis of several factors that include the number of rows of detectors in the CT scanner, the desired time for the entire scan, and the need for adequate Z-axis resolution. For example, a 4-row detector scanner may only be able to scan with no less than 3-mm collimation to scan the thoracic and abdominal aorta in 20 seconds (approximately one breath hold). If the collimation was set at 1.5 mm, the scan would take twice as long (40 seconds) and scanning could not be achieved in one breath hold. Furthermore, vascular contrast enhancement for 40 seconds is likely to require administration of an excessive amount of intravenous contrast during the study. By moving from a 4-row detector scanner to a 64-row detector scanner, simultaneous acquisition of extremely thin collimated images can made (0.5 mm to 1 mm) while keeping scanning time under 20 seconds.

Radiographic techniques for CTA studies, described at length in many publications, are now often preset in most current scanners, although these parameters can be modified if necessary. Detailed discussion of pitch, table speed, kVp, mA, field of view, and gantry speed is mostly of historical importance, although on occasion, consideration of these parameters is necessary.

IMAGE OUTPUT

Although there are many ways to produce CTA images, there are only three types of output. First, blood vessels can be seen in planar reconstruction. The simplest is the axial reconstruction that is produced by every CT scanner. When the plane is tilted, a planar oblique reconstruction is produced. It is possible to make a curved plane, such as one that follows the curve of the renal arteries. This is called a *curved planar reconstruction* (Figure 1A,B). It is also possible to curve the plane in the 3-D space, and this has been automated on several workstations. The complex 3-D curved planar reconstruction has become the standard method for renal and coronary artery analysis.

The second type of output is the maximum intensity projection, which shows the most dense volume elements (voxels) and usually demonstrates contrast in the blood vessels, as well as calcification in the

vessel wall (Figure 2). It is most useful when there are no vascular wall calcifications in the rendered volume.

The final type of output is volume rendering, which encodes different density voxels with varying colors at different intensities (Figure 3). The spectrum of color ranges between the very dense vascular voxels (eg, gold) to the moderately dense vascular voxels (eg, red). Less-dense voxels do not reach the threshold for display, and therefore soft tissues are mostly not seen. Volume rendering generates the colorful and very compelling 3-D renderings that are often associated with CTA (Figure 4), although in many situations, these volume-rendered images lack important information that is found in planar reconstructions (such as accurate measurements, soft tissue, and perivascular processes).

A number of studies have compared CTA with digital subtraction angiography of the aortoiliac, femoropopliteal, and renal arteries. Rubin[2] showed comparable diagnostic results between CTA and digital subtraction angiography for peripheral run-off vessels, with one-fourth the radiation dose using CTA. Willmann et al[3] demonstrated the utility of CTA for evaluating peripheral arterial bypass grafts. In the mid-1990s, Kaatee et al[4] and Beregi et al[5] showed comparable sensitivity and specificity for detecting and quantifying renal artery stenosis comparing CTA with digital subtraction angiography with early helical CT scanners using scanning techniques that are already outdated. CTA shows not only the degree of luminal stenosis, but also coexistent plaque (Figure 5A,B). CTA can be used as the sole angiographic technique before treatment of abdominal aortic aneurysm with endografts, rendering catheter angiography unnecessary for most cases.[6] There is a growing body of literature regarding CTA for evaluation of the coronary arteries, and with cardiac gating and further improvements in CT scanners and postprocessing, it is likely that many invasive cardiac catheterizations will be replaced by CTA.

CTA has been used in a wide variety of other conditions. Evaluation of renal vascular anatomy for a potential renal donor is accomplished almost exclusively with CTA.[7,8] Evaluation of surgical bypass graft complications, such as infection, stenosis, and pseudoaneurysm is also largely done with CTA (Figure 6A,B). CTA can demonstrate the pulmonary venous and left atrial anatomy to help guide the electophysiologist perform radiofrequency ablation of foci causing atrial fibrillation. Pulmonary artery CTA has mostly replaced catheter-based pulmonary angiography.[9] CTA is also gaining acceptance for evaluation of atherosclerotic stenosis of the carotid bifurcation and internal carotid artery (Figure 7),[10-12] as well as for evaluating the intracranial arterial circulation (Figure 8). Finally, coronary artery CTA is likely to replace diagnostic coronary arteriography in some situations,[13,14] although the exact applications for coronary CTA are still unclear.

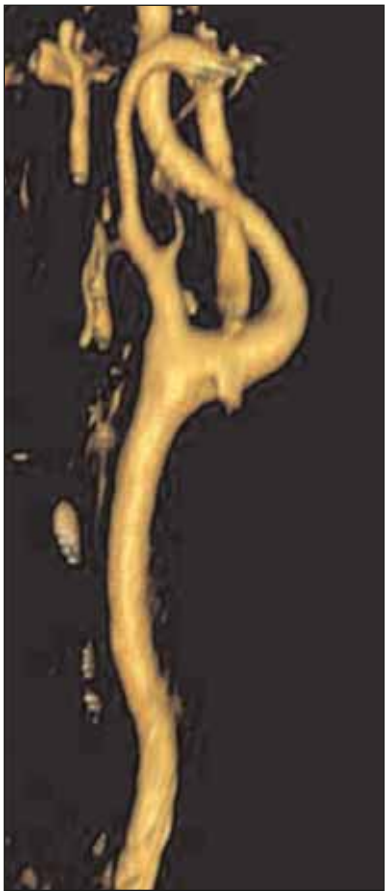

Figure 7. Volume-rendered carotid artery bifurcation.

CONTRAINDICATIONS

There are few situations in which CTA is not sufficient for vascular diagnosis. Dense and extensive mural calcification of Monckeberg's medical sclerosis, often seen in diabetics and/or renal failure patients, impedes accurate evaluation of stenosis in arteries that are smaller than 4 mm in diameter. Also, arteries that are smaller than 2 mm in diameter are not reliably evaluated, and therefore pedal, palmar, cerebrovascular, and visceral arterial branch studies for vasculitis or other small vessel occlusive diseases are better performed with invasive angiography. However, it is likely that both calcification and small vessels will be imaged more effectively as CTA develops further.

CTA is contraindicated in patients who have severe iodinated contrast allergy or those who should not receive iodinated contrast agents because of azotemia, who are not on dialysis. One possible solution is the use of gadolinium for intravenous contrast, which may become more widely used with 64-row detector scanners.

CONCLUSION

There are many unknowns regarding CTA. How will complex 3-D images be distributed to referring physicians? When will CTA technology coalesce with picture archiving and communication system infrastructure? What are the next advances in CT scanners, and will "rows of detectors" represent stable technology or is another concept likely to replace them? Although there are many questions, there seems to be one certainty—CTA has displaced many invasive angiographic diagnostic studies, and this trend will

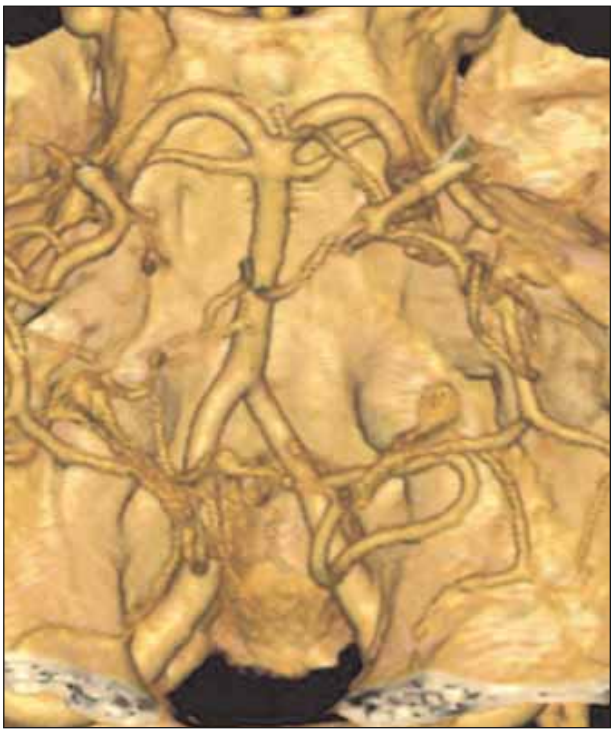

Figure 8. CTA of the basilar artery and its proximal branches.

continue into the future for both peripheral and coronary arteriography. ■

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Medicine is experiencing a molecular and cellular revolution, which has been spurred by the sequencing of the human genome and the development of research tools that permit high-throughput analysis of a variety of molecular and cellular systems. The endovascular specialist has begun to feel the effects of this revolution in the treatment of atherosclerotic occlusive disease with the introduction of drug-eluting stents for the prevention of in-stent restenosis. The next potential molecular or cellular therapy for treating peripheral arterial disease (PAD) is therapeutic angiogenesis, possibly involving stem cells. The purpose of this article is to familiarize the reader with this burgeoning field.

THE EXTENT OF PAD

The spectrum of symptomatic PAD ranges from intermittent claudication to chronic limb ischemia (CLI). Current practice treats only the patients in the middle of the spectrum (ie, disease severity that would warrant an invasive procedure, but within patients in whom revascularization is an option). It is estimated that approximately 5 million people[1] have intermittent claudication.[2] The vast majority of patients with intermittent claudication are typically managed conservatively with a walking program and cilostazol therapy.[2] Despite these therapies, most patients continue to have pain with ambulation, which affects their quality of life. The most severe manifestation of PAD is CLI, defined as rest pain and/or tissue loss. CLI develops in 500 to 1,000 individuals per million per year.[3] Psychologic testing of patients with CLI demonstrates quality-of-life indices similar to patients with terminal cancer.[4] Twenty percent of patients with limb-threatening ischemia have disease that is so extensive that revascularization, such as bypass surgery or angioplasty/stent placement, is not feasible.[5] The only option for these patients is amputation. Although the endovascular specialist is able to treat a portion of patients with PAD, there is a larger segment of PAD patients that currently receive suboptimal therapy.

THERAPEUTIC ANGIOGENESIS

There are two key processes that dictate the symptomatology of a patient with PAD. The first is the degree of the arterial occlusion. The second is the degree to which an endogenous arteriogenic response is mounted to compensate for the occlusion. Our current endovascular techniques can treat the former, but have no effect on the latter. In an attempt to augment the endogenous arteriogenic response, therapeutic angiogenesis is the