The Role of 3D Echocardiography in the Assessment of Valvular Heart Disease

Three-dimensional (3D) echocardiography is one of several emerging modalities to define cardiac anatomy and function. Although still in evolution, 3D echocardiography can complement current 2D echocardiographic techniques in the assessment of valvular heart disease. In a way not possible with 2D echocardiography, 3D echocardiography can allow images to be viewed at different angles that improve the visualization of cardiac structures. Image resolution remains a concern for transthoracic 3D imaging, but the recent development of 3D transesophageal echocardiography (TEE) (either real-time or reconstructed) has made this less of an issue.

Development of 3D echocardiography has made vast contributions to the understanding of mitral valve function. Although in the majority of patients with mitral stenosis, comprehensive 2D and Doppler echocardiography is sufficient, several clinical trials have demonstrated that 3D echocardiographic mitral valve planimetry can provide better correlation with invasively determined mitral valve area. An example of this technique using 3D transthoracic imaging is shown in Figure 1.

With the advent of real-time 3D TEE, rapidly obtainable views of the mitral valve, either from the left atrial perspective (“surgeon’s view”) or from the left ventricular perspective.

Points to Remember

- 3D echocardiography is an emerging modality with a diverse array of clinical applications, including assessment of valvular heart disease.
- Intraoperative transesophageal echocardiography during mitral valve surgery provides views of the mitral valve either from the left atrial perspective (“surgeon’s view”) or from the left ventricular perspective.
- 3D echocardiography can be helpful in identifying whether pacemaker or intracardiac defibrillator leads contribute to tricuspid regurgitation.

Figure 1. 3D planimetry for mitral stenosis. A, Multiplanar reconstruction views are used to manipulate the cutplanes (blue dashed lines) so that the mitral orifice can be visualized at its smallest point (B). B, The white arrow indicates the mitral valve area trace that is performed on a reconstructed image guided by the 3D echo images shown in A.
the left atrial perspective (“surgeon’s view”) or from the left ventricular perspective, are now possible with intraoperative TEE during mitral valve surgery. Mayo Clinic cardiologists have demonstrated the incremental value of 3D TEE in the recognition of mitral valve surgical pathology during operative repair. This is especially the case with respect to mitral valve anterior leaflet pathology and with commissural disease. Examples of typical 2D and corresponding 3D TEE pathology are shown in Figure 2. Although 2D TEE remains an excellent method for the assessment of mitral valve disease, 3D TEE allows for a more rapid assessment of surgical pathology and can increase diagnostic confidence.

Cardiologists at Mayo Clinic were among the first to report on the superiority of 2D TEE over transthoracic echocardiography for the diagnosis of complications of endocarditis. 3D TEE may also be useful in this setting by allowing for better visualization of leaflet perforations as well as a clearer description of adjacent cardiac structures. An example of an aortic valve leaflet perforation complicating a case of aortic valve endocarditis is shown in Figure 3.

Finally, 3D echocardiography can help identify whether pacemaker or intracardiac defibrillator leads are contributing to tricuspid regurgitation, something that can be difficult to do using 2D echocardiography. Ongoing investigations will also clarify whether 3D color Doppler imaging provides further clarification of regurgitant severity and whether 3D imaging can be of value during interventional procedures.

3D echocardiography is an emerging modality with a diverse array of clinical applications, including assessment of valvular heart disease. It complements current 2D echocardiographic techniques and its use continues to evolve as technologic advances are developed.

**Figure 2. Flail mitral valve posterior leaflet (middle scallop, P2).** A, Live 3D TEE view of the mitral valve at end systole from the left atrial perspective demonstrates the flail P2 scallop (asterisk) and clearly shows multiple torn chordae tendineae (arrows). B, 2D TEE end-systolic views demonstrate a flail middle scallop of the posterior mitral leaflet (P2). The flail P2 scallop is highlighted by the white arrows in the commissural 60° view on the left and a long-axis 110° view on the right; torn chordae tendineae are noted on the long-axis view (yellow arrow). LA, left atrium; LV, left ventricle.

**Figure 3. Aortic valve perforation.** A, This long-axis 2D TEE view in a patient with healed aortic valve endocarditis shows the aortic valve with multiple bright echodensities most consistent with healed vegetations. A large region of “echo dropout” (arrow) is consistent with a perforation. B, Using 3D TEE the true aortic valve orifice (asterisk) is well seen, as is the perforation (arrow). The size of the perforation as well as leaflet location is better defined using 3D TEE. Ao, aorta; LV, left ventricle; LA, left atrium.

**Carotid Angioplasty With Stent Placement**

Carotid angioplasty with stent (CAS) placement is an emerging alternative to carotid endarterectomy for the treatment of patients with carotid artery occlusive disease. Mayo Clinic neuroradiologists began using it in 1996 for patients at high risk for surgery.

The Cerebrovascular Clinic in Mayo Clinic’s Department of Neurology in Rochester, Minnesota, has a multidisciplinary CAS protocol in which a vascular neurologist, an interventionalist (from neuroradiology, neurosurgery, vascular surgery, or cardiology), and a neurosurgeon or vascular surgeon meet with the patient to help clarify the best treatment approach. Cardiology colleagues may also be involved if the patient has cardiac symptoms, which is not uncommon, since
so many patients with carotid occlusive disease also have coronary artery occlusive disease.

**Indications and Procedure for CAS Placement**

Candidates for CAS placement are patients with a severe narrowing of the carotid artery who have had symptoms such as transient ischemic attacks or cerebral infarction. Also candidates are selected patients who have severe narrowing of the carotid artery without symptoms.

Most patients arrive at Mayo Clinic after carotid ultrasonography, magnetic resonance angiography, or computed tomographic angiography has shown narrowing of the carotid artery. After performing a thorough medical history and patient examination, the multidisciplinary team members determine whether CAS placement is the optimal treatment, applying the recently published CREST data and individualizing the management decision.

During the CAS procedure, the patient is sedated but awake, and a small plastic catheter is inserted into a groin artery and tracked through the aorta to the carotid arteries. Next, contrast material is injected through the catheter to delineate the anatomy. If the angiogram confirms severe narrowing that could be best treated with CAS placement, then the procedure begins.

Before performing the CAS procedure, a protection device may be deployed distally in the carotid artery. This device functions something like a tiny mesh umbrella to catch material that may break free during the angioplasty. Then the angioplasty balloon is advanced across the plaque and inflated to push the plaque aside, thus reducing arterial narrowing. The stent—a small metallic scaffolding device—is put in place to keep the artery open (Figure). The procedure ends with withdrawal of the distal protection device and the catheter.

Typically, the patient is hospitalized for 1 day. Aftercare involves taking both clopidogrel and aspirin daily for 1 month to prevent blood clots from forming at the stent site and then aspirin alone indefinitely thereafter. Mayo Clinic specialists follow each patient long term, both to assess durability of the stent and to determine whether narrowing recurs. Follow-up may include intermittent carotid ultrasonography that begins several months after the procedure.

**Results, Risks, and Complications**

CAS placement is a logical extension of the balloon stenting used for coronary artery disease. Initially, in the late 1990s, CAS placement was performed on patients who were at high risk for conventional surgery. The outcomes of these early cases were excellent, and the risk of stroke and death was extremely low. Because these measures of success were so similar to those of the standard treatment, carotid endarterectomy, the use of CAS placement was cautiously and carefully expanded.

Since then, Mayo Clinic experience with CAS placement suggests that, when performed by an experienced, multispecialty team on appropriately selected patients, the procedure is approximately equal to carotid endarterectomy in terms of effectiveness, risks, and complications.

Because the procedures require the interventionalist to work within the artery, both carotid endarterectomy and CAS placement carry the risk of stroke during the procedure.

Mayo Clinic’s Cerebrovascular Clinic is a full-time clinic, providing consultations for patients with carotid stenosis and all other types of cerebrovascular disorders. To refer a patient for evaluation, call the Cerebrovascular Clinic at 507-284-1588.

**Points to Remember**

- Carotid angioplasty with stent (CAS) placement is appropriate for selected patients with transient ischemic attacks or cerebral infarction and also for certain patients who have severe stenosis of the carotid artery without symptoms.

- The National Institutes of Health selected Mayo Clinic to participate in the Carotid Revascularization Endarterectomy vs Stent Trial (CREST). CREST formally evaluated the comparative risks of stroke, myocardial infarction, and other adverse outcomes associated with the 2 procedures.

**Figure.** Left, Preoperative image of narrowed carotid artery. Right, Postoperative image showing stent in place and open artery after CAS placement.
Developed in the 1980s, deep brain stimulation (DBS) was principally used to treat movement disorders associated with essential tremor (ET) and Parkinson disease (PD). Today, its applications include other types of movement disorders and certain nonmotor syndromes and conditions. Successful DBS depends on careful patient selection, precise neural targeting, and extensive, individualized programming. It is generally reserved for symptoms that are unresponsive to other therapies.

For 14 years, neurologists, neurosurgeons, and members of the multidisciplinary DBS teams across Mayo Clinic’s 3 sites have gained experience, conducted research, and explored new clinical applications. Overall, they agree that for certain disorders in carefully selected patients, DBS and motor cortex stimulation (MCS) can markedly improve patient lives. The following update summarizes their findings and experience during the past several years.

Treatment of Primary Disorders

**Essential Tremor**
DBS for ET continues to have positive results, and other types of tremor are being addressed. Recently, Mayo physicians have reported success in using DBS to treat both orthostatic tremor, a variant of ET that affects the lower limbs on standing and spreads up the trunk, and rubral tremor, a rare tremor associated with the red nucleus.

**Parkinson Disease**
In the right patients, DBS continues to be effective in improving motor function and in reducing dyskinesias and symptom fluctuations related to on-off medication effects. The main indication is the patient’s need for increased frequency and levels of medication. Previously reserved for patients under the age of 70 years, DBS is now offered by Mayo Clinic physicians to selected older PD patients, some in their 80s.

**Dystonia**
Patients with focal and generalized dystonia represent a large percentage of patients treated with DBS at Mayo Clinic. Good results have been reported using DBS for early-onset primary dystonia or early-onset torsion dystonia. Most patients with other forms of dystonia are helped, although the response may not be dramatic. To improve outcomes, the Mayo Clinic DBS team is considering transcortical magnetic stimulation for some dystonias.

Possible Future Applications

**Epilepsy**
Mayo Clinic has completed a study of neurostimulation for focal epilepsy. Although the results are not yet in, several study participants whose seizures were intractable have become seizure-free.

**Centrally Mediated Neuropathic Pain**
Treatment of centrally mediated pain is experimental. The results at Mayo for trigeminal autonomic cephalgia, including cluster headaches, have been mixed. The use of preoperative positron emission tomography
scans to determine if hypothalamic sites should be stimulated unilaterally or bilaterally in a given patient is under consideration. Mayo physicians note that intractable face pain in the distribution of the trigeminal nerve may respond to MCS.

Psychiatric Disorders
Mayo researchers have performed DBS in patients with Tourette syndrome, considered both a movement and a psychiatric disorder. They are exploring DBS for other types of tics and are in the early stages of investigating neurostimulation for depression and obsessive-compulsive disorder.

Potential Secondary Symptom Benefits

Restless Legs Syndrome
Although DBS has not been used as a primary treatment for restless legs syndrome, Mayo researchers note that there is often a post-DBS reduction in restless legs associated with PD, a finding they confirmed in a retrospective study. Early study results and other case studies suggest DBS may be a promising option for primary treatment of restless legs syndrome.

Spasmodic Dysphonia
In 2008, Mayo researchers presented the first report on improved vocal control in a patient with spasmodic dysphonia—a primary focal dystonia of the vocal muscles during speech. Noting that there are now a growing number of reports of DBS for spasmodic dysphonia outside the United States, Mayo Clinic may explore this application in the future.

Figure 2. Final lead placement in motor cortex stimulation for neuropathic pain. Left, Conventional implantation of the motor cortex (green gyrus); right, more extensive implantation, covering motor, premotor (blue gyri), and some prefrontal cortices. The latter procedure is being performed at Mayo Clinic in Rochester.
Many clinicians use the term *pheochromocytoma* to refer to both adrenal pheochromocytomas and extra-adrenal catecholamine-secreting paragangliomas, because they have similar clinical presentations and are treated with similar approaches. However, the distinction between pheochromocytoma and paraganglioma is an important one because of implications for associated neoplasms, risk of malignancy, and genetic testing.

Catecholamine-secreting tumors are rare, with an annual incidence of 2 to 8 cases per 1 million people in all populations studied. There are several reasons to suspect, confirm, localize, and resect these tumors: 1) the associated hypertension is curable with surgical removal of the tumor, 2) a risk of lethal hypertensive paroxysm exists, 3) at least 10% of the tumors are malignant, and 4) 10% to 20% are familial, and detection of this tumor in the proband may result in early diagnosis in other family members.

Pheochromocytoma is frequently diagnosed before symptoms develop because of genetic screening for hereditary endocrine syndromes or incidental discovery of an adrenal mass on computed tomography (CT) or magnetic resonance imaging (MRI). Approximately 5% of all adrenal incidentalomas have proved to be pheochromocytomas. In the past, more than 95% of patients with pheochromocytoma had paroxysmal symptoms (spells) of palpitations, diaphoresis, and headaches. However, with the widespread use of CT and MRI, approximately 50% of all pheochromocytomas are initially detected as adrenal incidentalomas in patients without spells and, frequently, without hypertension.

In a patient with spells, the degree of increase in fractionated metanephrines and catecholamines in the blood or urine should be markedly abnormal (eg, increases more than 5 times the upper limit of the reference range). However, in an asymptomatic patient with pheochromocytoma, the biochemical test results may be normal because the neoplasm has been detected in the prebiochemical phase. In this situation, the clinician must rely on the features of the mass on CT or MRI (the imaging phenotype) to guide management.

Plasma-fractionated metanephrines have a 15% false-positive rate, usually because of increased plasma normetanephrine concentrations. Table 1 shows the upper limits of the reference ranges based on patients who are investigated for pheochromocytoma but are found not to have this rare tumor. Patients with values above these diagnostic cutoffs have pheochromocytoma, are severely ill (eg, hospitalized in an intensive care unit), or are taking a medication that is causing false-positive test results (Table 2). Use of antihypertensive agents (eg, β-adrenergic blockers, α-adrenergic inhibitors) and selective serotonin reuptake inhibitors does not result in false-positive biochemical test results.

### Points to Remember

- Catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla and the sympathetic ganglia are referred to as *pheochromocytomas* and *extra-adrenal catecholamine-secreting paragangliomas* (extra-adrenal pheochromocytomas), respectively.

- With the widespread use of computed tomography (CT) and magnetic resonance imaging (MRI), approximately 50% of all pheochromocytomas are initially detected as adrenal incidentalomas in patients without spells and, frequently, without hypertension.

- In an asymptomatic patient with pheochromocytoma detected in the prebiochemical phase, the clinician must rely on the features of the mass on CT or MRI (the imaging phenotype) to guide management.

### Table 1. Upper Limit of Reference Ranges for 24-Hour Urinary Fractionated Metanephrines and Catecholamines

- Metanephrine <400 mcg
- Normetanephrine <900 mcg
- Total metanephrine <1,000 mcg
- Norepinephrine <170 mcg
- Epinephrine <35 mcg
- Dopamine <700 mcg
After biochemical confirmation of pheochromocytoma, CT or MRI of the abdomen and pelvis is the first localization test. Approximately 90% of these tumors can be localized when in the adrenal glands and 98% when in the abdomen and pelvis. If the abdominal imaging result is negative, then scintigraphic localization with $^{123}$I-metaiodobenzylguanidine ($^{123}$I-MIBG) is indicated. Computer-assisted chest, neck, and head imaging provides additional localizing procedures that can be used, although they are rarely required.

The tumor can always be found in symptomatic patients with pheochromocytoma, because the average diameter of a pheochromocytoma in this situation is 4.5 cm. The typical imaging phenotype of a pheochromocytoma is a dense (Hounsfield units, >20) and vascular mass with slow contrast washout (<50% at 10 minutes after contrast medium administration) (Figure 1). By comparison, the much more common adrenocortical adenoma is usually hypodense (Hounsfield units, <10) and has rapid contrast washout (>50% at 10 minutes) (Figure 2).

When the clinician has trouble localizing a pheochromocytoma, it is usually because the patient does not have pheochromocytoma. Medication-induced false-positive biochemical test results and use of inappropriately low reference ranges can lead to imaging misadventures. Finally, it is important to understand that $^{123}$I-MIBG is taken up by healthy adrenal glands and the intensity of uptake is usually asymmetric. An adrenal gland should never be resected on the basis of asymmetric adrenal uptake of $^{123}$I-MIBG unless the uptake pattern correlates with a vascular adrenal mass on CT.

To refer a patient for diagnosis or management of pheochromocytoma, call 800-533-1564.

**Table 2. Medications and Situations That Can Cause False-Positive Results on Biochemical Testing for Pheochromocytoma**

- Tricyclic antidepressants (including cyclobenzaprine hydrochloride)
- Levodopa
- Ethanol withdrawal
- Withdrawal from clonidine and other drugs (eg, illicit drugs)
- Antipsychotics, buspirone hydrochloride, and bupropion hydrochloride
- Amphetamines
- Prochlorperazine
- Reserpine
- Major physical stress (eg, surgery, stroke)
- Obstructive sleep apnea syndrome

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**Figure 1.** Axial computed tomographic image of an asymptomatic patient with an incidentally discovered 5-cm left adrenal pheochromocytoma (arrow). This mass has an imaging phenotype consistent with pheochromocytoma: it is dense, vascular, and inhomogeneous. The Hounsfield unit density before contrast medium administration was 45. Ten minutes after administration, there was only 38% contrast washout.

**Figure 2.** Axial computed tomographic image of an asymptomatic patient with an incidentally discovered 2.5-cm left adrenal mass (arrow). This mass has an imaging phenotype consistent with a cortical adenoma: it is hypodense, not vascular, and homogeneous. The Hounsfield unit density before contrast medium administration was −5. Ten minutes after administration, there was 70% contrast washout.
Patient Care

Inpatient Video-EEG Monitoring for Epilepsy
Continuous video-EEG monitoring (inpatient) helps localize seizure focus, determine seizure type, and quantify the number of seizures in patients with intractable recurrent seizures and those with an unconfirmed seizure diagnosis.

Optimizing the Functional Performance of Cancer Survivors
There is a growing understanding of the importance of exercise and rehabilitation for cancer survivors. Physical Medicine specialists can help patients manage the negative long-term sequelae of cancer and its treatments and obtain a more satisfying, high-quality recovery.

New Endoscopic Treatment for Severe Gastrointestinal Bleeding
Endoscopic ultrasound-guided therapy appears to be a safe and effective treatment for patients with severe gastrointestinal bleeding for whom conventional therapies have failed. The therapy involves injecting various agents directly into the source to stop the bleeding.

Less Can Be More When Treating Some Kidney Cancer
A Mayo Clinic study suggests that removing the entire kidney from younger patients with small kidney tumors may lead to decreased overall survival compared with an operation that removes the tumor but leaves the kidney intact.

Research

Protecting Kidney Cells from Injury
In 1992, Dr. Karl Nath’s research team discovered the capacity of heme oxygenase