# Imaging Cardiac Masses in Patients with Cancer

Nicole Prabhu MD and Jeanne M. DeCara MD

Department of Medicine, Section of Cardiology, University of Chicago Medicine, Chicago, IL, USA

**ABSTRACT** Cardiac tumors are rare and the majority are from a primary source outside of the heart. Most are found, incidentally, with echocardiography but often additional cardiac imaging is needed to refine the differential diagnosis. For this purpose, cardiac magnetic resonance imaging (MRI) and to a lesser extent cardiac computed tomography (CT) or $^{18}$F-fluorodeoxyglucose positron-emission tomography/computed tomography ($^{18}$F-FDG PET/CT) are useful imaging modalities to better characterize a cardiac tumor and determine the likelihood of a neoplastic versus non-neoplastic origin. Cardiac CT may be useful to evaluate the effect of treatment while using $^{18}$F-FDG PET/CT to evaluate cardiac masses is under-studied but may be useful in patients who are already having a scan performed for oncologic reasons. It is through understanding the clinical context of a newly discovered cardiac mass, knowledge of the typical locations of various cardiac tumor types, combined with imaging techniques that avoid ionizing radiation that yield the greatest confidence in the noninvasive diagnosis of a cardiac mass.

*IMAJ* 2022; 24: 186–190

**KEY WORDS:** cancer, cardiac imaging, cardiac tumors, masses

In patients with cancer, cardiac and chest imaging is a common occurrence. In the course of this frequent imaging, cardiac masses can be discovered and must be categorized as either neoplastic or non-neoplastic. In patients with cancer, this differentiation has important prognostic and treatment ramifications. In this article, clinical and imaging features that help to narrow the differential diagnosis of cardiac tumors are reviewed.

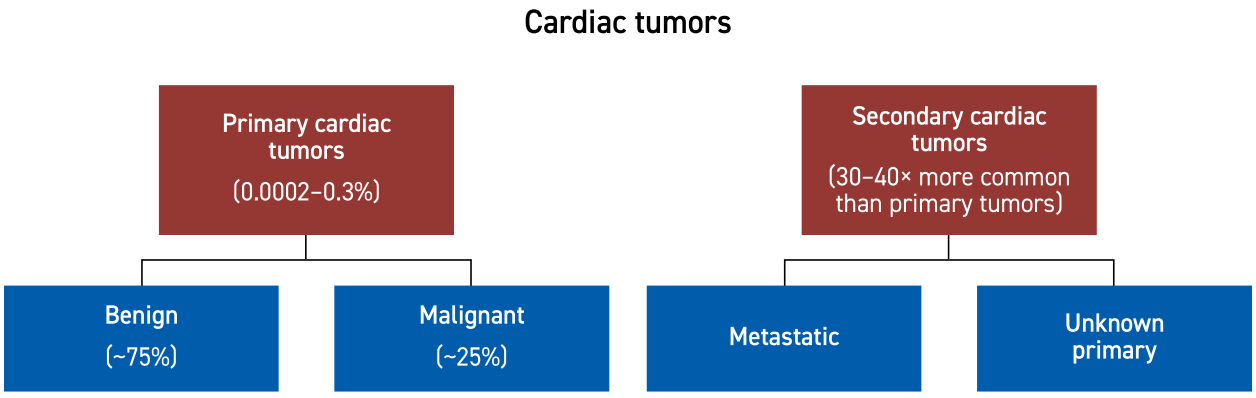
## PREVALENCE AND CLASSIFICATION

Cardiac tumors are uncommon, and are classified as either primary or secondary tumors [Figure 1]. Primary cardiac tumors originate within the heart. These are very rare, with an overall incidence of 0.001–0.3% [1]. Of these, 75% of primary cardiac tumors are benign, with myxomas being the most common [1,2]. A much smaller proportion of primary cardiac tumors are malignant, with sarcoma being the most commonly represented (64.8%), followed by lymphoma (27%) and mesothelioma (8%) [3].

Secondary cardiac tumors, meaning those originating outside of the heart, are far more common than primary cardiac tumors. A study of cardiac neoplasms at autopsy indicated that metastatic cardiac neoplasms were 132 times more common

**Figure 1.** Classification of cardiac tumors

Only a minority of tumors are primary, originating from within the heart, and the majority of these are benign: myxoma is the most common. Primary malignant tumors are much less common. Sarcomas and lymphomas are well represented. Secondary cardiac tumors are far more common than primary tumors. The majority of are metastatic from known primary tumors elsewhere in the body.



than primary cardiac neoplasms [4]. The bulk of these secondary tumors represent metastatic disease in patients with a known primary malignancy. In one series, the reported frequency of secondary metastatic tumors to the pericardium, myocardium, and coronary arteries in the general population was between 0.7% and 3.5%, whereas in patients with known malignancies it was 9.1% [5]. Melanomas are known to favor cardiac involvement [6]. However, other tumor types can metastasize to the heart. Primary lung cancer accounts for 36–39% of cardiac metastases, followed by breast cancer (10–12%) and hematological malignancies (10–21%) [5]. This distribution reflects the high prevalence of these tumors in the general population. Direct invasion, trans-venous extension, and lymphatic or hematogenous routes are well-described mechanisms for tumors to spread to the heart.

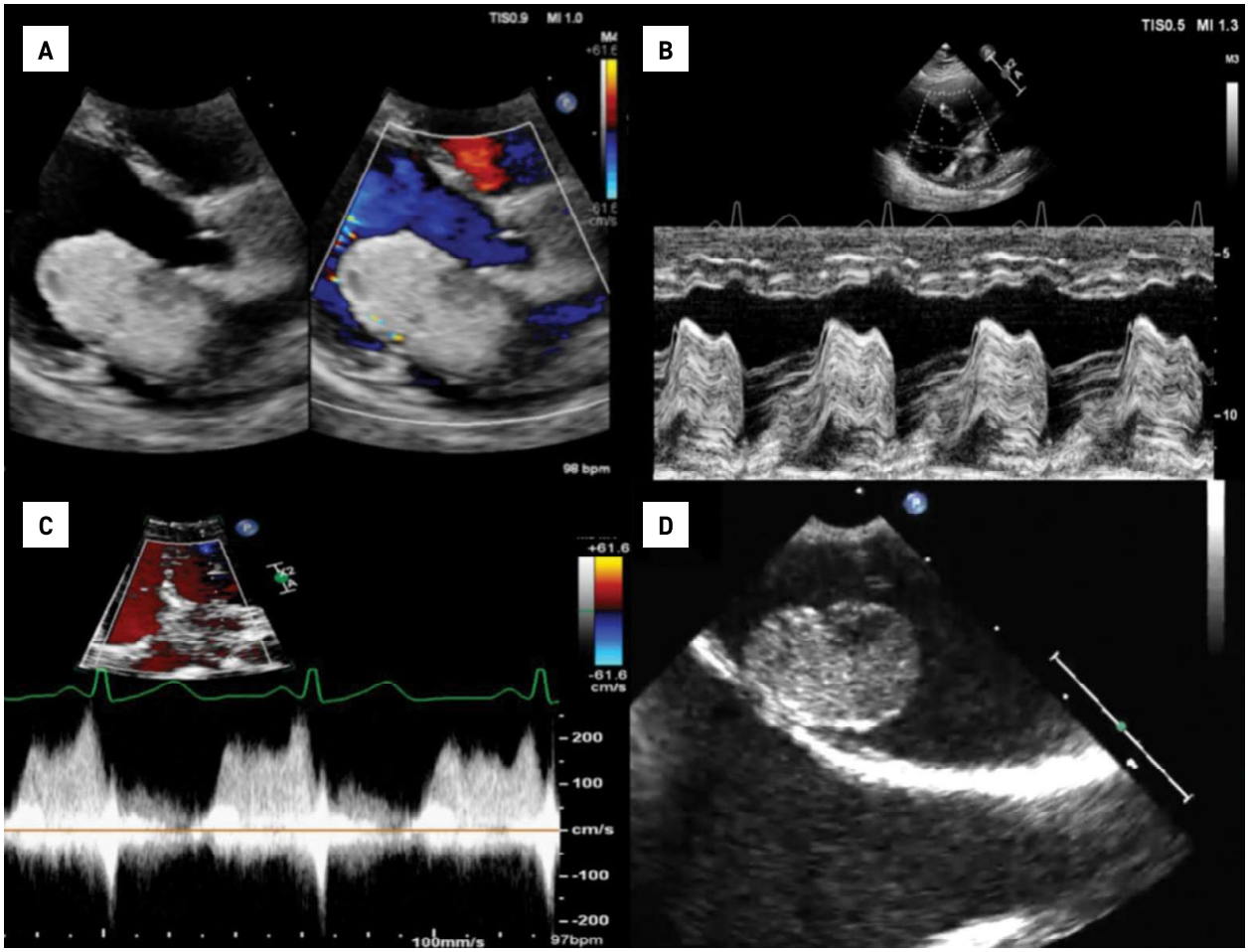
**MOST CARDIAC TUMORS ARE SECONDARY TUMORS THAT ORIGINATE FROM A PRIMARY TUMOR OUTSIDE OF THE HEART**

## CLINICAL DIAGNOSIS

### *Presentation and location*

Many cardiac tumors are found incidentally on cardiac or chest imaging. However, others are heralded by symptoms that then prompt imaging. Patients may experience new cardiovascular symptoms such as chest pain, dyspnea, palpitations, or syncope. They may even experience systemic symptoms such as fever or weight loss [7]. The size and location of the tumor can impact its clinical manifestation as well. Some cardiac tumors can interfere with valvular

**Figure 2.** Location as a clue to diagnosing an intracardiac tumor. This patient presented with syncope caused by mitral inflow obstruction by a large left atrial mass **[A]**. The mitral M-mode **[B]** and mitral inflow Doppler **[C]** show the hemodynamic impact of the tumor on mitral inflow causing functional mitral stenosis. Transesophageal echocardiography **[D]** shows the tumor adherence to the interatrial septum in the region of the fossa ovalis which is characteristic of left atrial myxoma. In this case, understanding the typical location of left atrial myxomas helped to narrow the differential diagnosis.



function while others invade the conduction system or myocardium leading to arrhythmias or cause systemic and/or pulmonary embolic phenomenon [7]. Location is extremely important in narrowing the differential diagnosis. Some benign primary tumors have typical locations [Figure 2]. For example, myxomas are typically found in the left atrium attached to the interatrial septum in the region of the fossa ovalis, and papillary fibroelastomas are usually found on the downstream side of the valves [8,9]. Malignant angiosarcomas are known to be large and infiltrate the right atrium [10]. The age of the patient can also help narrow the differential, as rhabdomyomas and fibromas are the most common benign cardiac tumors in children [11]. Unfortunately, cardiac tumors do not always adhere to the rules, and while these guidelines are helpful to acquire a differential diagnosis, tumors can still present with unexpected patterns.

**PRIMARY CARDIAC TUMORS ARE VERY RARE**

## CARDIAC IMAGING

Cardiac imaging plays a critical role in the evaluation of cardiac tumors. Quite often more than one imaging test is performed. Many cardiac tumors are first discovered on transthoracic echocardiogram (TTE) and then further characterized with advanced cardiac imaging such as cardiac magnetic resonance imaging (CMR), cardiac computed tomography (CT), and $^{18}$F-fluorodeoxyglucose positron-emission tomography/computed tomography ($^{18}$F-FDG PET/CT). Regardless of the imaging modality selected, the goals of cardiac imaging in evaluating a cardiac tumor are to determine the origin and size of the tumor, its borders, any hemodynamic impact, and its proximity to other cardiac and vascular structures. The latter can be useful in planning surgical resection. Last, imaging offers a means of assessing results post-resection, evaluating response to chemotherapy, or providing surveillance for reoccurrence. While the gold standard for tumor diagnosis is tissue biopsy, use of multimodality cardiac imaging can certainly refine the differential diagnosis in a noninvasive manner. Each imaging modality adds value in a unique way.

**CARDIAC IMAGING CAN HELP REFINE THE DIFFERENTIAL DIAGNOSIS OF CARDIAC TUMORS IN A NONINVASIVE MANNER BY EVALUATING TUMOR SIZE AND LOCATION, EXTENT OF INVASION, AND TISSUE CHARACTERIZATION INCLUDING PERFUSION**

### *Echocardiogram*

Two-dimensional (2D)-TTE is frequently the first step in the diagnostic evaluation of cardiac tumors due to its portability and widespread accessibility. It rapidly assesses tumor size, location, and hemodynamic consequence without using any ionizing radiation. However, the technique is limited in patients with poor acoustic windows, and the evaluation of peripheral vessels and extracardiac structures is constrained by the sector size [12]. With 2D-TTE and transesophageal echocardiography (TEE) one must mentally reconstruct a 3-dimensional (3D) structure from a series of 2D images. However, real time three-dimensional echocardiography (RT3DE) uses a volumetric method to capture the entire cardiac mass. The 3D dataset permits tumor visualization in any orientation, provides a more accurate assessment of size, shape and attachment point of the lesion as well as insight into the composition of the mass [13]. Transillumination (TI) is a new 3D echocardiographic imaging tool that uses freely movable virtual light source to enhance the contour and dimensionality of cardiac a mass [14]. While RT3DE allows for 3D rendering of the image, it is still displayed on a 2D monitor. Current studies are evaluating the feasibility of virtual reality (VR) to create true 3D visualization, which could translate to improved measurements of masses and conceivably be used in surgical and treatment planning [15]. Unfortunately, 2D-TTE, 3D-TTE, 2D-TEE, and 3D-TEE have limited ability to evaluate perfusion or other tissue characteristics of cardiac masses [12,16]. For this type of image, one must harness the advantages of advanced cardiac imaging modalities.

### *Cardiac magnetic resonance imaging*

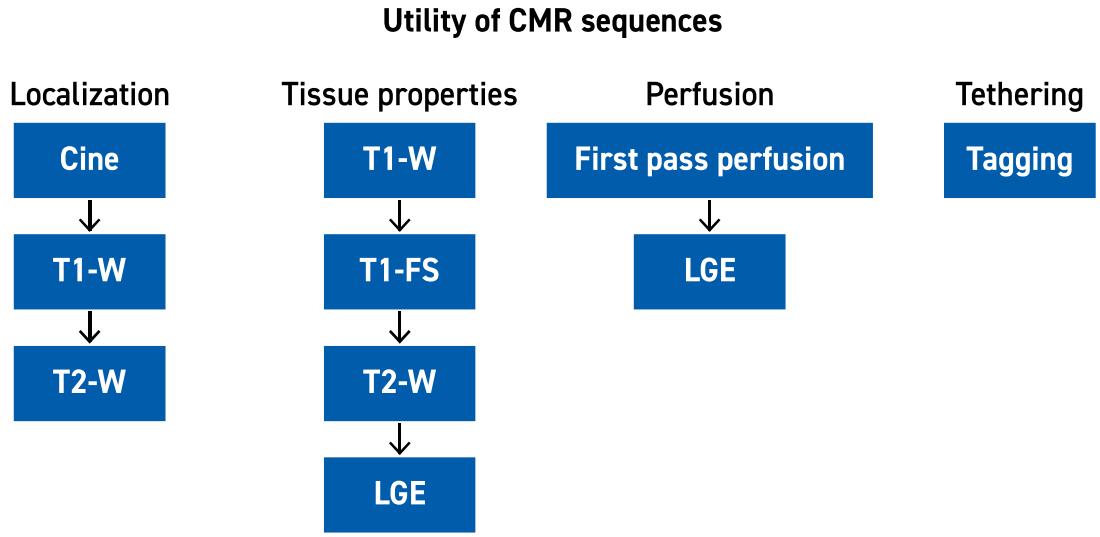
CMR allows for multiplanar imaging without restrictions on the field of view. CMR sequences are harnessed to enable localization, extension, and tissue characterization including perfusion [Figure 3]. When evaluating a cardiac tumor, features that favor a malignant lesion include size > 5 cm, involvement of more than one cardiac chamber, presence of pericardial or pleural effusions, extension into mediastinum or great vessel, and presence of perfusion [17,18]. Once the tumor is localized, T1-weighted, T2-weighted, and gadolinium-enhanced sequences provide information about tissue characterization. For example, cardiac masses have typical patterns on T1-T2-weighted imaging that can be used to help identify the tumor type, although not all tumors always adhere to these patterns [17]. Moderate or strong late gadolinium enhancement (LGE) or heterogenous LGE favors malignancy [19,20]. Last, with cine imaging and tagging, a tumor's functional impact on the myocardium and valves can be assessed. Disadvantages of CMR include its contraindication with older generation cardiac devices and also the need for electrocardiographic gating, which in the presence of an arrhythmia can lead acquisition artifacts and poor image quality [19,21]. CMR evaluation is also hampered when a cardiac tumor is calcified, a situation where cardiac CT may be more fruitful [19].

### *Cardiac CT*

Cardiac CT is a valuable imaging modality to evaluate cardiac tumors when other techniques are non-diagnostic or contraindicated. Electrocardiogram gating, which reduces artifact from cardiac motion, and submillimeter spatial resolution lead to high quality multiplanar images that can be obtained rapidly [22,23]. Cardiac CT is ideal for calcified masses. It is also helpful for

**Figure 3.** Use of cardiac magnetic resonance imaging for tumor characterization. Cine imaging is used to first localize a tumor within the heart and to assess its T1-weighted and T2-weighted properties in a multiplanar fashion. Malignant tumors tend to have longer T1 and T2 relaxation times due to high free water content compared to normal cells. Certain tumors have characteristic T1 and T2 properties that help to narrow the differential diagnosis. The behavior of a mass on first pass perfusion and the presence or absence of late gadolinium enhancement within it often determine whether the mass is vascularized as expected with a tumor, or rather a collection of necrotic or thrombotic material. Lastly, the adherence of a tumor to surrounding structures is assessed by myocardial tagging, which can be important when planning surgical resection.

T1-W = T1 weighted, T2-W = T2 weighted, FS = fat saturation, LGE = late gadolinium enhancement




pre-operative planning by showing the relationship of the tumor to surrounding vascular and extra-cardiac structures while also evaluating for coronary artery disease [23]. However, cardiac CT achieves this result using ionizing radiation and contrast agents. This technique lacks the temporal resolution and tissue characterization features of CMR, which spares the patient ionizing radiation [22].

### *$^{18}$F-fluorodeoxyglucose positron-emission tomography/computed tomography*

$^{18}$F-FDG PET/CT assesses the metabolic activity of a mass, which can help differentiate between benign and potentially malignant etiologies. It is frequently employed in the diagnosis and staging of non-cardiac malignancies and in treatment planning. Most such studies are not performed under any specific dietary instructions as they are not needed for this indication. However, if using $^{18}$F-FDG PET/CT to evaluate cardiac tumors, the European Association of Nuclear Medicine guidelines recommend a low-carbohydrate diet 24 hours prior to a $^{18}$F-FDG PET/CT scan [24]. This diet restriction shifts the myocardial metabolism toward fatty acid consumption and prevents false positive results that might otherwise arise from failure to suppress carbohydrate metabolism [24]. While there are no large-scale studies evaluating the diagnostic value to $^{18}$F-FDG PET/CT for cardiac tumors, reports on its utility in differentiating malignant from benign cardiac tumors based on standardized uptake values and target blood pool ratios are emerging from small case series [25-27]. While this technique may have an expanded role for cardiac tumor imaging in the future, the dietary preparation can be limiting for some. In addition, radiation exposure associated with $^{18}$F-FDG PET/CT is a consideration, particularly if done as a stand-alone procedure and not in combination with extra-cardiac PET scans already being performed as part of patient's oncological assessment.

**CARDIAC IMAGING IS USEFUL FOR SURGICAL PLANNING AND POST-CANCER TREATMENT ASSESSMENT**

## CONCLUSIONS

Although cardiac tumors are rare, it is important to recognize the clinical presentation and typical location for the more common tumor types. Many imaging tools are available to aid in the evaluation of cardiac tumors, each with specific features that can be harnessed to considerably narrow the differential diagnosis. Transthoracic and transesophageal 2D- and 3D-echocardiography and CMR are the most commonly deployed, providing key information on tumor location, size, extent, and tissue characterization. The lack of ionizing radiation for both CMR and TTE make them sensible initial choices not only for diagnostic assessment but also for surgical planning and post-treatment assessment.

**Correspondence**

**Dr. J.M. DeCara**
Dept. of Medicine, Section of Cardiology, University of Chicago Medicine, Chicago, IL 60637, USA
**Phone:** (1-773) 834-7354
**Fax:** (1-773) 702-1034
**email:** jdecara@medicine.bsd.uchicago.edu

## References

1. Leja MJ, Reardon, MJ. A Review of Malignant Primary Cardiac Tumors. *Am Coll Cardiol* 2018 [Available from https://www.acc.org/latest-in-cardiology/articles/2018/04/20/08/41/a-review-of-malignant-primary-cardiac-tumors].
2. Habertheuer A, Laufer G, Wiedemann D, et al. Primary cardiac tumors on the verge of oblivion: a European experience over 15 years. *J Cardiothorac Surg* 2015; 10 (1): 56.
3. Cresti A, Chiavarelli M, Glauber M, et al. Incidence rate of primary cardiac tumors: a 14-year population study. *J Cardiovasc Med (Hagerstown)* 2016; 17 (1): 37-43.
4. Butany J, Leong SW, Carmichael K, Komeda M. A 30-year analysis of cardiac neoplasms at autopsy. *Can J Cardio* 2005; 21 (8): 675-80.
5. Goldberg AD, Blankstein R, Padera RF. Tumors metastatic to the heart. *Circulation* 2013; 128 (16): 1790-4.
6. Patel JK, Didolkar MS, Pickren JW, Moore RH. Metastatic pattern of malignant melanoma: a study of 216 autopsy cases. *Am J Surg* 1978; 135 (6): 807-10.
7. Yanagawa B, Mazine A, Chan EY, et al. Surgery for tumors of the heart. *Semin Thorac Cardiovasc Surg* 2018; 30 (4): 385-397.
8. Karabinis A, Samanidis G, Khoury M, Stavridis G, Perreas K. Clinical presentation and treatment of cardiac myxoma in 153 patients. *Medicine* 2018; 97 (37): e12397.
9. Ikegami H, Andrei A-C, Li Z, McCarthy PM, Malaisrie SC. Papillary fibroelastoma of the aortic valve: analysis of 21 cases, including a presentation with cardiac arrest. *Tex Heart Inst J* 2015; 42 (2): 131-5.
10. Patel SD, Peterson A, Bartczak A, et al. Primary cardiac angiosarcoma - a review. *Med Sci Monit* 2014; 20: 103-9.
11. Delmo Walter EM, Javier MF, Sander F, Hartmann B, Ekkernkamp A, Hetzer R. Primary cardiac tumors in infants and children: surgical strategy and long-term outcome. *Ann Thorac Surg* 2016; 102 (6): 2062-9.
12. Buckley O, Madan R, Kwong R, Rybicki FJ, Hunsaker A. Cardiac masses, part 1: imaging strategies and technical considerations. *AJR Am J Roentgenol* 2011; 197 (5): W837-41.
13. Zaragosa-Macias E, Chen MA, Gill EA. Real time three-dimensional echocardiography evaluation of intracardiac masses. *Echocardiography* 2012; 29 (2): 207-19.
14. Genovese D, Addetia K, Kebed K, et al. First clinical experience with 3-dimensional echocardiographic transillumination rendering. *JACC: Cardiovasc Imaging* 2019; 12 (9): 1868-71.
15. Narang A, Hitschrich N, Mor-Avi V, et al. Virtual reality analysis of three-dimensional echocardiographic and cardiac computed tomographic data sets. *J Am Soc Echocardiogr* 2020; 33 (11): 1306-15.
16. Kirkpatrick James N, Wong T, Bednarz James E, et al. Differential diagnosis of cardiac masses using contrast echocardiographic perfusion imaging. *J Am Coll Cardiol* 2004; 43 (8): 1412-19.
17. Jeong D, Patel A, François CJ, Gage KL, Fradley MG. Cardiac magnetic resonance imaging in oncology. *Cancer Control* 2017; 24 (2): 147-60.
18. Kassi M, Polsani V, Schutt RC, et al. Differentiating benign from malignant cardiac tumors with cardiac magnetic resonance imaging. *J Thorac Cardiovasc Surg* 2019; 157 (5): 1912-1922.e2.
19. Sparrow PJ, Kurian JB, Jones TR, Sivananthan MU. MR Imaging of cardiac tumors. *Radiographics.* 2005; 25 (5): 1255-76.
20. Mousavi N, Cheezum MK, Aghayev A, et al. Assessment of cardiac masses by cardiac magnetic resonance imaging: histological correlation and clinical outcomes. *J Am Heart Assoc* 2019; 8 (1): e007829.
21. Tyebally S, Chen D, Bhattacharyya S, et al. Cardiac tumors. *JACC: CardioOncology.* 2020; 2 (2): 293-311.
22. Liddy S, McQuade C, Walsh KP, Loo B, Buckley O. The assessment of cardiac masses by cardiac ct and cmr including pre-op 3d reconstruction and planning. *Curr Cardiol Rep* 2019; 21 (9): 103.
23. Kassop D, Donovan MS, Cheezum MK, et al. Cardiac masses on cardiac CT: A Review. *Curr cardiovasc imaging rep* 2014; 7 (8): 9281.
24. Boellaard R, Delgado-Bolton R, Oyen W, Giammarile F, Tatsch K, Eschner W. European Association of Nuclear Medicine (EANM). FDG PET/CT: EANM procedure guidelines for tumour imaging: Version 2.0. *Eur J Nucl Med Mol Imaging* 2015; 42: 328-54.
25. Meng J, Zhao H, Liu Y, et al. Assessment of cardiac tumors by (18)F-FDG PET/CT imaging: Histological correlation and clinical outcomes. *J Nucl Cardiol* 2021; 28 (5): 2233-43.
26. Rahbar K, Seifarth H, Schäfers M, et al. Differentiation of malignant and benign cardiac tumors using $^{18}$F-FDG PET/CT. *J Nucl Med* 2012; 53 (6): 856-63.
27. Shao D, Wang S-X, Liang C-H, Gao Q. Differentiation of malignant from benign heart and pericardial lesions using positron emission tomography and computed tomography. *J Nucl Cardiol*2011; 18 (4): 668-77.

Capsule

## AAV gene therapy for Tay-Sachs disease

Tay-Sachs disease (TSD) is an inherited neurological disorder caused by deficiency of hexosaminidase A (HexA). **Flotte** and colleagues described an adeno-associated virus (AAV) gene therapy expanded-access trial in two patients with infantile TSD (IND 18225) with safety as the primary endpoint and no secondary endpoints. Patient TSD-001 was treated at 30 months with an equimolar mix of AAVrh8-HEXA and AAVrh8-HEXB administered intrathecally (i.t.), with 75% of the total dose (1 × 1014 vector genomes (vg)) in the cisterna magna and 25% at the thoracolumbar junction. Patient TSD-002 was treated at 7 months by combined bilateral thalamic (1.5 × 1012 vg per thalamus) and i.t. infusion (3.9 × 1013 vg). Both patients were immunosuppressed. Injection procedures were well tolerated, with no vector-related adverse events (AEs) to date. Cerebrospinal fluid (CSF) HexA activity increased from baseline and remained stable in both patients. TSD-002 showed disease stabilization by 3 months after injection with ongoing myelination, a temporary deviation from the natural history of infantile TSD, but disease progression was evident at 6 months after treatment. TSD-001 remains seizure-free at 5 years of age on the same anticonvulsant therapy as before therapy. TSD-002 developed anticonvulsant-responsive seizures at 2 years of age. This study provides early safety and proof-of-concept data in humans for treatment of patients with TSD by AAV gene therapy.

*Nature Med* 2022; 28: 251
Eitan Israeli