The role of cardiac MRI is growing in the management of cardiotoxicity associated with therapies used to treat cancer.

Cardiac Magnetic Resonance Imaging in Oncology
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Background: Cardiac magnetic resonance imaging (MRI) is emerging as an important diagnostic modality in the management of cardiovascular-related dysfunction in oncological diseases. Advances in imaging techniques have enhanced the detection and evaluation of cardiac masses; meanwhile, innovative applications have created a growing role for cardiac MRI for the management of cardiotoxicity caused by cancer therapies. Methods: An overview is provided of the clinical indications and technical considerations of cardiac MRI. Its role in the evaluation of cardiac masses and cardiac function is reviewed, and novel sequences are discussed that are giving rise to future directions in cardio-oncology research. A review of the literature was also performed, focusing on cardiac MRI findings associated with cardiac dysfunction related to cancer treatment.

Results: Cardiac MRI can be used to differentiate benign and malignant primary cardiac tumors, metastatic disease, and pseudotumors with high spatial and temporal resolution. Cardiac MRI can also be used to detect the early and long-term effects of cardiotoxicity related to cancer therapy. This is accomplished through a multiparametric approach that uses conventional bright blood, dark blood, and postcontrast sequences while also considering the applicability of newer T1 and T2 mapping sequences and other emerging techniques.

Conclusions: Cardio-oncology programs have an expanding presence in the multidisciplinary approach of cancer care. Consequently, knowledge of cardiac MRI and its potential applications is critical to the success of contemporary cancer diagnostics and cancer management.

Introduction
Cardiac magnetic resonance imaging (MRI) is emerging as an important diagnostic modality in the management of cardiovascular-related dysfunction in oncological diseases. With survival rates becoming longer in patients with cancer and in those with chronic cardiovascular disease, new strategies are being developed to manage the increasing overlap between these groups of patients. Cardio-oncology programs have an expanding presence in the multidisciplinary approach to cancer care. Thus, knowledge of cardiac MRI and its potential applications is important to the success of contemporary oncological diagnosis and management.

Expert consensus published in 2010 on cardiac MRI includes several important indications related to oncological evaluation and monitoring. Cardiac MRI may be used to characterize tissue within cardiac masses and may aid in the early differentiation be-
between cardiac pseudotumors, benign or malignant cardiac tumors, and thrombi. Furthermore, cardiac MRI can help the health care professional characterize extracardiac structures, including pericardial masses, and delineate the physiological sequelae of tissue involvement such as pericardial constriction.

In patients with heart failure or nonischemic heart disease, cardiac MRI is indicated to quantitatively evaluate chamber size, ventricular mass and morphology, wall motion abnormalities, and systolic and diastolic function. These evaluations are useful in patients with cardiomyopathies related to cardiotoxicity or infiltrative diseases, including amyloidosis or sarcoidosis. Patients receiving chemotherapy who frequently receive blood transfusions are at risk for iron overload, which may also be evaluated with cardiac MRI. In patients with cancer and comorbid, chronic cardiovascular conditions, such as coronary artery disease and ischemic heart disease, cardiac MRI may be used to assess for myocardial viability, necrosis, and scar tissue, and can be used to identify subendocardial ischemic processes. Structural abnormalities, including coronary artery anomalies and valvular disorders, can also be evaluated. In pediatric patients with cancer, cardiac MRI may be an important adjunct for assessing congenital heart disease without exposing these children to ionizing radiation.

Cardiac MRI can assess a range of parameters and provides advantages over other imaging modalities. Most pulse sequences of cardiac MRI can achieve spatial resolutions of 1 × 1 × 3 mm voxel size and temporal resolutions of 20- to 40-millisecond frame rates with cine sequences (Table). In addition, studies have shown high reproducibility rates and low variance of quantitative measures of cardiac MRI across different observers, scanners, and institutions. Although a description of the underlying physics and components of pulse sequences for imaging are beyond the scope of this article, sequences of cardiac MRI can generally be categorized into bright blood (gradient echo-based or steady-state free precession [SSFP] acquisition) or dark blood (inversion recovery or spin echo acquisition) imaging sequences. Cine bright-blood imaging sequences are optimally used to assess cardiac function, ventricular mass and volume, myocardial perfusion, and blood flow. Dark-blood imaging sequences, including T1-weighted, T2-weighted, and gadolinium-enhanced sequences, are used to assess cardiac and tumor morphology. Standard cardiac MRI takes approximately 1 hour at 1.5 T or 3 T and involves localizers, cine SSFP left ventricular (LV) short- and long-axis (2-, 3-, and 4-chamber) views, and postcontrast delayed viability imaging. In oncological imaging, T2-weighted, fast-spin echo or inversion recovery gradient echo and T1-weighted fast-spin echo sequences allow further lesion characterization. When lesions involve the right ventricle (RV), axial cine SSFP will offer RV structure and function evaluation. First-pass arterial perfusion offers vascularity evaluation of the suspected tissue. Refer to the Table for indications of each sequence of cardiac MRI.

Compared with imaging modalities — including fludeoxyglucose F 18 positron emission tomography, thallium Tl 201, single-photon emission computed tomography (CT), CT alone, and echocardiography — cardiac MRI allows the qualitative and quantitative assessment of cardiac anatomy, function, perfusion, and tissue characteristics in a single examination. It avoids exposing patients to ionizing radiation, radioactive isotopes, or iodinated contrast with highly reproducible, noninvasive imaging that has significant advantages over alternative imaging modalities. Cardiac MRI also offers superior tissue characterization, with high spatial and temporal resolution and multiplanar imaging with a larger field of view, that can be performed in patients of various body habitus.

Limitations of cardiac MRI include the time necessary for the examination, reactions to contrast media, and its cost. The need for breath holds and electrocardiographical gating can also reduce image quality, particularly in patients with poor pulmonary reserve or in the presence of arrhythmias. Patients who have claustrophobia and those with non–MRI-compatible medical devices may be unable to undergo cardiac MRI. Cardiac MRI also has limited abilities for the detection of calcium in the coronary arteries; thus, it should be used in conjunction with other modalities if the presence of calcium is being investigated.

Evaluation of Cardiac Masses

Cardiac masses can be categorized as primary cardiac tumors, secondary or metastatic cardiac tumors, intracavitary thrombus, or cardiac pseudotumors. Primary cardiac tumors are rare and typically benign, whereas metastatic masses are approximately 40 times more prevalent than primary cardiac tumors. Cardiac MRI allows for accurate tissue characterization and localization of cardiac masses, and it can be used to help the health care professional determine the extent of involvement and functional impact of the mass. In a study evaluating 59 patients with cardiac masses, Zhu et al reported 96% accuracy in differentiating benign from malignant tumors and 100% accuracy in differentiating neoplasms from pseudotumors when using cardiac MRI compared with pathological examination. Hoffman et al showed that characteristics on MRI, including location, tissue composition, and associated pleural or pericardial effusions, have a diagnostic accuracy of 0.92 (area under curve) for diagnosing a cardiac or paracardiac mass as malignant. The superior tissue characterization of cardiac MRI can inform clinical decision-making and help to risk stratify patients for surgical resection, chemo-
therapy, or observation.17

Cardiac masses are best characterized using T1- and T2-weighted fast-spin echo in addition to multiplanar cine SSFP for LV and RV structure and function.12 First-pass perfusion imaging through the mass provides the clinician with real-time evaluation of regional tissue perfusion, whereas late, gadolinium-enhanced imaging has added sensitivity for the

| Table. — Sequences of Cardiac Magnetic Resonance Imaging |
|---------------------------------|-----------------|----------------|-----------------|
| Sequence                        | Indication      | Approximate Spatial Resolution | Temporal Resolution | Comment                                                                 |
| Basic                           |                 |                               |                  |                             |
| Cine SSFP                       | Structural and functional evaluation | 1.4–1.8 mm² | ≤ 50 ms | Bright-blood sequence used to assess cardiac function and effect of tumor on cardiac function |
| Inversion recovery              | Late gadolinium enhancement | 1.4–1.8 mm² | NA | Used to identify areas of myocardial fibrosis or infiltration. Phase sensitive and black-blood preparation versions potentially more robust |
| Additional                      |                 |                               |                  |                             |
| T2-weighted, double-inversion recovery | Tissue characterization | 1.4–1.8 mm² | NA | Black-blood sequence used to characterize masses and detect the presence of water or edema |
| T2-weighted, triple-inversion recovery | Tissue characterization | 1.4–1.8 mm² | NA | Black-blood sequence with fat suppression used to characterize masses and detect presence of water or edema |
| Myocardial tagging              | Cardiomyopathy evaluation myocardial strain | 1.3 × 2.0 mm | ≤ 50 ms | Used to assess regional wall motion, adherence of masses to the pericardium, constrictive pericarditis |
| Phase-contrast flow             | Congenital disease valvular disease | — | ≤ 50 ms | Analysis planes must be prospectively prescribed |
| T2*                             | Cardiac iron quantification | 1.6–3.0 mm² | NA | Repeated blood transfusions, primary hemochromatosis |
| T1-weighted                     | Tissue characterization | — | NA | Black-blood sequence used to characterize masses. Can be performed with fat saturation. Melanoma metastases are inherently hyperintense on T1-weighted imaging |
| First-pass arterial perfusion   | Tissue characterization | 1.8 × 1.8 × 8.0 mm | — | Saturation recovery sequence used to assess perfusion and early enhancement of masses. Can also be used to evaluate for myocardial ischemia |
| Contrast-enhanced MRA           | MRA             | 1.3 × 1.8 × 2.0 mm | NA | Timing of image acquisition based on vascular territory of interest (ie, pulmonary arteries for pulmonary embolism, aorta for acute aortic syndrome) |
| Emerging                        |                 |                               |                  |                             |
| T1 mapping                      | Native T1 and extracellular volume quantification | 2.1 × 1.1 × 8.0 mm | — | Used in myocardial characterization |
| T2 mapping                      | T2 signal can be altered by myocardial infarction or myocarditis | 2.6 × 2.1 × 8.0 mm | — | Limited utility because T2 relaxation sensitive to mild infections and large interpatient variability |
| 3D cine SSFP single-breath hold | Single breath-hold 3D cine short-axis sequence (< 22 sec) vs > 8.5 min standard 2D cine SSFP, including pauses² | 2.0 × 2.0 mm in-plane | 36–70 ms² | Could have a role in cardiotoxicity left ventricular evaluation. Shorter time, no radiation exposure compared with MUGA |
| 4D flow magnetic resonance      | Advanced multiplanar flow analysis and visualization | 1.3 mm isotropic³ | — | Allows retrospective phase-contrast analysis |
| CMR/FDG PET fusion              | Evaluation of myocardial perfusion imaging, localization, and differentiation of tumors | CMR: 1.4–1.8 mm² PET: 5–8 mm² | ≤ 50 ms | — |

*Depends on body habitus and scanner prescription.

⁴Based on heart rate.

²Using phase contrast vastly undersampled isotropic projection reconstruction.

⁵Using phase contrast vastly undersampled isotropic projection reconstruction.

2D = 2-dimensional, 3D = 3-dimensional, 4D = 4-dimensional, CMR = cardiac magnetic resonance, FDG = fludeoxyglucose F 18, MRA = magnetic resonance angiography, MUGA = multigated acquisition, NA = not applicable, PET = positron emission tomography, SSFP = steady-state free precession.
evaluation of soft-tissue enhancement. Additional techniques, such as myocardial tagging utilizing radiofrequency prepulses, can be used to evaluate secondary myocardial dysfunction or strain potentially arising from large or invasive masses.

Benign Primary Cardiac Tumors

**Myxoma:** Myxomas are the most common type of benign cardiac tumor, typically presenting between the fourth and seventh decades of life with a classic triad of cardiac obstructive symptoms, embolic events, and constitutional symptoms such as fever, weight loss, and dyspnea. Most myxomas are solitary masses found in the left atrium, and they often arise from the interatrial septum. These masses appear heterogeneous, containing myxomatous tissue originating from primitive mesenchymal cells with mucoid and other elements. Myxomatous tissue is hypointense relative to myocardium on T1-weighted imaging. Depending on the degree of associated fibrous tissue, myxomas can have a heterogenous, T2-weighted appearance. Areas of intratumoral hemorrhage may be hypointense or hyperintense. Cine bright-blood imaging sequences reveal characteristic mobility associated with myxomas, with the masses typically hyperintense relative to the myocardium and hypointense or isointense relative to the blood pool on SSFP. Myxomas demonstrate heterogeneous enhancement and calcify approximately 50% of the time when found in the right atrium.

**Papillary Fibroelastoma:** Papillary fibroelastomas are benign endocardial lesions that predominantly affect cardiac valves. These are the second most common benign primary cardiac tumor and account for 75% of all cardiac valvular tumors. Although these lesions are generally asymptomatic, tumor fragments or surface thrombus can result in embolic events leading to stroke, pulmonary embolism, or myocardial infarction. Papillary fibroelastomas are typically small (<1.5 cm), mobile, pedunculated masses arising from valve leaflets or the endocardium. They demonstrate a hypointense signal on SSFP and T2-weighted sequences due to their high fibrous content; however, this can make differentiating fibroelastomas from thrombus difficult. In certain cases, valvular location, papillary contour, and small

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**Fig 1A–F.** — (A) Axial- and (B) short-axis steady-state free precession, bright-blood imaging demonstrates an irregular mass involving the right atrial wall extending into the right atrial cavity and pericardial space (white arrows). Asterisks indicate moderate pericardial effusion. (C) Axial T2 spectral presaturation with inversion recovery, dark-blood imaging shows heterogeneous increased signal within the mass. (D) Axial-arterial phase, first-pass perfusion imaging shows peripheral rim enhancement in the mass suggestive of a vascularized tumor. (E) Short-axis, late gadolinium-enhanced imaging shows minimal central enhancement of the mass. (F) Axial positron emission tomography/computed tomography fused imaging shows peripheral increased metabolic activity in the mass. The extension of the mass into multiple cardiac compartments with heterogeneous, high T2 signal, and enhancement support the diagnosis of primary cardiac angiosarcoma.
size may offer support in diagnosing fibroelastomas. When they are large in size, fibroelastomas can result in turbulent flow, which can be observed on cine SSFP.

**Lipoma:** Typically, lipomas are incidentally discovered, and they occur across a wide range of ages. They have a homogeneous appearance with encapsulated tissue that is hyperintense on T1-weighted imaging and less hyperintense on T2-weighted imaging. Lipomas demonstrate signal intensity similar to subcutaneous or mediastinal fat on fat-saturated imaging and do not show enhancement after the administration of contrast. These lesions usually arise from the epicardial surface, but they can extend to the pericardial region; they do not warrant intervention if the patient is asymptomatic. Rarely, however, giant lipomas can lead to symptomatic obstruction that warrants resection — this is particularly true if the pericardial space is involved.

**Rhabdomyoma:** Rhabdomyomas are the most common benign cardiac tumor in children and are usually asymptomatic; however, they are often associated with tuberous sclerosis. Most cases of rhabdomyomas present with multiple masses predominately found in the ventricles. Rhabdomyomas can extend into the ventricular cavities and cause obstruction; however, most remain asymptomatic and spontaneously regress by 4 years of age. These masses appear isointense to the myocardium on T1-weighted imaging and hyperintense on T2-weighted imaging, without enhancement after the administration of gadolinium contrast.

**Fibroma:** Fibromas are the second most common congenital cardiac tumor seen in infants and children, with clinical presentations ranging from asymptomatic to heart failure and ventricular arrhythmias. Typically, fibromas are located within the ventricular walls, but they can be seen in the atria, particularly when associated with polyposis syndromes. On T1-weighted imaging, these masses typically appear as solitary masses that have a T1-weighted isointense or hypointense signal, whereas they characteristically appear homogeneously hypointense on T2-weighted imaging. Following the administration of gadolinium contrast, fibromas do not enhance during perfusion but will show intense enhancement on late gadolinium-enhanced imaging.

**Hemangioma:** Cardiac hemangiomas present in a wide variety of ages, often with dyspnea on exertion;
Fig 4A–F. — Prior to anticoagulation, (A) axial- and (B) short-axis SSFP, bright-blood imaging demonstrate a well-defined, low-signal structure in the right atrium (arrow). (C) T2 spectral presaturation with inversion-recovery axial, dark-blood imaging demonstrates heterogeneous, T2 hyperintensity in the mass. (D) T1 axial, precontrast, fat-saturated imaging demonstrates an isointense to mildly increased T1 signal within the mass. (E) Early and (F) later dynamic, first-pass perfusion imaging show peripheral rim enhancement of the mass. Increased T1 signal within a mass is a distinguishing feature of melanoma metastases, the diagnosis in this case.

Fig 3A–F. — (A) Long-axis, 4-chamber, and (B) axial steady-state free precession, bright-blood imaging show a lobulated mass arising from the lateral right atrial wall. (C) T2 spectral presaturation with inversion-recovery axial, dark-blood imaging demonstrates heterogeneous, T2 hyperintensity in the mass. (D) T1 axial, precontrast, fat-saturated imaging demonstrates an isointense to mildly increased T1 signal within the mass. (E) Early and (F) later dynamic, first-pass perfusion imaging show peripheral rim enhancement of the mass. Increased T1 signal within a mass is a distinguishing feature of melanoma metastases, the diagnosis in this case.
however, they can also be asymptomatic.\textsuperscript{28,29} Hemangiomas appear heterogeneous, with isointensity or hypointensity on T1-weighted imaging and are typically hyperintense on T2-weighted imaging.\textsuperscript{30,31} Following intravenous contrast, a heterogeneous-enhancement pattern has been reported.\textsuperscript{5,30} Cardiac hemangiomas have also been described as having flow voids on T2-weighted imaging with calcifications best seen on CT.\textsuperscript{32}

**Malignant Primary Cardiac Tumors**

Findings suggestive of primary malignant or metastatic cardiac tumors include a diameter of more than 5 cm, invasive behavior with irregular borders, right-sided or pericardial involvement, tissue heterogeneity on T1- and T2-weighted imaging, a broad base of attachment, enhancement after the administration of gadolinium contrast, and associated hemorrhagic pericardial or pleural effusions.\textsuperscript{10,13,15,33}

**Angiosarcoma:** Among primary cardiac malignancies, cardiac angiosarcoma is the most common in adults.\textsuperscript{34} Angiosarcomas are often found in the right atrium, but they are usually metastatic at the time of presentation.\textsuperscript{34,35} Clinically, patients present with symptoms related to right-sided heart failure, hemorrhagic pericardial effusions, and tamponade.\textsuperscript{10,13,15} These tumors appear as a large, heterogeneous, broad-based mass with mixed signal intensity on T1-weighted imaging and a predominantly hyperintense signal on T2-weighted imaging.\textsuperscript{35,36} Following the administration of gadolinium, these tumors are typically heterogeneous with marked surface enhancement and central areas of necrosis; on SSFP, they are predominantly hyperintense relative to the myocardium.\textsuperscript{37} In addition, the postcontrast appearance of cardiac angiosarcomas has, rarely, been described as having a “sun-ray” configuration of enhancement when extensive pericardial involvement is present; the “rays” are radially oriented, enhancing lines that extend from the epicardium to the pericardium separated by nonenhancing pericardial regions.\textsuperscript{38,39} Fig 1 demonstrates the typical features of primary cardiac angiosarcoma.

**Rhabdomyosarcoma:** Rhabdomyosarcoma is the most common primary cardiac malignancy in children.\textsuperscript{40} Symptoms of heart failure may be present, and the tumors may involve multiple sites such as the valves without any definite chamber predominance.\textsuperscript{40} These tumors appear as an infiltrative mass with irregular margins isointense relative to the myocardium on T1-weighted imaging.\textsuperscript{41} After the administration of contrast, these masses typically show homogeneous enhancement, although areas of hypointense necrosis or hemorrhage may be observed within the tumor.\textsuperscript{10,41}

**Other Sarcomas:** Other malignant primary cardiac tumors are usually sarcomatous in origin, and they may include undifferentiated sarcomas, leiomyosarcomas, fibrosarcomas, liposarcomas, and osteosarcomas.\textsuperscript{13,35} These tumors often present in adults in the fourth or fifth decade, and they commonly arise from the left atrium.\textsuperscript{29,42} Appearances on cardiac MRI may be heterogeneous on T1- and T2-weighted imaging, with variable contrast enhancement depending on their composition and the presence of necrosis or hemorrhage.\textsuperscript{10,43}

**Lymphoma:** Primary cardiac lymphomas are rare and have a poor prognosis; they often present with rapidly worsening heart failure, obstructive symptoms, or arrhythmias.\textsuperscript{44} Typically, lymphomas are of the non-Hodgkin B-cell type and found in the right atrium;
however, they may invade other cardiac chambers or the pericardium. Primary cardiac lymphomas are often characterized by multiple, infiltrative nodular masses that are isointense relative to the myocardium on T1-weighted imaging and heterogeneously hyperintense on T2-weighted imaging. They can also demonstrate diffuse pericardial infiltration with an associated hemorrhagic pericardial effusion. Following the administration of gadolinium contrast, they show heterogeneous enhancement with areas of low enhancement centrally relative to the periphery.

Metastatic Cardiac Tumors
Metastatic cardiac tumors are significantly more common than primary cardiac malignancies. Autopsy studies have shown that known malignant neoplasms also have cardiac metastases in 10% to 12% of cases. The neoplasms that most commonly metastasize to the heart include melanoma, bronchogenic carcinoma, lymphoma, leukemia, breast carcinoma, and esophageal carcinoma. Metastatic disease may spread to the heart by direct invasion or via hematological, retrograde lymphatic, or transvenous spread. The pericardium is most often involved, although one-third of patients with metastatic cardiac involvement will die due to pericardial tamponade, congestive heart failure, or coronary artery invasion. Patients may present with dyspnea, angina, obstructive symptoms, or arrhythmia. Although metastatic lesions in the heart do not have exclusive appearances on cardiac MRI, they generally demonstrate low T1- and high T2-weighted signal with variable enhancement patterns (Fig 2). However, melanoma is an exception, because it has a high T1-weighted signal due to the presence of paramagnetic melanin (Fig 3). Metastatic lesions may demonstrate necrosis with peripheral enhancement. In patients with diffuse metastatic disease that also involves skeletal muscle, thoracic lesions may be useful to include in the examination.

Thrombus
Cardiac MRI may be used to characterize cardiac masses and can help the health care profession differentiate true cardiac tumors from thrombus. Thrombus more commonly occurs in the left atrium — especially in the setting of atrial fibrillation or dysfunctional left ventricles — and is often misinterpreted as atrial myxoma. Acute thrombus appears as intermediate to hyperintense on T1- and T2-weighted imaging. Subacute thrombus appears hyperintense on T1-weighted imaging with areas of hypointensity on T2-weighted imaging. Chronic thrombus appears hypointense on T1- and T2-weighted imaging (Fig 4). Although mild surface enhancement has been reported with organized thrombus, thrombus does not typically enhance, whereas true cardiac tumors often enhance following the administration of gadolinium contrast due to the presence of tumoral vascularity.

Cardiac Pseudotumors
Cardiac pseudotumors include anatomical structures such as prominent eustachian valves, the Chiari network, crista terminalis, and lipomatous interatrial septum that may mimic true cardiac tumors but can...
be distinguished by cardiac MRI.2,10,13,15 The Chiari network is an embryological remnant of mobile, fenestrated, fibrous threads commonly attached to the right atrial wall.5 The crista terminalis is a fibromuscular ridge separating the posterior right atrium and the trabeculated right atrial appendage (Fig 5).53 Lipomatous hypertrophy is characterized by hyperplasia of cardiac adipose tissue and can sometimes be mistaken for lipomas due to the similarities in fat content.13 Lipomatous hypertrophy is nonencapsulated and typically involves the limbus of the fossa ovalis with sparing of the fossa ovalis, thus creating a characteristic, bilobed, dumb-bell shape on cardiac MRI without enhancement and with a homogeneous, hyperintense signal on T1-weighted imaging.13,53 Lipomatous hypertrophy can take an atypical form with nodular fatty deposition along the coronary sinus or lateral right atrial wall that can mimic masses on echocardiography (Fig 6).

**Infiltrative Cardiomyopathies in Oncology**

Infiltrative cardiomyopathies are characterized by the deposition of abnormal substances within myocardial tissue leading to cardiac dysfunction.55 Additional cardiac abnormalities can arise, including ventricular wall thickening, chamber dilatation, and conduction disruption, which can lead to heart failure and arrhythmia.55 Cardiac amyloidosis and cardiac iron deposition are important infiltrative cardiomyopathies, which are encountered more frequently in patients with cancer.6,56 Although endomyocardial biopsy is the gold standard for diagnosing certain infiltrative cardiomyopathies, such as amyloidosis, typical features on cardiac MRI with a noncardiac tissue sample positive for amyloidosis can infer the diagnosis in cases where endomyocardial biopsy samples are not easily obtained.57 Moreover, the sensitivity rate of biopsies may be limited in early cardiac iron overload, which can have an uneven patchy distribution, and increases the utility for quantitative cardiac MRI in the diagnosis of cardiac iron overload.58

Amyloidosis is a heterogenous group of deposition diseases resulting in the extracellular accumulation of abnormal fibrillar protein deposits. Whereas cardiac MRI or echocardiography can show concentric LV wall thickening with bialtrial enlargement suggestive of nonspecific, underlying restrictive cardiomyopathy, cardiac MRI classically demonstrates circumferential, ventricular, late gadolinium enhancement with a subendocardial or transmural pattern more specific for amyloidosis (Fig 7).59 In addition, abnormal gadolinium kinetics seen particularly with amyloidosis leads to difficulty in myocardial nulling on late gadolinium-enhanced imaging. T1-mapping research has shown the expansion of extracellular volume fraction related to amyloid deposition and possible fibrosis.60

Cardiac iron overload is a leading cause of morbidity and mortality in patients receiving repeat blood transfusions and can be seen in certain patients with cancer.6,61 Patients who are transfusion dependent receive approximately 20 times the normal physiological iron intake.8 Excess iron is initially taken up by the reticuloendothelial system; however, once overwhelmed, iron is deposited into other organs such as the liver, spleen, and heart. Serum iron, transferrin, and ferritin levels show some correlation with liver iron levels but not with cardiac iron levels.62 In addition, liver iron...
stores do not reliably correlate with cardiac iron stores. Echocardiography cannot be used to directly detect iron overload, but it can detect secondary cardiac injury. Endomyocardial biopsy also offers iron quantification, but this procedure is prone to sampling error due to possible patchy iron deposition in early disease.

Cardiac MRI offers a reliable, noninvasive biomarker to evaluate cardiac iron stores. T2\* cardiac MRI allows quantification of cardiac iron level with a normal value of 52 ± 16 milliseconds at 1.5 Tesla. R2\* is the inverse signal sequence of T2\* and allows for a more accurate quantification of iron overload in severe disease, in which a brighter R2\* signal corresponds to iron overload (Fig 8). Regions of interest on T2*/R2* maps should be drawn over the interventricular septum to avoid susceptibility from the adjacent lung; susceptibility correction techniques have helped keep consistent measurements. Although early cardiac iron overload may present with restrictive cardiomyopathy, progressive disease can result in dilated cardiomyopathy with systolic dysfunction. When T2\* drops below 20 milliseconds due to cardiac iron overload, the LV ejection fraction (LVEF) has been shown to decrease with an associated increased mortality rate.

**Evaluation of Cardiac Function and Cardiotoxicity**

Although cardiac MRI has become a decisive modality for identifying and diagnosing cardiac masses, it also has a growing role in monitoring cardiac function in patients with cancer, especially in the setting of cardiotoxicity related to radiotherapy and chemotherapy. Although no universally accepted definition exists, an expert consensus statement from the American Society of Echocardiography and the European Association of Cardiovascular Imaging published in 2014 defined cardiac dysfunction related to use of cancer therapeutics as a decrease in LVEF of more than 10%, to a value below 53%, and confirmed by repeat cardiac imaging performed 2 to 3 weeks later. However, cardiovascular effects of chemotherapeutic agents may range from hypertension to arrhythmias and to ventricular dysfunction. The timing and severity of cardiac dysfunction associated with use of cancer therapeutics depend on the agent, dosing, and patient-related factors.

Among chemotherapeutic agents, anthracyclines were first recognized in the 1960s to cause irreversible cardiotoxicity, including cardiomyopathy and heart failure. Tyrosine kinase inhibitors such as erb-B2–positive targeted therapies and vascular endothelial growth factor inhibitors are often associated with reversible cardiotoxicity; in addition, irreversible dysfunction can also occur. Fluorouracil, taxanes, and methotrexate have been associated with myocardial ischemia and arrhythmia, and alkylating agents such as cyclophosphamide has been linked to heart failure, myopericarditis, and arrhythmia. Radiotherapy to the mediastinum with a cumulative dose of more than 30 Gy and a daily fractioning of more than 2 Gy may contribute to restrictive cardiomyopathy, accelerated atherosclerosis, valvular dysfunction, and pericardial effusion or constriction.

Using cardiac MRI, the earliest findings of cardiotoxicity can be seen within weeks of chemotherapy in the form of myocardial edema and decreased LVEF, which can be asymptomatic. LV short-axis, T2-weighted imaging will demonstrate an abnormal,
hyperintense myocardial signal in the setting of edema. T2-weighted signal ratios of myocardium to skeletal muscle have been proposed to detect edema that is not visually apparent.\textsuperscript{71} Chronic cardiotoxicity related to chemotherapy can present with further decreased LVEF, myocardial fibrosis, and a decreased LV mass index seen months to years following the use of chemotherapy.\textsuperscript{71} In addition, Ylanen et al\textsuperscript{72} showed that both RV and LV function can be decreased in the absence of focal myocardial fibrosis in long-term survivors of childhood cancer treated with anthracyclines, which raises the possibility of interdependence of the RV and LV with regard to anthracycline cardiotoxicity.

A pilot study of 22 patients by Wassmuth et al\textsuperscript{73} demonstrated that the use of early myocardial gadolinium contrast enhancement on fast-spin echo predicted a significant loss of ejection fraction at 28 days after anthracycline therapy (Fig 9). Myocardial fibrosis is also a common finding on cardiac MRI in patients with anthracycline-induced cardiac dysfunction.\textsuperscript{74} Jordan et al\textsuperscript{74} showed that changes in T1-weighted signal intensity could serve as an early marker of anthracycline-related subclinical injury, and Drafts et al\textsuperscript{75} showed low to moderate doses of anthracycline-based chemotherapy were associated with subclinical abnormalities of cardiac function. In a study of 114 adult survivors of childhood cancer who received anthracycline therapy, Armstrong et al\textsuperscript{76} found that 2-dimensional (2D) echocardiography had a sensitivity rate of 25% and a false-negative rate of 75% for detection of ejection fraction less than 50%. Given the increased sensitivity rate of cardiac MRI, Heck et al\textsuperscript{77} incorporated cardiac MRI to follow LV function in patients with breast cancer who were treated with adjuvant cardiotoxic chemotherapy and prophylactic angiotensin-receptor blockers or beta blockers. They found a higher detection rate of cardiac dysfunction by cardiac MRI compared with echocardiography, suggesting that cardiac MRI should be considered for survivors with an ejection fraction between 50% and 59% for more comprehensive cardiac assessment.\textsuperscript{1,76,77} Early radiation-related injury can present as myocarditis or pericarditis, whereas late radiation-related effects can manifest as coronary artery disease, myocardial fibrosis, restrictive cardiomyopathy, and pericardial effusions.\textsuperscript{39} A case of constrictive pericarditis following radiotherapy for esophageal cancer is shown in Fig 10.

**Future Directions**

Cardiac MRI has become an important tool in the evaluation of cardiac tissue and function, and further developments will continue to advance the role of cardiac MRI in the diagnosis and management of cardio-oncological diseases. Three-dimensional (3D) cine SSFP imaging allows LV functional analysis during 1 breath hold, which would reduce the short-axis LV series to 22 seconds from 8.5 minutes using 2D cine SSFP without sacrificing clinically significant imaging quality.\textsuperscript{7} Combination positron emission tomography/MRI is promising for evaluating myocardial perfusion as well as in the localization and differentiation of select tumors.\textsuperscript{13}

In addition to monitoring ventricular dysfunction, via T1-mapping techniques, cardiac MRI may be used to evaluate myocardial fibrosis sometimes seen in chemotherapy-induced cardiomyopathies and restrictive...
cardiomyopathy. T1 mapping and postcontrast extracellular volume can be used to quantify edema in acute coronary syndromes and the myocardial deposition of T1-altering substances, including amyloid, lipid, or protein. T2 mapping is a new technique based on a bright-blood T2-prepped SSFP sequence, which allows the quantification of myocardial T2 relaxation times. However, T2 mapping is limited by large interindividual variability of myocardial T2 relaxation times and relative rates of sensitivity to minor disturbances, including the common cold. Kubler et al showed how T1 and T2 mapping can be applied to characterize tissue within cardiac myxomas. Future studies may show an increasing role of T1 and T2 mapping in cardiac MRI for other oncological applications.

Four-dimensional flow MRI allows for the advanced evaluation of blood flow in the heart where blood flow velocities can be retrospectively quantified in any plane, and flow can be visualized in streamlines, resolved path lines, or vector graphs. Four-dimensional flow MRI could have an increasing role in scenarios in which cardiac or great vessel blood flow is compromised by a tumor. However, more studies are needed to determine the added benefits of these emerging cardiac MRI sequences in the management of cardio-oncological disease.

Conclusions
Imaging advances in cardiac magnetic resonance techniques have improved the rate of detection and evaluation of cardiac masses. In addition, novel applications have created a role for cardiac magnetic resonance imaging (MRI) in the management of cardiovascular-related dysfunction seen in oncological disease. Cardio-oncology is a growing field in the management of cancer. Therefore, use of cardiac MRI — in conjunction with other imaging modalities — and a multidisciplinary approach are both crucial to the contemporary model of cancer care. Knowledge of cardiac MRI and its applications will help health care professionals deliver the best care possible to their patients with cancer.

References


