

Onco-Cardiology: Value of Cardiac Imaging by Using CT and MRI after Radiation Therapy

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Conflicts of interest are listed at the end of this article.

See also the article by Takagi et al in this issue.

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It has been estimated that the number of cancer survivors will double from 12 million in 2012 to 24 million by the end of the next decade in the United States alone, raising awareness and concern for health problems during follow up of these patients. Among cancer survivors, half will die of cancer recurrence, but a third will die of cardiovascular disease (1). The recognition of the challenges and opportunities related to heart disease in cancer survivors has led to the inception of onco-cardiology as a new discipline. Onco-cardiology is a medical discipline that focuses on the identification, prevention, and treatment of cardiovascular complications related to cancer therapy.

A combination of surgical procedures, radiation therapy, and chemotherapy is the main therapeutic option for many malignancies including intrathoracic cancers. It is increasingly recognized that chemotherapy–radiation therapy may have adverse cardiac effects, although radiation therapy technology for treating chest malignancies has markedly improved by delivering therapeutic doses to well-defined targets while minimizing radiation injury to surrounding normal organs (2). However, despite advances in radiation therapy planning, there are still concerns about the acute and long-term effects of radiation therapy to surrounding thoracic organs, particularly the heart. Radiation-induced heart disease may occur at even relatively low radiation doses, in contrast to the outdated notion that the heart is a radio-resistant organ. The latency period for radiation-induced heart disease may range from months to many years and is dependent on radiation dose, age, preexisting cardiovascular disease, traditional risk factors, and concurrent chemotherapy (2).

Cardiac disease after radiation therapy may manifest in various ways, including as coronary artery disease, valve disease, pericardial disease, or as direct injury to the myocardium. The hallmark of radiation-induced myocardial damage is fibrosis, which is initiated through various cellular mechanisms that result in endothelial damage of the myocardial microvasculature and the large epicardial coronary vessels (3). Structures that may be affected are the myocardium, main coronary arteries, microvasculature, conduction system, pericardium, cardiac valves, and proximal aorta. Coronary artery disease after radiation therapy may manifest with more fibrous plaques because of intimal hyperplasia and ostial stenoses, in addition to stenoses that are smoother, longer, and more concentric than are those in conventional coronary artery disease. Radiation-induced heart disease conforms to radiation portals. For example, women with left-sided chest radiation have a higher risk

of cardiovascular complications compared with women who undergo right-sided radiation. Myocardial interstitial fibrosis after radiation involves a number of cellular processes that result in cardiomyopathy because of direct myocardial injury (3). Various cytokines and inflammatory pathways have been implicated in myocardial fibrosis after irradiation, resulting in a proliferation of fibroblast activity and an expansion of the myocardial interstitium and extracellular matrix. Myocardial fibrosis consists of a proliferation of collagen bands, separating and replacing myocytes (4).

Noninvasive cardiac imaging plays an important role in the diagnosis of symptomatic and asymptomatic cardiovascular disease during cancer therapy. The echocardiogram is the most widely used tool for serial evaluation of the heart during cancer therapy (5). According to the American Society of Echocardiography guidelines, ejection fraction should be determined by using the biplane method of discs. However, the temporal variability of estimating ejection fraction with echocardiography may be up to 10%, which can be higher than the thresholds used to define cardiotoxicity (5). Another major limitation of the use of ejection fraction as a biomarker is the late occurrence of reduction in ejection fraction (5). Hence, there is a growing interest in identifying markers of early myocardial injury to predict heart failure. Myocardial strain analysis with tissue Doppler imaging and speckle tracking strain imaging have been advocated for the detection of global and regional mechanical dysfunction as an early, more sensitive marker of heart disease. This echocardiographic technique has a number of technical limitations, but may detect early systolic left ventricular dysfunction before a decrease in ejection fraction is observed in patients with cardiotoxicity.

Coronary CT angiography, MRI, and radionuclide perfusion imaging may provide alternative noninvasive imaging approaches that can depict the major manifestations of radiation-induced heart disease more comprehensively and directly compared with echocardiography. CT angiography is well suited to assess coronary artery disease, evaluate the extent, characterize plaque features, and assess coronary calcifications; it may also help to assess the functional status of a coronary artery stenosis. Screening for radiation-induced heart disease with coronary CT angiography yields high prevalence of coronary artery disease, but the benefit of screening on survival is unknown. For example, the prevalence of significant coronary artery disease is high after mediastinal irradiation in survivors of Hodgkin lymphoma, while asymptomatic even in the presence of life-threatening

coronary artery disease (6). A recent health-related quality of life analysis of survivors of Hodgkin lymphoma was performed to assess the emotional and practical burden as well as perceived benefits of screening and counseling on patient satisfaction. Screening by means of CT angiography and subsequent cardiac intervention was highly valued and the benefits were felt to outweigh the emotional and practical burden (7).

Cardiac MRI may be useful to identify perfusion defects similar to CT perfusion and radionuclide perfusion techniques. However, the main advantage of cardiac MRI is myocardial tissue characterization by using multiparametric imaging, including late gadolinium enhancement to detect gross scar, T1 mapping to define interstitial fibrosis, and extracellular matrix expansion and T2 mapping to assess myocardial edema.

In the current issue of *Radiology*, Takagi et al report the use of serial T1 mapping of the left ventricle to assess the potential detrimental effects of chemotherapy–radiation therapy to the heart in patients who underwent treatment for esophageal cancer (8). Radiation therapy–induced complications are increasingly reported in survivors of esophageal cancer as the survival rate of this malignancy is growing (2). Takagi et al performed serial T1 mapping of the heart in a prospectively defined study before and at two time points (0.5 year and 1.5 years) after chemotherapy–radiation therapy, thereby providing insight into the evolution over time of myocardial injury after radiation therapy (8). In addition, the authors evaluated a differential effect on the basal left ventricular septum, which is included in the radiation field versus the nonirradiated lateral wall of the left ventricle. The imaging protocol included cine MRI to assess function, precontrast and postcontrast T1 mapping to assess myocardial injury and expansion of the extracellular matrix, and late gadolinium enhancement to assess myocardial scar tissue. The main observation was that myocardial native T1 values and extracellular volume reveal myocardial changes earlier (already at 6-month follow-up) than changes in global left ventricular function or gross scar seen at late gadolinium

imaging. Furthermore, the myocardial tissue alterations were confined to the basal septum, which received the higher radiation dose. The strengths of the study by Takagi et al were the prospective design, the serial assessment starting before radiation therapy, and the use of multiparametric cardiac MRI to depict early myocardial changes in an important and growing patient population. A number of limitations may be noted related to relatively small sample size, lack of cardiac events during follow-up period, the uncertainty about the prognostic implications of the findings, and the confounding effect of concurrent chemotherapy. However, this study provides an impetus to explore the utility of cardiac MRI in diagnosing early myocardial injury in patients who underwent chemotherapy–radiation therapy. In addition, the study illustrates how cardiac MRI may be of potential value for early diagnosis of radiation-induced myocardial injury. Hopefully, future studies will define how early diagnosis by using cardiac MRI may translate to therapy and prevention of radiation-induced heart disease in the growing population of cancer survivors in general.

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