CMR Imaging of Myocardial Amyloidosis Using Late Contrast Enhanced Imaging: Challenges and Potential Solutions

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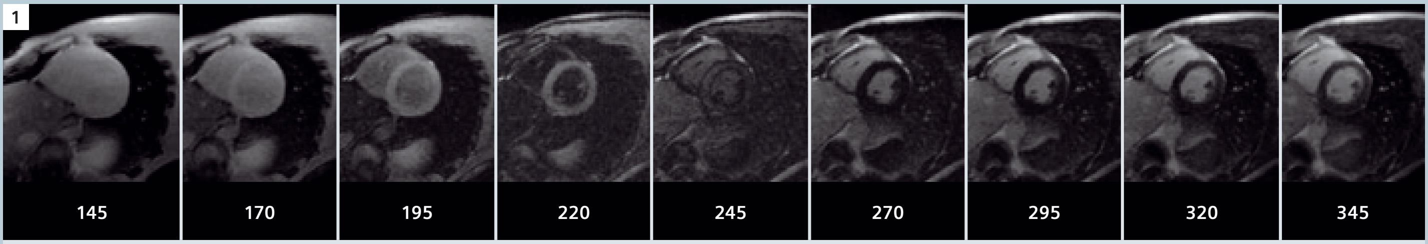
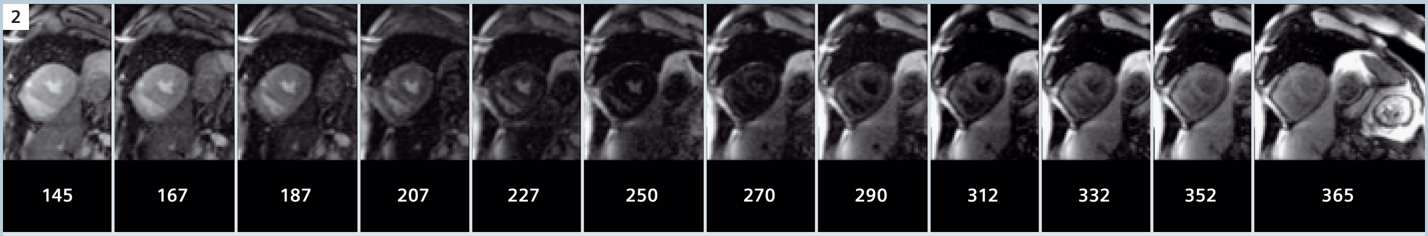
Late Contrast Enhancement (LCE, also known as Delayed Enhancement) is a CMR technique that was initially developed as a method for imaging the extent and transmurality of myocardial infarction. However, since this technique detects gadolinium retention in tissue, it is useful for the detection of a variety of pathological conditions where gadolinium is retained in the heart due to fibrosis of ischemic or inflammatory etiology and infiltrative disorders. Therefore, this technique has proven to be useful in the evaluation of non-ischemic cardiomyopathies, including evaluation of fibrosis in hypertrophic cardiomyopathies, myocarditis and infiltrative diseases (e.g. amyloidosis).
The technique is based on maximizing contrast between "abnormal" and "normal" myocardium by use of an inversion recovery magnetization preparation scheme where the inversion time (TI) is selected to eliminate signal from the "normal" myocardium and areas where there is abnormal accumulation of contrast agent and subsequent T1 shortening.



1 Individual frames from a TI-scout - the appropriate TI [in ms] where "normal" myocardium is completely nulled is easily seen to be 270 ms.



2 In this subject with amyloid the null point for myocardium is reached before the blood pool is nulled indicating that the T1 of myocardium is shorter than that of blood. Typically, for infarct imaging, with conventional contrast agents and scan timing the blood pool will have a T1 which is shorter than the T1 of "normal" myocardium.

Selection of TI

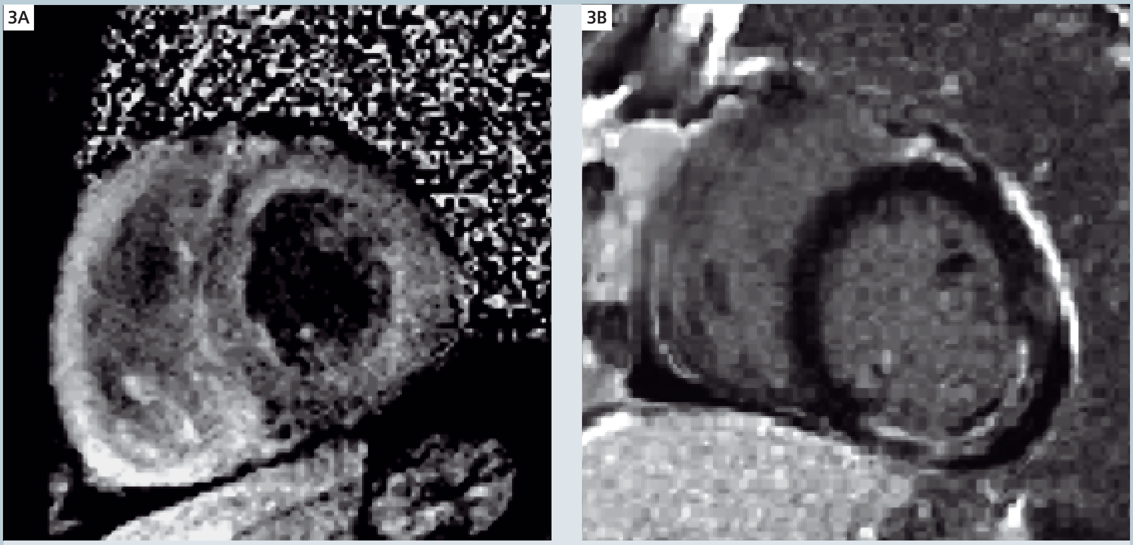
The required TI varies with the contrast agent, contrast dose, time after injection, heart rate and other physiological parameters such as the rate of elimination of the contrast agent from the blood pool via the kidneys or other mechanisms.
The traditional method of selecting the optimal TI is to use the "TI Scout" sequence where, in essence, each frame of a cine sequence is acquired after an initial inversion pulse and consequently has a different TI.
This strategy is effective when regional differences exist in gadolinium retention, such as in infarcted tissues, where these regions can be compared to a significant amount of "remote", non-infarcted myocardium. However, diseases that affect the entire myocardium without regional variation pose a challenge with this approach, since no "normal" myocardium can be detected to choose an optimal null-point. This is particularly true for cardiac amyloidosis, where typically the entire myocardium is involved in a circumferential manner and the contrast wash-in and wash-out kinetics are also significantly altered.
The pitfall of the traditional approach is that the operator determining the optimal null-point for the myocardium erroneously may choose an inversion time that nulls signal in the abnormal and not in the normal myocardium. This can result in false negative examinations. This typically does not occur in ischemic heart disease, since the infarcted myocardium is well-delineated and it can be clearly distinguished from normal myocardium.
In amyloid heart disease, the deposition of the abnormal protein occurs in a circumferential manner, starting in the endocardial layers and spreading through the myocardium in a transmural fashion, particularly in the most advanced cases. Therefore, choosing an optimal TI time is difficult, since the amount of normal myocardial tissue is quite minimal. Using the traditional TI-scout approach invariably will lead to incorrect TI selection – the TI chosen, when looking for the "black myocardium", will be significantly shorter than the TI which would have been selected if normal myocardium was in the TI scout slice.
Another important issue is that contrast wash-in and wash-out kinetics are significantly altered in cardiac amyloidosis. Due to the infiltration of tissues, gadolinium is extracted faster from the blood pool, compared to normal myocardial tissue. Therefore, the optimal time to image after contrast injection is shorter than in typical cases of myocardial infarction.
Therefore, timing is critical in patients with suspected cardiac amyloidosis. Both the time after injection as well as the inversion time needs to be modified when looking for this disease.

To identify when this is a problem there are a few indicators which can help:

- when identifying the optimal null point with the TI-scout is more challenging than in most cases, it should raise the suspicion of "global hyperenhancement" due to cardiac amyloidosis,
- when a TI-scout is performed, in the majority of cases the blood pool will reach its null point before the myocardium. If it appears that in a given patient the myocardium reaches the null point before the blood pool, it might also raise the possibility of cardiac amyloidosis,
- use of a Phase Sensitive Inversion Recovery (PSIR) sequence will reduce the need for a precise TI setting, however the lack of "normal" tissue still makes identification of "abnormal" difficult . Again, if the tissue contrast between the blood pool and myocardium is poor, it should raise the issue of cardiac amyloidosis,
- global hyperenhancement in cardiac amyloidosis typically spreads from the subendocardial layers to the subepicardium. Therefore, except in the most advanced cases, a rim of normal tissue might be seen in the epicardial layer.

The best way to make the diagnosis of cardiac amyloidosis is to adjust image acquisition in patients in whom there is sufficient suspicion. At our institution, referring physicians are asked to specifically note on the order sheet when there is any suspicion of cardiac amyloidosis, so the imaging protocol can be adjusted accordingly. We alter our usual "delayed hyperenhancement" imaging protocol as follows:

- Perform an SSFP-based TI-scout in a mid-ventricular short axis slice EARLY (approximately 5 minutes after gadolinium injection).
- Adjust the TI time for the PSIR sequence if needed.
- Perform the PSIR delayed enhancement coverage of the myocardium as usual (2-chamber, 4-chamber, 3-chamber and short axis stack).
- REPEAT the TI-scout in a mid-ventricular short



3 Cardiac amyloidosis (left) vs Ischemic heart disease illustrated by PSIR images - the amyloidosis patient shows „patchy" enhancement pattern and the myocardium is brighter than the blood pool. In the ischemic patient the normal tissue is homogenously dark.
(Images courtesy of Dr. Glenn Coates, Wake Radiology, Raleigh, NC, USA.)

axis slice 15 minutes after the injection of the contrast agent.
- Adjust the TI-time for the PSIR sequence again
- REPEAT the typical PSIR coverage of the heart as above

Summary

CMR is the most powerful non-invasive tool to detect cardiac amyloidosis, but it is critical that appropriate technique is utilized. The most important approach is to alter the image acquisition scheme upfront in order to follow the abnormal contrast wash-in and wash-out kinetics seen in this disease. Although some features described above can help to identify the disease with the usual approach, it is much easier if the imaging protocol is altered accordingly. The pointers and indicators in the preceding text may help to identify these scenarios, both by the abnormal behavior of the TI-scout sequence (with reference to "normal" behavior in ischemic heart disease patients) and in the close examination
of the PSIR sequences to look for heterogeneity in the texture of hyperenhancement and the abnormal contrast of the myocardial signal with reference to the blood-pool.
It should be noted that many of these observations are based on the assumption of a certain contrast agent dose and timing of the scan at a certain time after contrast administration. Significant variation in contrast agent dose may invalidate some of these indicators outlined in this document.