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Issue Highlights

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A Vision for Magnetic Resonance Imaging to Assess Cardiotoxicity

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1. Introduction

A cancer survivor, as defined by the NCI, encompasses individuals from diagnosis throughout life. In the U.S., there were 18.1 million survivors in 2022, projected to be 26 million by 2040, with 60% surviving past 5 years and 40% past 10 years [1]. Having survived cancer, they face ongoing risks of treatment-related toxicities and comorbidities that could compromise their hard-earned quality of life [2]. Cardiovascular toxicity is a major cause of morbidity and mortality during or after cancer therapy [3,4]. It is very challenging to evaluate cardiotoxicity with cardiac imaging and circulating biomarkers findings, so clinical heart failure may serve as sole reliable evidence of toxicity [3,4,5]. Once heart failure occurs, near normal cardiac recovery is unlikely, and even with guideline-directed medical therapy (GDMT), there continues to be an elevated long-term risk for cardiovascular issues. Cardiotoxicity may present as tissue inflammation, fibrosis, edema associated with cancer therapies or toxicities relating to infiltration into the myocardial interstitium by various substances like proteinaceous amyloid fibrils, immune and inflammatory cells, iron-related deposits, and liposaccharides.

Cardiac MRI (cMRI) is a well-recognized “gold-standard” quantitative imaging reference. However, cMRI’s benefits outside of academic centers are limited by barriers. To implement cMRI effectively, experienced technologists who understand cardiac anatomy and function are needed for precise imaging such as obtaining appropriate scout scans, accurate slice placement and precise magnetic focusing (shimming). Post-processing approaches of cMRI require time, expertise and dedicated software which are not typically available in nonacademic institutions, such as global and regional strain analyses, T1 and T2 mapping, extracellular volumes (ECV), and late gadolinium enhancement (LGE; so-called “scar imaging”).

To make advanced cMRI accessible to all patients, future MRI scanners should simplify and speed up the entire process. Automation and AI-enhanced systems will assist technologists in producing reproducible imaging data and analyses in less time (Figure 1). This benefits older or sicker patients and allows for more efficient use of MRI scanners, improving diagnostic quality and patient management.

2. Scout Scans

cMRI begins with scout scans with breath-holds to obtain the four standard views (Figure 1). UIH EasyScan™, previously reported (1), is a new technique enabling a single acquisition of transverse images in one breath-hold that are quickly AI-processed into the four standard views for slice placement (Figure 2). EasyScan™ allows accurate slice planning with minimal effort and high reproducibility, esp. for less-experienced technologists. Experienced cMRI technologists may stick to traditional approach to “tweak” plane positioning, but when patient movement requires redoing scout scans, EasyScan™ is the quick and preferred solution.

Magnetic Shimming: To accurately evaluate cardiac anatomy and functions qualitatively and quantitatively, cMRI sequences require “magnetic field focusing”, typically achieved by adjusting the B0 field. UIH AIshim™ optimizes the B0 field for the entire cardiac image in one go, delivering faster better images and improved quantification (Figure 3) [1].

3. Structural and Functional Metrics

Since 2020, the UIH MR scanner has automatically used AI to quantify LV and RV size, volume, mass and function. After initial acquisition of short axis slices (SAX), the MR technologist verifies or tweaks the segmentation map. The adjustments propagate through the slices and a table of key quantitative LV and RV data is generated. Because that segmentation map was not transferable to other processes in the previous version, a new AI approach that segments the LV and RV images and computes the structural and functional data is being developed and currently under final testing. In

the current version, the segmentation maps are available for other pipeline processes including: 1) feature tracking estimates of global and regional longitudinal, circumferential and radial strains; 2) conversion of T1 and T2 (T2*) relaxation time maps into maps of abnormal T1 and T2 myocardium estimates and processing of ECV; and 3) mapping and quantitating LV LGE for tissue viability estimates ("scar imaging") (Figure 1).

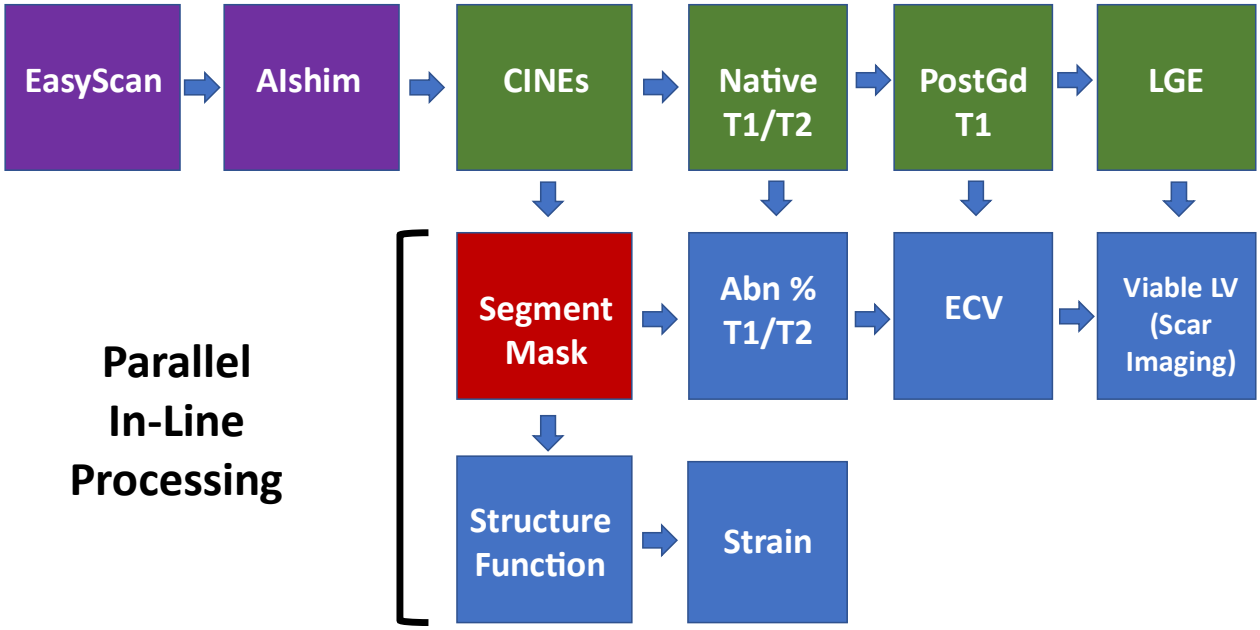


Figure 1. Schematic of the automated workflow pipeline with parallel in-line image processing. Purple boxes reflect new, AI-enabled and simplified scout scan acquisition and shimming. Green boxes represent current standard cMR imaging data obtained in typical non-ischemic cardiomyopathy evaluation which further processed for complete evaluation. The Red box reflects image segmentation performed on CINE images. Blue are image post-processing results generated automatically with AI and reported to the reader with the images for final interpretation.

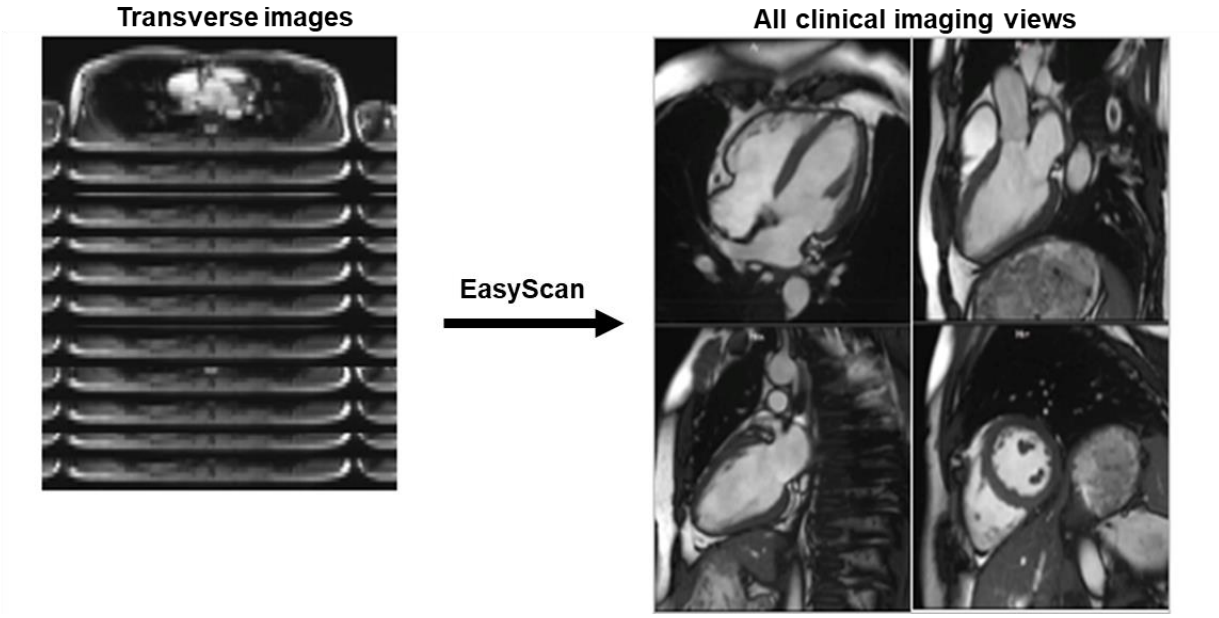


Figure 2.UIH EasyScan™ automatically acquires transverse images and uses AI/Deep learning to generate clinical views with 1 breath hold (Ref 1).

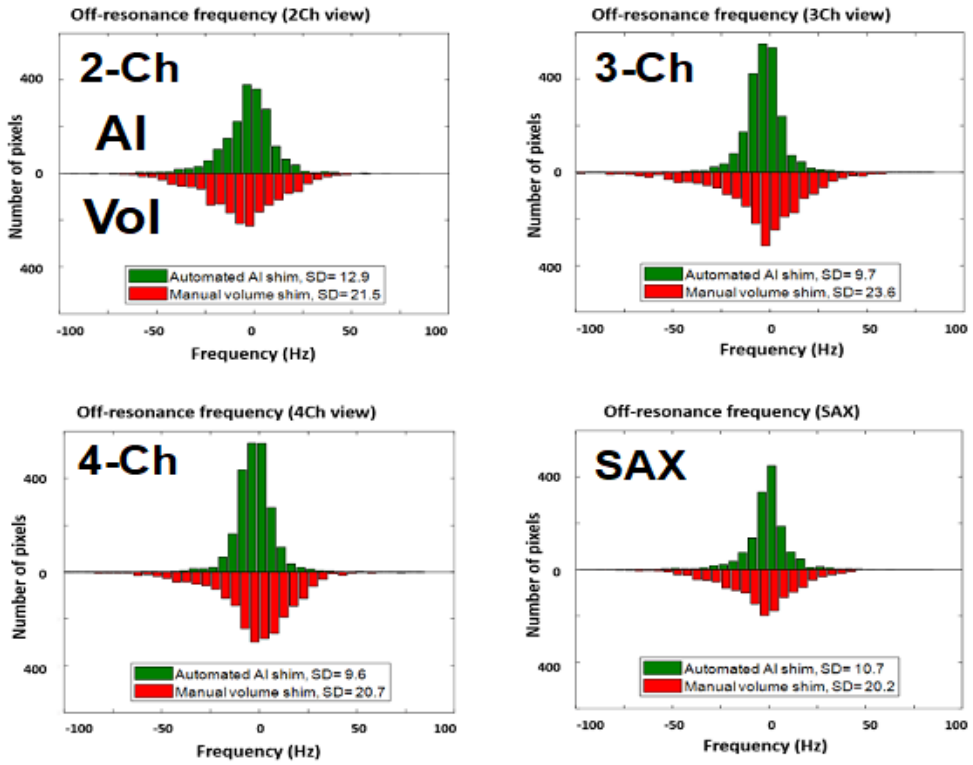


Figure 3. Four standard views illustrating improved on-frequency image distribution with UIH AIshim. AIshim (Green) vs Volume shim (Red) yields crisper images, higher SNR, and improved quantitative results (Ref 1).

4. Myocardial Strain

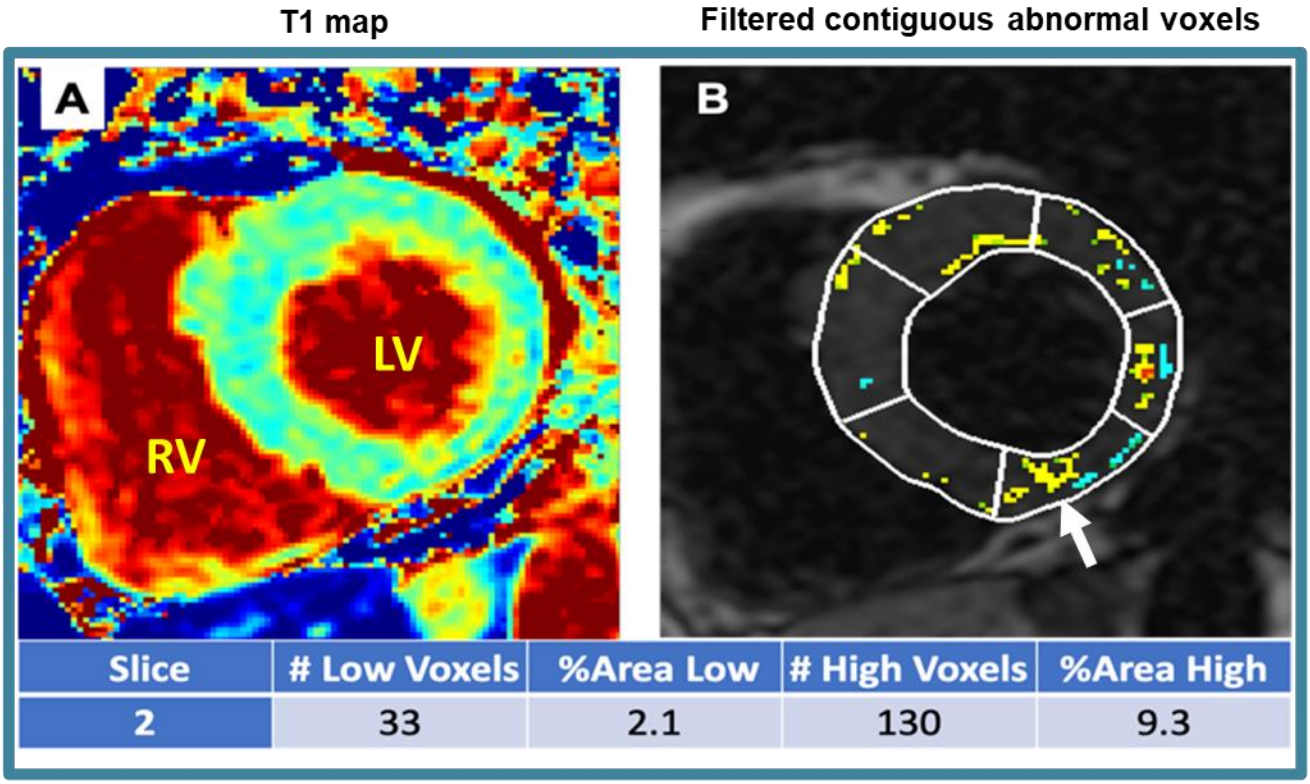
Global myocardial deformation, i.e., strain imaging, with AI enhanced speckle is now integrated into cardiology management guidelines. Strain estimates in MRI have been studied for many years using tagging approaches including DENSE (University of Virginia, Charlottesville, VA) and SENC (MyoScan; Myocardial Solutions, Inc.; Morrisville, NC). SENC images are acquired rapidly (6 sec/plane). AI off-line processing of the images yields a complete report in several minutes. Alternative non-tagging and AI feature tracking (FT) methodology are similarly used for off-line post-processing by CIRCLE Cardiovascular Imaging (Calgary, Canada) and by UIH. UIH scanners have a built-in data processing approach, where CINE images are transferred to a powerful multi-GPU workstation and processed automatically to generate the report. AI FT methods reprocess the balanced steady state free precession (bSSFP) CINE images used for structure and function assessments to obtain strain analyses. This in-line AI approach saves time by processing the data while the scanner operating system acquires additional study images.

5. Myocardial Characterization

The Washington University in Saint Louis -UIH approach to myocardial characterization enhances the utility of the T1/T2 maps by covering the entire heart (up to 9 slices). Voxels that deviate 2 or 3 standard deviations above or below expected nominal myocardial T1 or T2 relaxation times are color-coded yellow or red, respectively. We retain abnormal myocardium voxels that are contiguous with two or more such voxels, eliminating the remaining isolated abnormal and normal voxels. The resultant color map is superimposed on a grayscale image slice, offering an easily-interpretable quantitative abnormal map of each slice. The percent volume of abnormal myocardium (high and low) is calculated for each slice and the entire heart. We empirically categorize the percent volume into ranges of normal, mild, moderate, high, and very high, and such sensitive, quantitative metrics can aid cardiomyopathy diagnoses and support longitudinal progression determinations (Figure 4). Moreover, while T1/T2 maps typically require a short breath-hold per slice, free breathing sequences for acquiring T1/T2 maps under

investigation show potential to improve patient comfort without compromising accuracy of mapping.

T1 maps pre- and post-gadolinium are acquired, segmented, and aligned to estimate ECV normalized for hematocrit for each slice and the entire heart. ECV, structural/function metrics, global longitudinal strain and T1/T2 indexes of abnormal myocardium form a comprehensive dataset for characterizing cardiotoxicity associated with myositis, myocardial edema, and differentiating cardiac fibrosis from amyloid infiltration (Figures 5, 6). Renal dysfunction can preclude the use of gadolinium for ECV estimates. In our experience, cardiac amyloidosis shows a long insidious progression associated with increasing abnormal T1 myocardium and expanding ECV. In the late phase, it is associated decreased LV contractility, increased EDV, increasing wall thickness and diminishing GLS. In contrast to cardiac amyloid infiltration, diffuse fibrosis is associated with reduced GLS earlier in its progression, often followed by declining cardiac function, changes EDV, ESV or wall thickness. Regardless, these diagnoses require confirmation with biochemical tests, biopsy, or Tc-99m pyrophosphate scan.



Slice	# Low Voxels	%Area Low	# High Voxels	%Area High
2	33	2.1	130	9.3

Fig 4. Conversion of colorized T1 or T2 relaxation maps into abnormal myocardium displaying only the abnormal voxels 2 std dev above or below nominal values for myocardium superimposed on grayscale slice image. (A) Typical T1 parameter map of color coded T1 value. (B) Filtered contiguous abnormal T1 voxels on an MR image. Percent abnormal myocardium is determined for each slice and the entire heart. Current Grading: Normal, <20%; Mild, 20 to 35%; Moderate, 35 to 50%; High 50 to 75%; Very High, 75+ %.

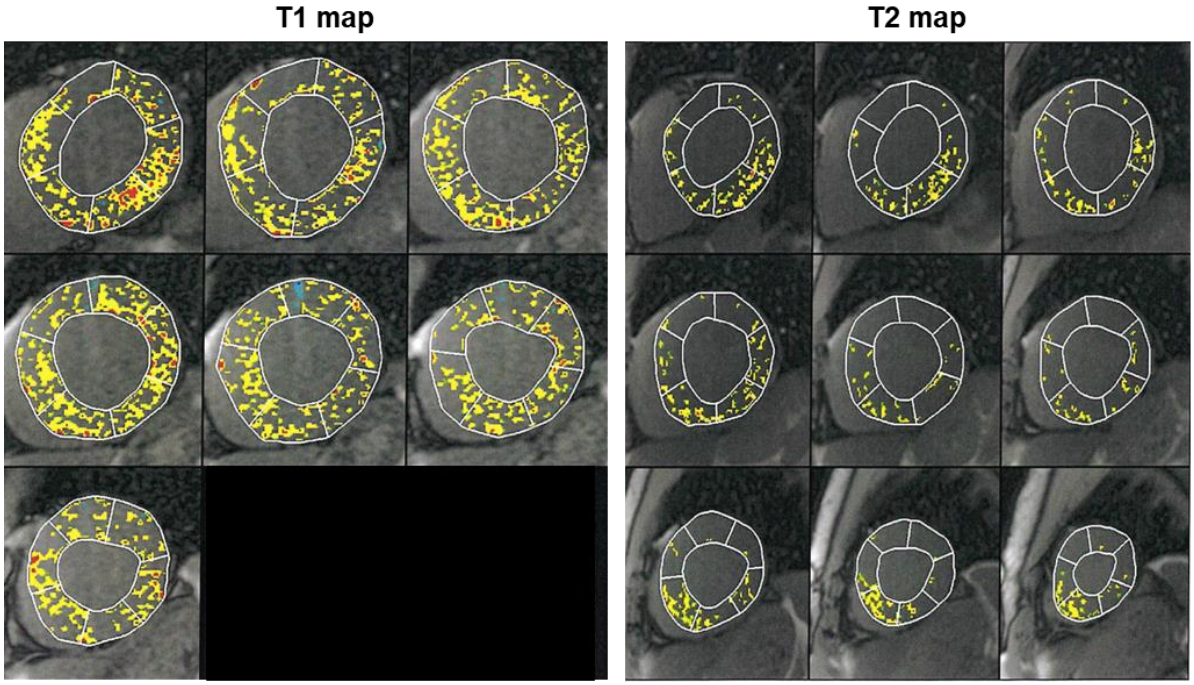


Fig. 5. A patient with hypertension and cocaine use and interventricular septum diastole at 1.5 cm is referred to rule out amyloidosis due to declining ejection fraction and increased septal thickening by echocardiography. The patients is diagnosed with dilated cardiomyopathy with moderately reduced ejection fraction, severely decreased global longitudinal strain of left ventricle, normal extracellular volume, and mildly increased T1 abnormal myocardium consistent with fibrosis.

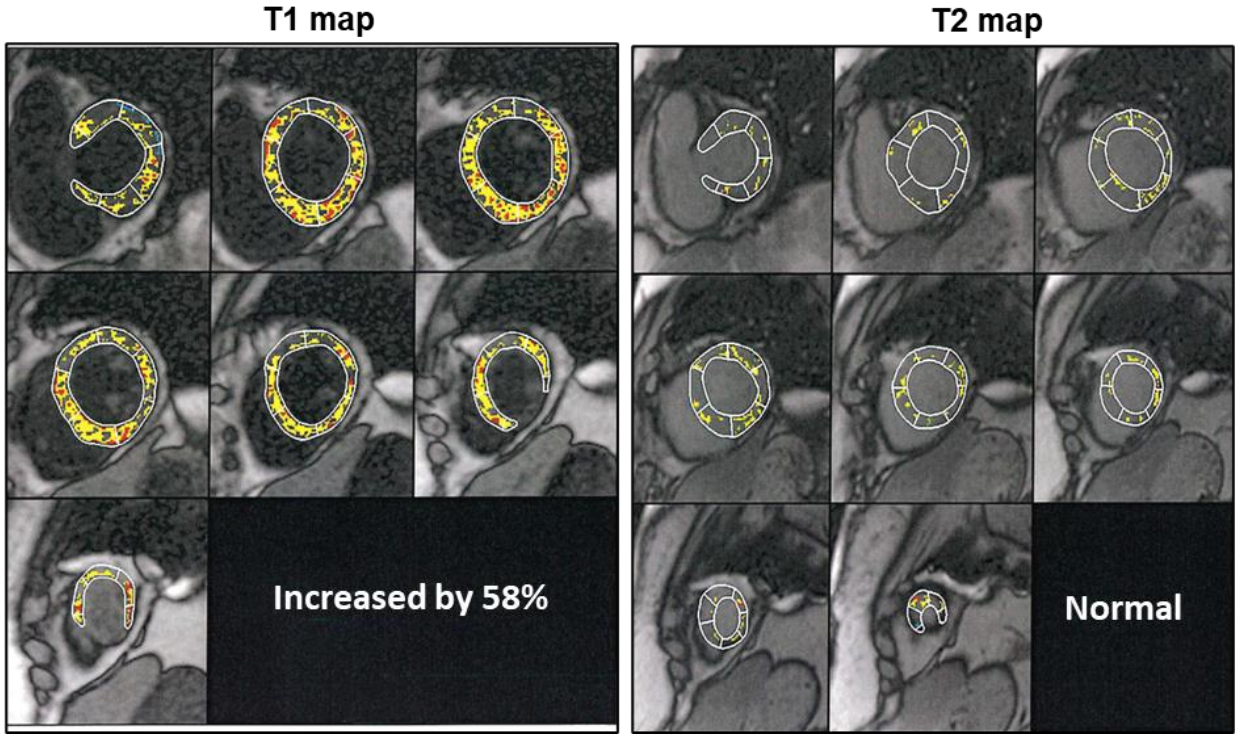


Fig. 6. A patient with carpal tunnel syndrome is referred to rule out amyloidosis. The patients is diagnosed with normal LV end diastolic volume and function with normal LV and RV global longitudinal strains. T1 abnormal myocardium (%) is highly increased associated with a marked extracellular volume increase (>3 std dev). The findings are consistent with amyloidosis.

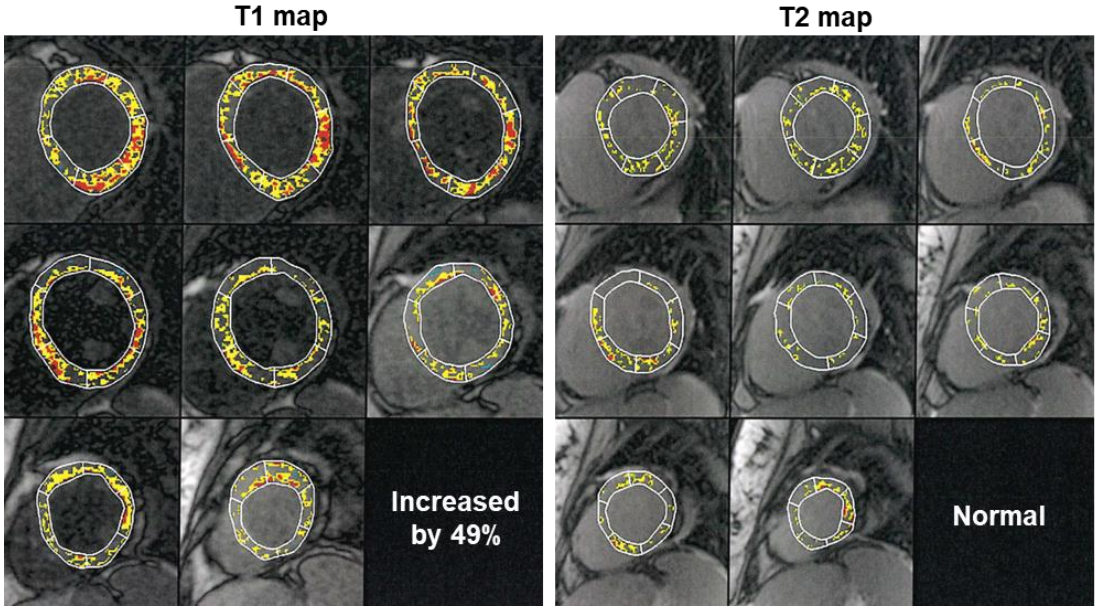


Fig 7A. A 77-year-old patient with cardiomyopathy is referred to rule out cardiac amyloidosis. Note, the LV dilates to preserve cardiac output (or EF). Increased abnormal myocardium associated with amyloid can be differentiated from diffuse fibrosis by changes in ECV and strain. In our lab, increased ECV > 3 standard deviations above nominal (i.e., ≥ 36%) is associated with amyloid infiltration. Strain decreased at higher levels fibril infiltration as noted by higher percentages T1 abnormal myocardium. The patient is diagnosed with mildly dilated LV with minimally decreased systolic function and moderately decreased LV global longitudinal strain. T1 abnormal myocardium (%) is moderately increased associated with moderately high extracellular volume increase (>3 std dev). The findings are consistent with amyloidosis.

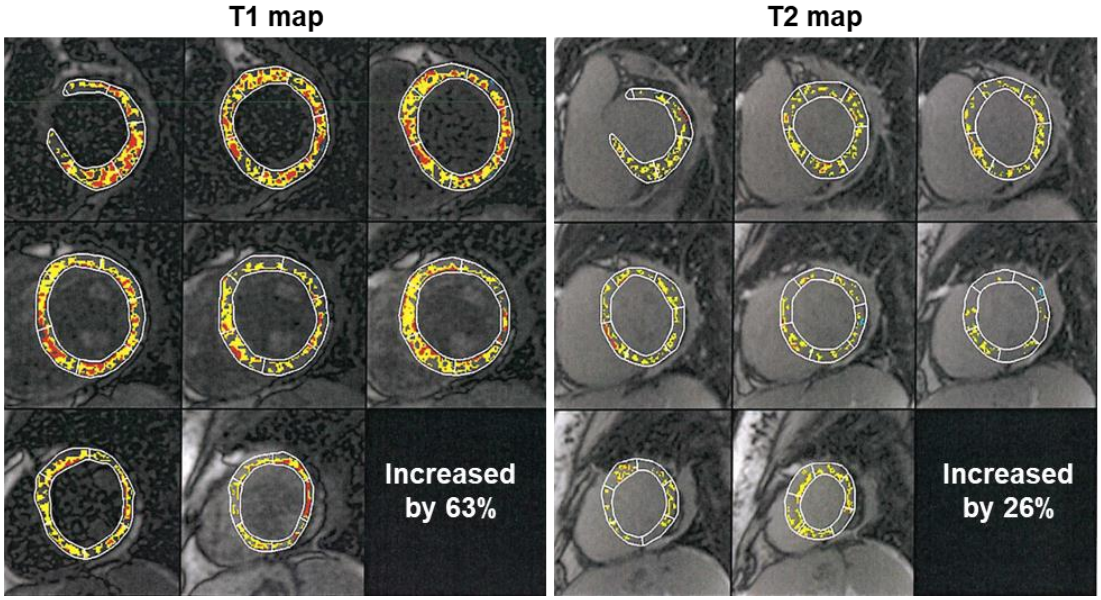


Fig 7B. A patient was followed up at 6 months after the diagnosis of cardiomyopathy to assess cardiac function and amyloid progression. While progressive amyloid infiltration can be monitored by its impact on ECV, IV access was not obtained in this patient. Direct assessment of percent T1 abnormal myocardium demonstrated considerable progression of infiltrative disease, while cardiac structure, function, and strain metrics improved with guideline directed medical management (GDMT). Using percent T1 abnormal myocardium to assess progression rather than ECV, reduced patient study time (20-30 min), and eliminated: 1) the need for recent hematocrit and serum creatinine assays, 2) placement of IV access, 3) the use of gadolinium, and 4) physician supervision. The patients was diagnosed with normal LV EDV with minimally decreased systolic function and mildly decreased LV global longitudinal strain. T1 abnormal myocardium (%) is highly increased. T2 abnormal myocardium (%) is mildly increased reflecting tissue edema. Amyloid tissue infiltration progressed (T1 abnormal myocardium: 49% to 63%) while cardiac structure, function and strain improved.

As illustrated in Fig 7 A and B, following the diagnosis of cardiac amyloid, disease progression can be monitored using ECV to assess the interstitium expansion effects of fibril infiltration. Alternatively, serial changes in native T1 map of abnormal myocardium directly reflect fibril accumulation. This metric eliminates the need for gadolinium contrast, IV access, recent hematocrit and serum creatinine levels, and physician supervision. It also shortens patient study time by

20 to 30 minutes.

6. Conclusion

Cardiac MRI offers a wide range of advanced imaging techniques and quantitative metrics to diagnose or differentiate various cardiomyopathy, ischemic disease, and myocarditis disease. It is crucial to understand that no single measurement can capture the entire picture. Our collective vision is to achieve “Equal Healthcare for All”, making strengths of cMRI accessible to all patients, regardless of hospital size, location and availability of image post-processing resources. Cardio-oncology patients will benefit from robust serial cMRI studies conducted over months to years, facilitated by an automatic workflow that minimizes personnel requirements, reduces resource demands, and enhances longitudinal quality control.

7. Image/Figure Courtesy

All images are the courtesy of Division of Cardiology, Washington University Medical School, St. Louis, MO, USA

8. References

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