PARAMETRIC MAPPING AND MYOCARDIAL ECV MEASUREMENT FOR NON-ISCHEMIC CARDIOMYOPATHY IN INDIAN COHORT

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A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF MD RADIODIAGNOSIS (BRANCH VIII) EXAMINATION OF THE TAMIL NADU DR M.G.R MEDICAL UNIVERSITY, CHENNAI TO BE HELD IN MAY 2020

CERTIFICATE

This is to certify that the dissertation entitled “parametric mapping and myocardial ECV measurement for non-ischemic cardiomyopathy in Indian cohort” is the bonafide original work of Dr Linu Oommen Varghese submitted in partial fulfillment of the requirement for MD Radiodiagnosis(Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in May 2020.

Guide:

Dr Leena Robinson Vimala

Associate Professor

Department of Radiodiagnosis

Christian Medical College

Vellore – 632004

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Head of the Department:

Dr Sridhar Gibikote

Professor

Department of Radiodiagnosis

Christian Medical College

Vellore – 632004.

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Principal:

Dr Anna B Pulimood

Professor

Christian Medical College

Vellore – 632004.

DECLARATION

I hereby declare that this dissertation titled “parametric mapping and myocardial ECV measurement for non-ischemic cardiomyopathy in Indian cohort” is carried out by me under the guidance and supervision of Dr. Leena Robinson Vimala, Associate Professor of Radiodiagnosis, Christian Medical College, Vellore. This dissertation is submitted in partial fulfillment of the requirement for MD Radiodiagnosis(Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in May 2020.

Dr Linu Oommen Varghese

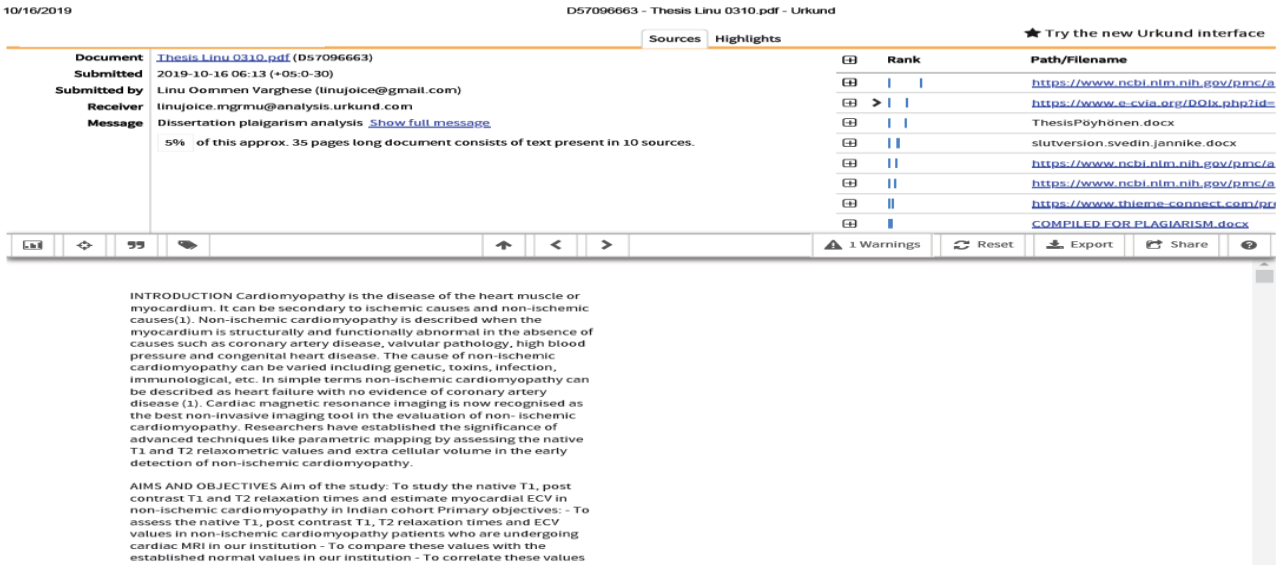
Post graduate resident

Department of Radiodiagnosis

Christian Medical College

Vellore – 632004.

ORIGINALITY CERTIFICATE



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Dr Leena Robinson Vimala

Associate Professor

Department of Radiodiagnosis

Christian Medical College

Vellore – 632004

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CONTENTS

INTRODUCTION

Cardiomyopathy is the disease of the heart muscle or myocardium. It can be secondary to ischemic causes and non-ischemic causes(1). Non-ischemic cardiomyopathy is described when the myocardium is structurally and functionally abnormal in the absence of causes such as coronary artery disease, valvular pathology, high blood pressure and congenital heart disease. The cause of non-ischemic cardiomyopathy can be varied including genetic, toxins, infection, immunological, etc. In simple terms non-ischemic cardiomyopathy can be described as heart failure with no evidence of coronary artery disease (1). Cardiac magnetic resonance imaging is now recognised as the best non-invasive imaging tool in the evaluation of non-ischemic cardiomyopathy. Researchers have established the significance of advanced techniques like parametric mapping by assessing the native T1 and T2 relaxometric values and extra cellular volume in the early detection of non-ischemic cardiomyopathy.

AIMS AND OBJECTIVES

Aim of the study: To study the native T1, post contrast T1 and T2 relaxation times and estimate myocardial ECV in non-ischemic cardiomyopathy in Indian cohort

Primary objectives:

- To assess the native T1, post contrast T1, T2 relaxation times and ECV values in non-ischemic cardiomyopathy patients who are undergoing cardiac MRI in our institution
- To compare these values with the established normal values in controls done in the same scanner setting in our institution
- To correlate these values with qualitative assessment of late gadolinium enhancement

Secondary objective: - To compare the native T1, post contrast T1, T2 relaxation time and ECV values with the other ethnic groups which is already published in literature

REVIEW OF LITERATURE

Non ischemic cardiomyopathy is disease of the myocardium characterised by mechanical or electrical dysfunction with inappropriate ventricular hypertrophy or dilation (2). The causes of non-ischemic cardiomyopathy are numerous as outlined in figure 1.

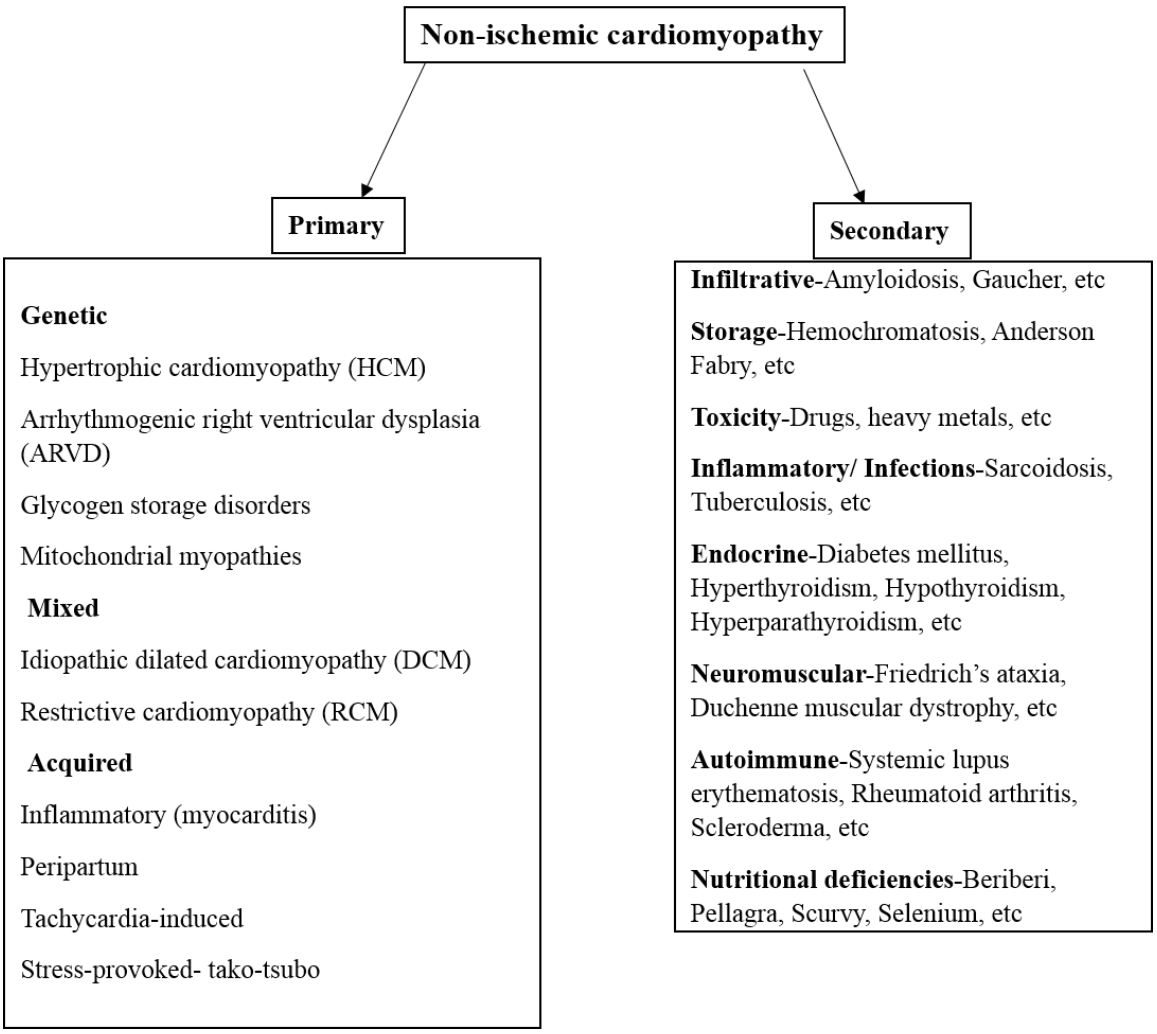


Figure 1- Classification of non-ischemic cardiomyopathies

Source- Maron BJ, Towbin JA, Thiene G, Antzelevitch C, Corrado D, Arnett D et al. Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. Circulation 2006; 113:1807–16.

Non ischemic cardiomyopathy can be also categorized as restrictive cardiomyopathy (amyloidosis, storage disorders like Fabry's, sarcoidosis, hemochromatosis), dilated (non-ischemic cardiomyopathy), hypertrophic cardiomyopathy, myocarditis and arrhythmogenic right ventricular dysplasia(3). Prevalence of inherited hypertrophic and dilated non-ischemic cardiomyopathy is more as compared to the other types [Table 1].20% cases of sudden cardiac death are due to non-ischemic cardiomyopathy(4).

Table 1: Prevalence of most common inherited non-ischemic cardiomyopathies

	Children (1-puberty)	**Adults (19-64 years)**
HCM	Uncommon	1:250/500
DCM	Uncommon	1:250/500
ARVD	Uncommon	1:2000/5000
RCM	Uncommon	Uncommon

Source- McKenna WJ, Maron BJ, Thiene G et al, Classification, Epidemiology, and Global Burden of Cardiomyopathies.Circ Res. 2017 Sep 15; 121(7):722-730.

Evaluation of non-ischemic cardiomyopathy:

Non-ischemic cardiomyopathy eventually leads to myocardial injury which in turn causes ventricular dysfunction. Blood investigations, electrocardiogram are used in preliminary evaluation of non-ischemic cardiomyopathy followed by cardiac magnetic resonance imaging (MRI). Electrocardiograms are helpful to assess conduction delays and atrial fibrillation. Echocardiography assesses the size and function of the ventricles, valvular function, etc.(1).

Blood investigations include serum electrolytes, serum ferritin, serum total iron binding capacity levels, thyroid functions, blood alcohol levels and toxins, viral serologies, antinuclear antibodies, ESR and CRP to determine the causes like iron overload, toxicity induced, inflammation, systemic involvement of autoimmune diseases or inflammatory pathologies, etc. Genetic testing for work up for genetic aetiology of cardiomyopathy is essential (5).

Electrocardiogram findings include arrhythmias, atrio-ventricular block which can signal towards genetic or inflammatory cause, QRS duration and QT interval are the other factors to evaluate non ischemic cardiomyopathy (5).In non-ischemic dilated cardiomyopathy, ventricular tachycardia, ventricular arrhythmias and premature ventricular depolarization's are estimated with electrocardiogram which is also an important factor for prognosis as these patients are prone for arrhythmias. Prolonged QRS duration, QRS notching and fragmentation with sinus rhythm is also seen in idiopathic dilated cardiomyopathy (5). Ventricular arrhythmias and non-sustained ventricular tachycardia is also seen in hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy. However in arrhythmogenic right ventricular cardiomyopathy there are precordial T wave inversions, epsilon waves and parietal block or delayed terminal QRS activation with sinus rhythm (5). The electrocardiogram finding in hypertrophic cardiomyopathy also includes septal Q waves in the lateral and inferior leads. However in the apical variant there are no septal Q waves, instead giant T wave inversion. Wolff-Parkinson- White syndrome is also seen in hypertrophic cardiomyopathy (6). The Romhilt-Estes point score can be used to detect left ventricular hypertrophy in the electrocardiogram of hypertrophic

cardiomyopathy (7).The electrocardiogram findings in restrictive cardiomyopathy are biphasic P waves which are also tall, narrow QRS complex, notched biphasic T waves and abnormal ST-T segments (8). Acute myocarditis show ST elevation with absent reciprocal depression and abnormal Q waves (9).

Echocardiogram findings in dilated cardiomyopathy include dilated left ventricle with normal or decreased wall thickness, decreased left ventricular function, higher end diastolic diameter and ventricular dyssynchrony with global hypokinesia of the ventricular wall. The left ventricular indexed end diastolic volume is greater than 100ml/m2 in patients with dilated cardiomyopathy(5). In hypertrophic cardiomyopathy echocardiogram findings include thickened left ventricular wall, asymmetric septal hypertrophy, septal wall thickness greater than 15 mm, systolic anterior motion of the mitral valve and left ventricular outflow tract obstruction(10). Additionally, Doppler techniques are complemented with echocardiogram for measuring velocity across left ventricular outflow tract at rest and with Valsalva manoeuvres (11). The echocardiogram findings in restrictive cardiomyopathy shows decreased indexed end diastolic volume <40 ml/m2, left ventricular wall can be thickened in amyloidosis and Fabry disease. The typical echocardiographic finding in amyloidosis is of myocardial speckled pattern due to deposition of amyloid proteins in the myocardium. The left ventricular ejection fraction can be normal or reduced with diastolic dysfunction (12).Arrhythmogenic right ventricular cardiomyopathy findings on echocardiogram include right ventricular dilatation with akinesia or dyskinesia (5). However the sensitivity and specificity for the diagnosis of this condition is limited with echocardiogram (13).

CARDIAC MRI IN NON-ISCHEMIC CARDIOMYOPATHY

Physics of MRI

Magnetic resonance imaging (MRI) is depended on the electromagnetic movement of the atomic nuclei. The atomic nuclei are comprised of protons and neutrons which spin on their axis. Hydrogen nuclei are used for magnetic resonance imaging study as it is bountiful in human body. These nuclei spin on its own axis and their movement generate a magnetic field. When the human body is exposed to external magnetic field of magnetic resonance imaging machine, the hydrogen nuclei in the human body starts to wobble or precess [figure 2]. The frequency at which this precession of the hydrogen atoms occur is called precessional frequency and is defined by Larmor equation (ϾϽ0=B0*ɣ). The nuclei of the hydrogen atoms will be aligned randomly until exposed to the external magnetic field. Once this radiofrequency pulse is applied by a transmit radiofrequency coil, these nuclei align in parallel and anti-parallel direction, and two magnetization vector components are produced (longitudinal and transverse). The protons relax once the radiofrequency pulse is removed, this generates a current in the receiving radiofrequency coil by the principle of Faraday law of induction which is the MRI signal [figure 3](14). There are gradient coils in the MRI machine which are in x-axis, y-axis and z-axis which are section-selective gradient, phase encoding gradient and frequency encoding gradient, help in localizing MRI signal. The pulse sequences are waveforms obtained from the radiofrequency pulses and gradients which helps in image acquisition (15).The MR system processor with all these information, is stored in the k-space. This raw imaging data is Fourier transformed and the final image is obtained(14).

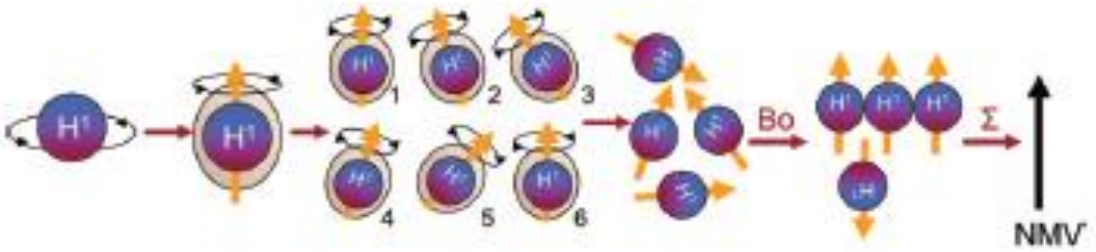


Figure 2. Spinning of hydrogen nuclei in their own axis (External magnetic field (B0, Aligning parallel and anti-parallel, net magnetization vector (NMV).

Bitar R, Leung G, Perng R, Tadros S, Moody AR, Sarrazin J, MR pulse sequences: what every radiologist wants to know but is afraid to ask.Radiographics. 2006 Mar-Apr; 26(2):513-37.

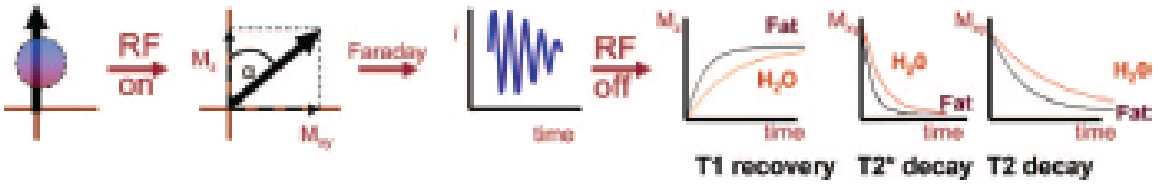


Figure 3. RF pulse applied flips the net magnetization vector at an angle producing longitudinal and transverse magnetization (Mz and Mxy respectively).

Bitar R, Leung G, Perng R, Tadros S, Moody AR, Sarrazin J, MR pulse sequences: what every radiologist wants to know but is afraid to ask.Radiographics. 2006 Mar-Apr; 26(2):513-37.

T1 recovery is T1 sequence acquired in MRI, which is produced by realignment of the net magnetization vector as longitudinal magnetization increases in magnitude. The spinning nuclei recover by discharging energy into the environment in T1. T2 recovery which is the T2 sequence in MRI, which is produced through decay of transverse magnetization. The interplay amidst the spinning nuclei and their magnetic fields interaction causes the transverse magnetization to dephase. T2* sequence in MRI is produced by the transverse magnetization dephasing by magnetic field inhomogenities [figure 4]. T1 weighted images helps to interpret the anatomy and T2 weighted images helps to interpret the disease(14).

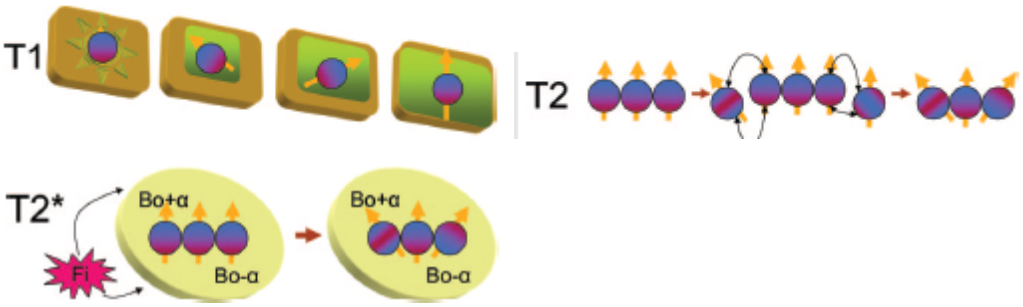


Figure 4. T1 recovery (spin-lattice relaxation), T2 decay (spin-spin relaxation), T2* decay.

Bitar R, Leung G, Perng R, Tadros S, Moody AR, Sarrazin J, MR pulse sequences: what every radiologist wants to know but is afraid to ask.Radiographics. 2006 Mar-Apr;26(2):513-37.

Technique of Cardiac MRI:

Cardiac MRI (CMR) is done for several indications some of which are to assess myocardial viability for hibernation and stunning, congenital heart diseases, cardiomyopathies, myocarditis, valvular heart diseases, tumours, pericardial disease, etc.(16).Advantages of doing MRI are that it has no ionizing radiation, greater soft tissue resolution, etc.(17). It is contraindicated in patients having aneurysmal clips, pacemakers, ocular implants, etc. As the risk for foetus is unknown, MRI during pregnancy is a relative contraindication (17).The technical obstacle in acquiring the images of the heart are due to its complex motion and pulsations of the vessels. These technical challenges can be lightened with the use of ECG gating, breath hold techniques, respiratory gating, etc.(17). The magnetic resonance imaging in 1.5 Tesla (T) and 3 T provide good quality images. A pile of short axis cine from the base to the apex of heart is accrued in approximately six breath holds for 10-12 seconds. The technique depends on a regular R-R interval on the ECG(18).

ECG gating is done as prospective or retrospective. In prospective gating image acquisition is begun with R wave triggering. The advantage is that only the necessary data are collected. However, this approach is limited due to heart rate fluctuation. Other disadvantage is that this technique is inclined to artefacts. Retrospective gating on the other hand acquires image throughout the cardiac cycle and the required data is selected during post processing. It is not affected by the heart rate variations. However, it is more time consuming. Respiratory gating enables the images to be acquired at the end of expiration by tracking the patient's breathing (17).

Image acquisition of Cardiac MRI: Planes

Cardiac MRI image acquisition is dependent on cardiac planes and the body planes Body planes are axial, coronal and sagittal planes which are orthogonal to the long axis of the body [Figure 5]. The cardiac morphology is better depicted with these planes. Axial plane helps us to view the four chambers of heart and the pericardium. The sagittal plane depicts great vessels arising from the ventricles. The coronal plane illustrates the left atrium, left ventricular outflow tract and the pulmonary veins. Nevertheless, the obliquity (~45°) of these planes to the walls of the heart deters definite anatomic and functional characterization. These information are better depicted by specialized cardiac planes (17).

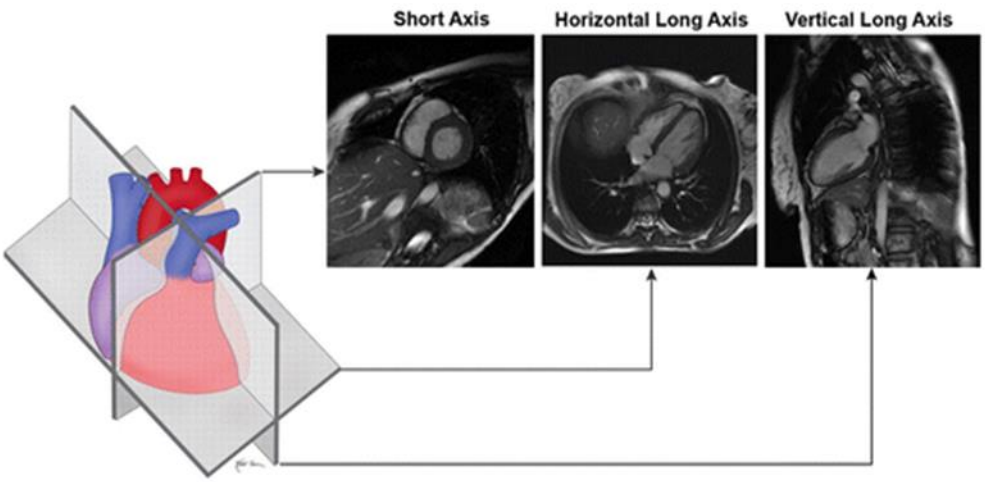


Figure 5. Body planes for image acquisition.

Daniel T. Ginat, Michael W. Fong, David J. Tuttle, Susan K. Hobbs and Rajashree C. Vyas, Cardiac imaging: Part I, MR pulse sequences, imaging planes, and basic anatomy, American Journal of Roentgenology. 2011: 197: 808-815

The cardiac planes included are short axis, four chamber view (horizontal long axis) and two chamber view (vertical long axis) [figure 6]. A line is drawn from the cardiac apex to the centre of the mitral valve in the axial body plane images. The short axis plane is perpendicular to the long axis of the heart at the mid left ventricular level. The four chamber view is perpendicular to the short axis. The two chamber view is orthogonal to the short axis. Three chamber view is obtained in short axis view when the axis intersects the left ventricular outflow tract and the posterolateral wall of the left ventricle and also in four chamber view when the axis intersects the mitral valve and apex of the left ventricle. Other cardiac planes are the right ventricular outflow track, right ventricular vertical long axis, right ventricular axial and oblique sagittal plane (parallel to the aorta and three points plane (17).

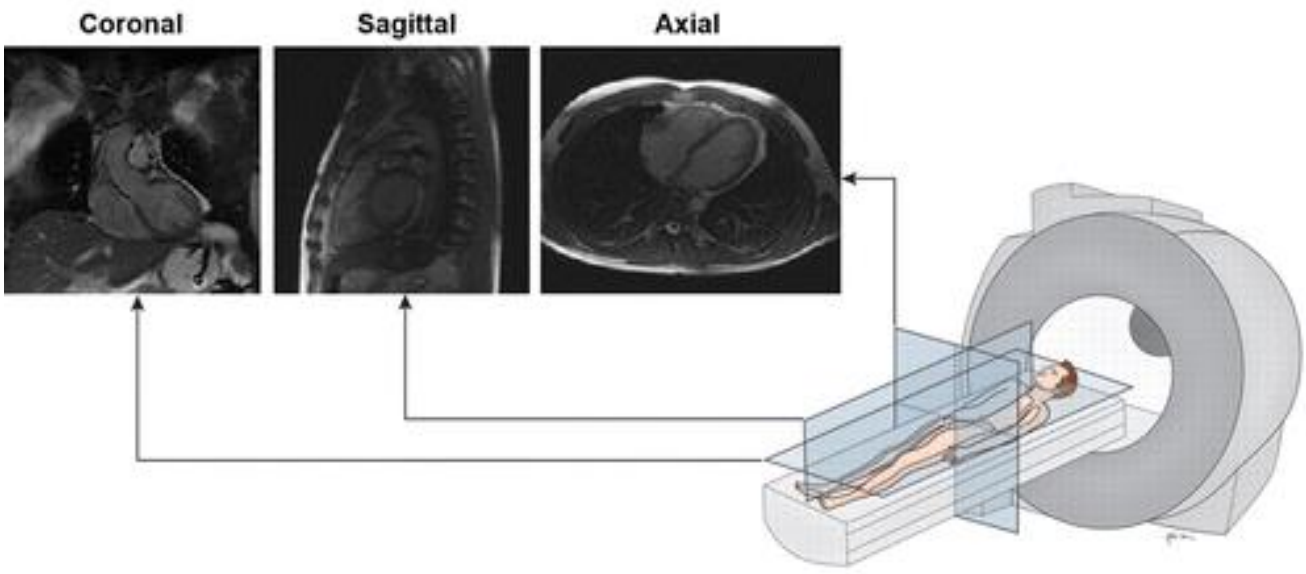


Figure Cardiac planes for image acquisition.

Daniel T. Ginat, Michael W. Fong, David J. Tuttle, Susan K. Hobbs and Rajashree C. Vyas, Cardiac imaging: Part I, MR pulse sequences, imaging planes, and basic anatomy, American Journal of Roentgenology. 2011: 197: 808-815

Image acquisition of Cardiac MRI : Pulse sequences

Numerous pulse sequences are available for image acquisition. The factors in the pulse sequence are called imaging engines and modifiers(17). Imaging engines are comprised of echo planar imaging, gradient echo, fast spin echo and steady state free precession. Modifiers are comprised of fat suppression, parallel imaging, inversion and saturation prepulse and velocity encoded imaging. Imaging engine is the back bone of image acquisition and modifiers assist in diagnostic interpretation(17).

Dark blood imaging

Dark blood imaging is used to depict anatomic structures. It is low signal intensity imaging of slow flowing blood. Spin echo imaging sequences are used to acquire dark blood imaging. Fast spin echo [Figure 7] and turbo spin echo sequences are the novel techniques. The artefact with this technique is that the slow flowing blood can appear

bright and can merge with the anatomic structures. Gadolinium is delivered only after dark blood imaging as it can interfere with this sequence (17).

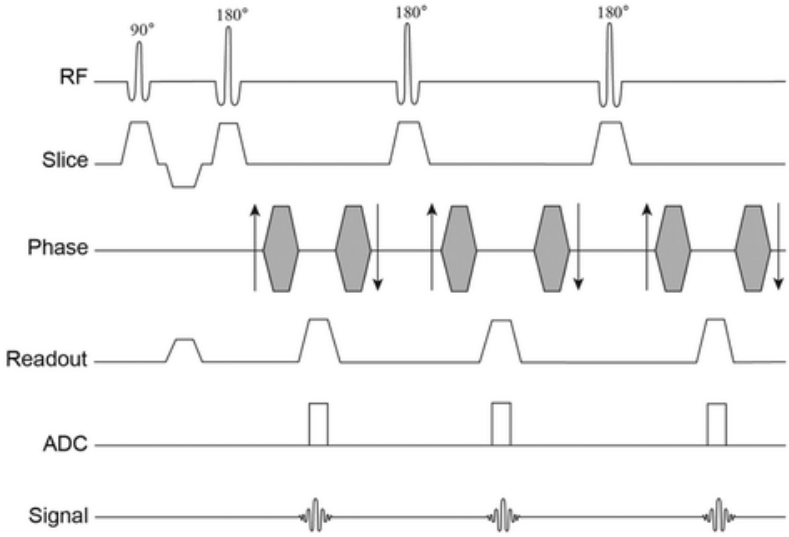


Figure 7. Radiofrequency pulse and signals readout in fast spin echo sequence.

Daniel T. Ginat, Michael W. Fong, David J. Tuttle, Susan K. Hobbs and Rajashree C. Vyas, Cardiac imaging: Part I, MR pulse sequences, imaging planes, and basic anatomy, American Journal of Roentgenology. 2011: 197: 808-815.

Bright blood imaging

Bright blood imaging is used to assess the cardiac function. It is high signal intensity imaging of fast flowing blood. Gradient echo imaging sequences are used to acquire bright blood imaging. Steady state free precession [Figure 8], FIESTA, turbo field echo, fast field echo, etc. are the novel techniques (17).

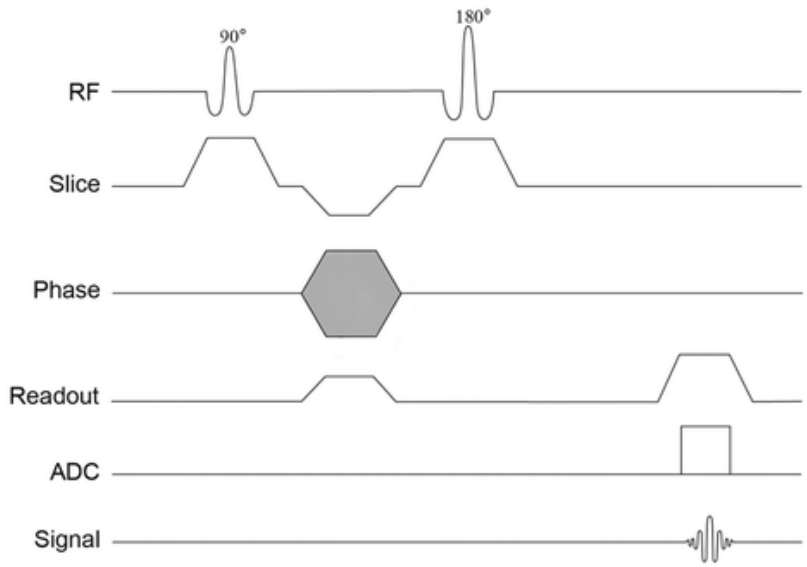


Figure 8. Radiofrequency pulse and signals readout in steady state free precision echo sequence.

Daniel T. Ginat, Michael W. Fong, David J. Tuttle, Susan K. Hobbs and Rajashree C. Vyas, Cardiac imaging: Part I, MR pulse sequences, imaging planes, and basic anatomy, American Journal of Roentgenology. 2011: 197: 808-815.

Contrast enhanced Imaging:

Gadolinium is the contrast agent used for contrast enhanced imaging. The use of contrast material in cardiac MRI is dependent on delayed enhancement. The imaging, which is inversion recovery, is done after ten minutes of gadolinium injection intravenously. The contrast agent is administered as 0.1-0.2 mmol/kg with a saline chase bolus of 20 ml. There will be enhancement of myocardium in the areas of abnormality when myocardium is nulled utmost (17).

Delayed contrast enhanced cardiac MRI customarily used to assess ischemic heart disease for infarction and viability of the myocardium. Nonetheless, nowadays it is being used for assessment of non-ischemic cardiomyopathies. The diagnosis of non-ischemic cardiomyopathy can be simplified with the help of discrete enhancement

patterns. These areas of enhancement are also subjected to endomyocardial biopsy for confirming the diagnosis. Different patterns of enhancement are midmyocardial (or mesocardial), subendocardial, subepicardial, patchy and transmural, each of these have separate list of differential diagnosis [figure 9](19).

Myocardial fibrosis can also be detected with delayed enhancement pattern. There is collagen within the myocardium, leading to scar formation or fibrosis, which leads to heart failure. The different types of myocardial fibrosis are reactive interstitial fibrosis due to diabetes, hypertension, etc., infiltrative interstitial fibrosis due to deposition of infiltrates like amyloid, granulomas in sarcoidosis, glycosphingolipids in Anderson Fabry, etc. and replacement fibrosis which primarily scarring due to damage and necrosis as seen in myocardial ischemia (20). The delayed contrast enhancement in myocardial fibrosis is dependent on higher distribution of contrast with protracted wash out time of contrast due to lower capillary density within the fibrotic tissue. There is increased extracellular volume within the scarred myocardium which leads to increased distribution of the contrast within the same (20). Interpretation of scar on cardiac imaging is significant as it is responsible for arrhythmias, which can be dangerous for life and can lead to sudden cardiac death(18).

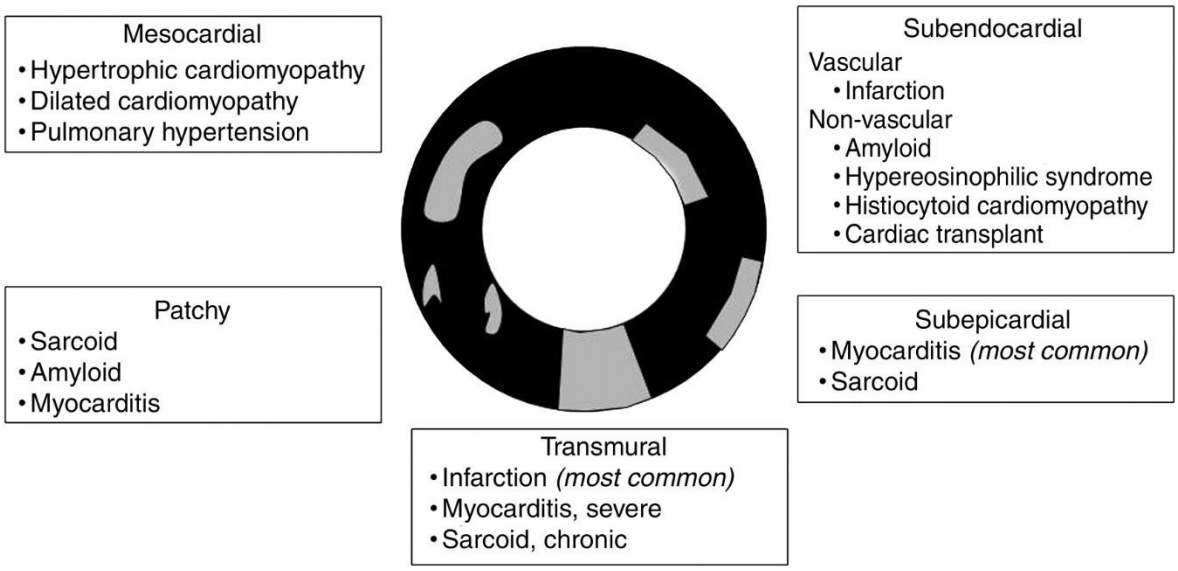


Figure 9. Patterns of delayed enhancement in cardiac MRI.

Cummings KW, Bhalla S, Javidan-Nejad C, Bierhals AJ, Gutierrez FR, Woodard PK, A pattern-based approach to assessment of delayed enhancement in nonischemic cardiomyopathy at MR imaging.Radiographics. 2009 Jan-Feb;29(1):89-103. doi: 10.1148/rg.291085052.

Subendocardial enhancement

The subendocardium is the inside part of the myocardium adjacent to the blood pool. The area if involved is within the vascular territory it is considered infarction and non-vascular territorial involvement there is uniform subendocardial enhancement in conditions like amyloidosis, hypereosinophilic syndrome, histiocytoid cardiomyopathy and in cardiac transplant(19).In patients with AL amyloidosis, the prevalent patterns subendocardial, subepicardial and patchy nodular enhancement.

Subepicardial enhancement

The subepicardium is the outward part of the myocardium adjacent to the pericardium, most distant from the blood pool. It is dominant pattern in myocarditis and sarcoidosis. These enhancement areas can also be used as a tool to guide for endomyocardial biopsy. In myocarditis, this pattern resolves after 6-8 weeks, with

resolution of the disease (19).In patient with TTR amyloidosis, the subepicardial pattern of enhancement was more common in basal and mid cavity lateral segments as compared to the AL amyloidosis patients.

Mid myocardial or mesocardial enhancement

The mid myocardium is the part between the subendocardium and subepicardium of the myocardium. This pattern is seen predominantly with dilated and hypertrophic cardiomyopathy. Hypertrophic cardiomyopathy is characterized with abnormal myocardial wall thickening and restrained diastolic filling of the left ventricle in cardiac MRI. These areas of abnormal wall thickening can show enhancement secondary to fibrosis or ischemia due to microvascular obstruction by hypertrophy. Dilated cardiomyopathy is the most common non-ischemic cardiomyopathy. Dilated left ventricle with reduced ejection fraction in cardiac MRI with delayed enhancement pattern of mid myocardial due to fibrosis are diagnostic of dilated cardiomyopathy (19).

Transmural Enhancement

The transmural involvement is the involvement of the entire musculature of the myocardium. However, there can be difference in the percentage of involvement of the myocardium and this can in turn predict the functional recovery in myocardial infarction. The transmural enhancement pattern is commonly seen in ischemic heart disease due to myocardial infarction. Myocarditis can also demonstrate transmural enhancement in later stages due to fibrosis. However the prevalent pattern in myocarditis is subepicardial (19).

Nodular or Patchy Enhancement

Patchy delayed enhancement can be seen in sarcoidosis, myocarditis and amyloidosis. Nodular pattern of enhancement in sarcoidosis is due to non-caseating granulomas. Other associated features of lymphadenopathy and parenchymal involvement are also seen. Isolated cardiac involvement in sarcoidosis is rare. Again these areas of enhancement are a guide for biopsy(19).

Sarcoidosis diagnosis can be a challenge in tuberculosis endemic countries.

Significance of cardiac MRI in non-ischemic cardiomyopathy:

The significance of cardiac MRI in non-ischemic cardiomyopathy are varied.

1. The visualization of right ventricle is of higher quality with MRI, especially in arrhythmogenic right ventricular dysplasia. Both sides of heart are frequently involved with non-ischemic cardiomyopathy than with ischemic cardiomyopathy. Abnormal wall thickness are better appreciated on cardiac MRI (18).Wall motion abnormalities like dyskinesia and akinesia and hypokinesia in ARVD and myocardial infarction respectively are better appreciable on cardiac MRI.

2. The volume and systolic functional parameters can be better assessed as compared to echocardiogram.

3. Late gadolinium enhancement patterns help in differentiating between various pathologies and come to a diagnosis. Myocardial fibrosis can also be detected with cardiac MRI with delayed enhancement pattern. The causes for myocardial fibrosis include myocardial infarction, hypertensive cardiomyopathy, hypertrophic

cardiomyopathy, myocarditis, infiltrative diseases like sarcoidosis, amyloidosis, etc(20). Myocardial fibrosis could only be assessed with endomyocardial biopsies previously. However, cardiac MRI has improvised the diagnostic standard in the recent past with better tissue characterization abilities. The late gadolinium enhancement and parametric mapping has revolutionized the diagnosis of myocardial fibrosis, which is a prognostic factor (20).

3. The other tissue characteristics like iron deposition and edema can also be detected using cardiac MRI with the help of parametric mapping, specifically T2* and T2 mapping respectively (18).

Parametric mapping in cardiac MRI for non-ischemic cardiomyopathy:

Parametric mapping are quantitative parameters, which are perfusion parameters alternatively also relaxation time of the myocardium. These are T1, T2, T2*, T1 post contrast relaxation times and extracellular volume. These are exclusive tissue parameters that are measured using cardiac MRI (21). T1 and T2 mapping techniques provide myocardial tissue characterisation in addition to late gadolinium enhancement(22).Cardiac MRI is the principal imaging modality for myocardial tissue characterisation. CMR parametric mapping allows the spatial visualisation of quantitative changes in myocardium based on the differences in myocardial parameters T1, T2, T2*(star) and ECV. These changes are due to specific disease pathways related to the intracellular disturbances of the cardiomyocyte (for e.g., iron overload, or glycosphingolipid accumulation in Anderson-Fabry disease); extracellular derangements in the myocardial interstitium (for e.g., myocardial fibrosis of cardiac amyloidosis); or both (for e.g. myocardial edema from infarction with

increased intracellular and/or extracellular fluid). Unlike the routine T1-, T2- and T2*-weighted images, mapping allows visualisation and quantification of the disease independent of whether the myocardial disease is focal or diffuse. This is important as diffuse myocardial disease is related to specific disease pathways and has been difficult to non-invasively quantify or appreciate(23).T1 and T2 mapping are capable in identification and quantification of myocardial diseases without biopsy. Native T1 mapping is superior to T2-weighted imaging and late gadolinium enhancement as it provides a high level of diagnostic accuracy and can detect myocardial abnormalities to a greater extent. It has superior positive and negative predictive value. Hence, parametric mapping is now considered as an essential tool in the quantitative analysis of non-ischemic cardiomyopathy(4).

Native T1 mapping:

Native T1 or T1 relaxation time, also known as spin-lattice or longitudinal relaxation time is a tissue-specific time constant, to characterise different tissues. T1 mapping is driven by protons that align their spins briskly following excitation by a radiofrequency pulse. The T1 relaxation time is depended on the rate of energy transfer roman excited proton to its surroundings. This varies according to the state of the molecular size, shape, viscosity, temperature and magnetic field strength. T1 values are directly proportional to the field strength. The T1 values also vary with age and sex (men and elderly have slightly higher values)(24). All tissues have constitutional T1relaxation time, based on their cellular and interstitial constituents like water, fat, iron, etc. Myocardial diseases alter these constituents, thus changing

the native T1 and T2 signals. Normal myocardial T1 relaxation time ranges from 941–1029 msec at 1.5 Tesla and 1158-1169 msec in 3 Tesla (4) [figure 10].

Table 1: Select Reported Myocardial T1 Relaxation Times in Healthy Subjects

Magnet	Technique	No. of Subjects*	Age (y)	Native T1 (msec)†	Contrast-enhanced T1 (msec)	Authors	Year
1.5 T	LL	14 (8)	38 ± 10.9	1000.4 ± 126	523.3 ± 72.8	Nacif et al (27)	2011
1.5 T	MOLLI	15 (9)	33.1 ± 8.5	982 ± 46	NR	Messroghli et al (13)	2006
1.5 T	MOLLI	10 (7)	35 ± 7	976 ± 46/80	NR	Piechnik et al (19)	2010
1.5 T	MOLLI	14 (8)	38 ± 10.9	1029.4 ± 56.8	462.4 ± 62.2	Nacif et al (27)	2011
1.5 T	MOLLI	13 (7)	38.1 ± 11.1	NR	466 ± 14	Sibley et al (23)	2012
1.5 T	ShMOLLI	10 (7)	35 ± 7	966 ± 48/88	NR	Piechnik et al (19)	2010
1.5 T	ShMOLLI	21 (8)	55 ± 13	944 ± 17	NR	Ferreira et al (40)	2012
1.5 T	ShMOLLI	45 (32)	42 ± 14	941 ± 18	NR	Ferreira et al (41)	2013
1.5 T	ShMOLLI	342 (170)	38 ± 15	962 ± 25	NR	Piechnik et al (14)	2013
1.5 T	ShMOLLI	36 (22)	59 ± 4	958 ± 20	NR	Karamitsos et al (42)	2013
3 T	MOLLI	10 (7)	35 ± 7	1169 ± 45/73	NR	Piechnik et al (19)	2010
3 T	MOLLI	24 (8)	29 ± 6	1159.0 ± 39.2	NR	Liu et al (21)	2012
3 T	MOLLI	60 (30)	48 ± 17	1158.7	411.2	von Knobelsdorff-Brenkenhoff et al (43)	2013
3 T	ShMOLLI	10 (7)	35 ± 7	1166 ± 60/91	NR	Piechnik et al (19)	2010

Note.—NR = not reported.
*Number in parentheses indicates number of male subjects.
†Some values are represented as mean ± standard deviation/mixed standard deviation, as defined by Piechnik et al (19).

Figure 10. Normal myocardial T1 relaxation time.

Hamlin SA[1], Henry TS, Little BP, Lerakis S, Stillman AE. Mapping the future of cardiac MR imaging: case-based review of T1 and T2 mapping techniques.Radiographics. 2014 Oct;34(6):1594-611. doi: 10.1148/rg.346140030.

Techniques of T1 mapping:

a. Look and Locker, in 1970, suggested a design to estimate T1 relaxation times by achieving data consecutively after magnetisation inversion [figure 11]. These techniques have been further modified and acquisition times shortened. Currently widely used technique, the Modified Look-Locker Inversion recovery (MOLLI) pulse sequence measures T1 relaxation time in a single breath hold and 17 consecutive heart beats(24).

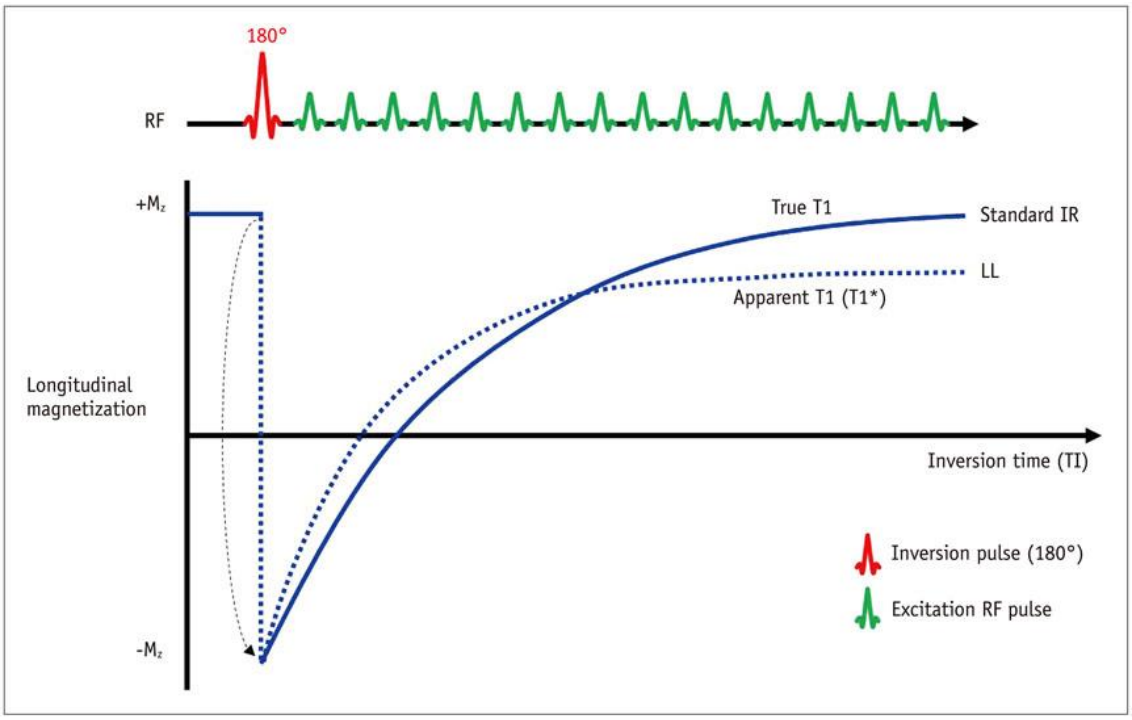


Figure 11. Look Locker technique of T1 mapping.

Pan Ki Kim, PhD,[1] Yoo Jin Hong, MD, PhD,[1] Dong Jin Im, MD,[1] Young Joo Suh, MD, PhD,[1] Chul Hwan Park, MD,[2] Jin Young Kim, MD,Myocardial T1 and T2 Mapping: Techniques and Clinical Applications. Korean J Radiol. 2017 Jan-Feb; 18(1): 113–131.

b. In MOLLI technique, inversion recovery images are amassed at diverse inversion times in one breath hold and in single cardiac cycle with single shot readouts and in single slice. The initial code for modified Look Locker technique was 3(3)3(3)5. The numbers within the bracket are the number of RR intervals in T1 recovery and the ones outside the bracket are the number of images obtained after the inversion pulse. Currently, a simpler protocol used for MOLLI is 5(3)3 [figure 12]. These modifications in protocol improves the accuracy and precision(24).The equilibrium magnetization is inverted alternatively nulled by radiofrequency pulse for T1 measurement. Subsequently these images are procured at separate times after inversion or following saturation pulse (25).

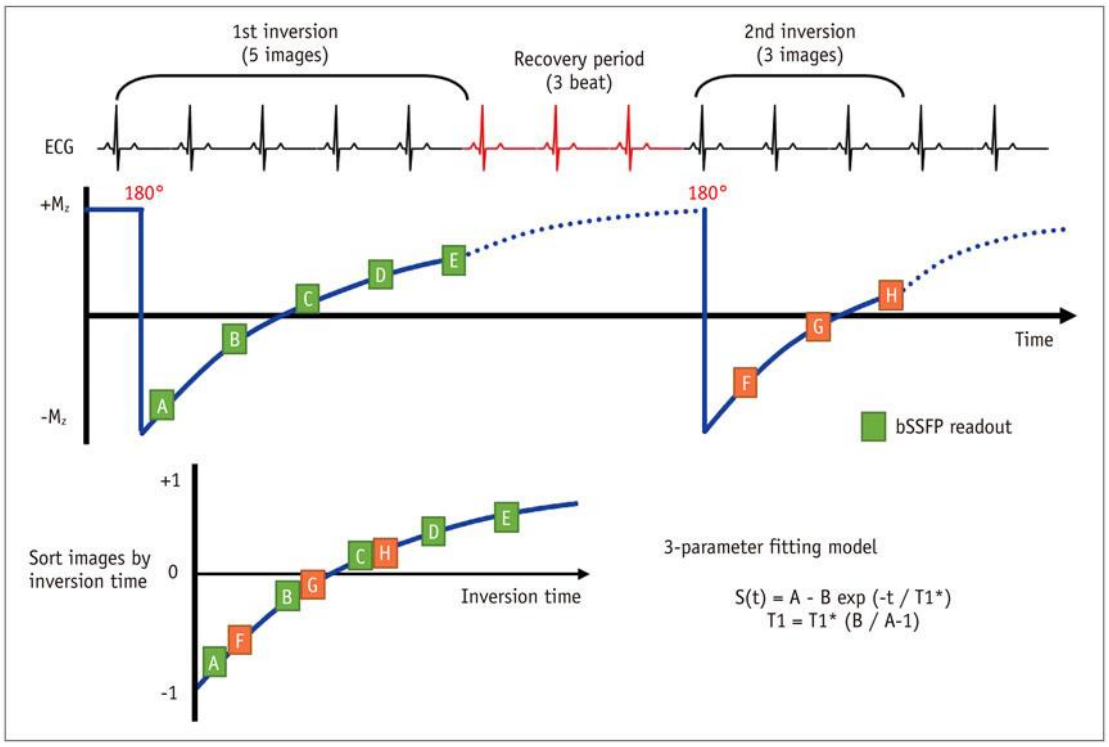
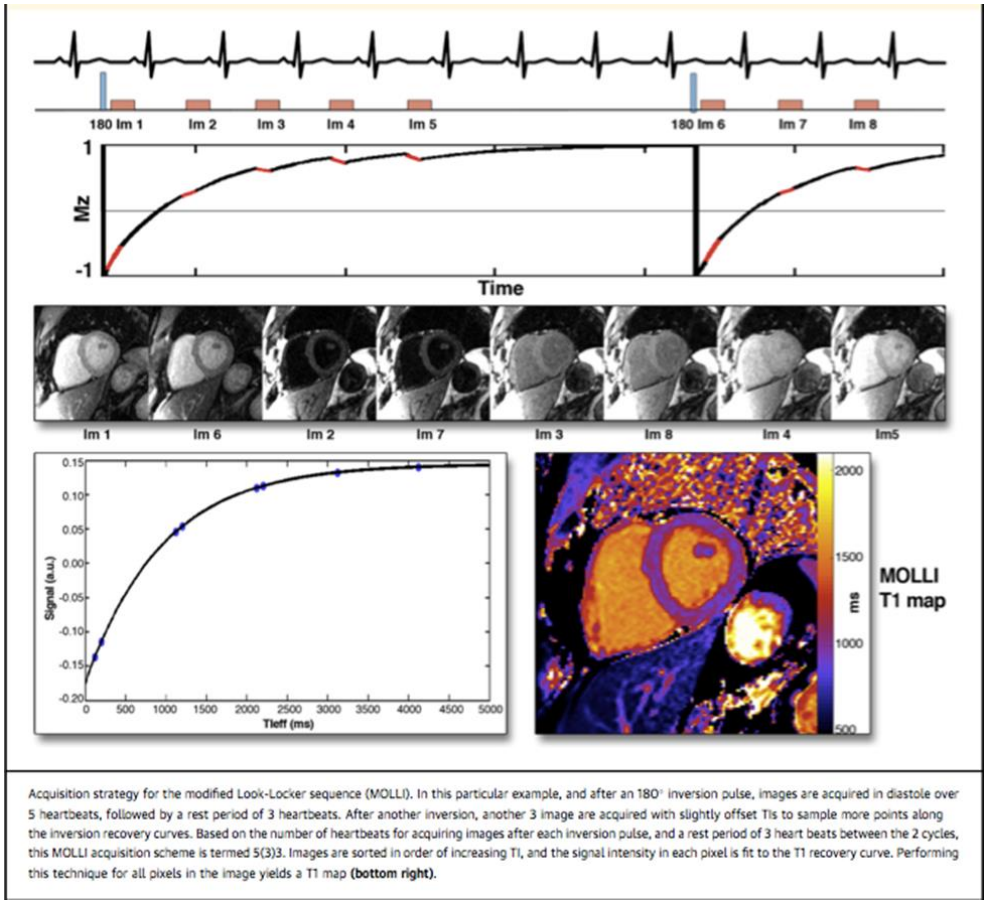


Figure 12. Modified Look Locker technique of T1 mapping.

Pan Ki Kim, PhD,[1] Yoo Jin Hong, MD, PhD,[1] Dong Jin Im, MD,[1] Young Joo Suh, MD, PhD,[1] Chul Hwan Park, MD,[2] Jin Young Kim, MD,Myocardial T1 and T2 Mapping: Techniques and Clinical Applications. Korean J Radiol. 2017 Jan-Feb; 18(1): 113–131.

The latest technical progress enables myocardial T1 mapping to be acquired with 1.5 Tesla MRI scanners in a single breath hold. The differences in enhancement and windowing are reduced with T1 mapping techniques. Hence, the quantification of relaxation time is standardized better. In MOLLI technique the images are obtained in the constant cardiac phase as compared to the conventional technique(26). The curve fitting of all images in a sequence generates a pixel map of the T1 values which is represented as a single image, the T1 map (4). Native T1 is an assuring method for detecting myocardial abnormalities without gadolinium administration(24)[figure 13].



Acquisition strategy for the modified Look-Locker sequence (MOLLI). In this particular example, and after an 180° inversion pulse, images are acquired in diastole over 5 heartbeats, followed by a rest period of 3 heartbeats. After another inversion, another 3 image are acquired with slightly offset TIs to sample more points along the inversion recovery curves. Based on the number of heartbeats for acquiring images after each inversion pulse, and a rest period of 3 heart beats between the 2 cycles, this MOLLI acquisition scheme is termed 5(3)3. Images are sorted in order of increasing TI, and the signal intensity in each pixel is fit to the T1 recovery curve. Performing this technique for all pixels in the image yields a T1 map **(bottom right)**.

Figure 13. MOLLI technique for T1 mapping.

Andrew J.TaylorMD, PhD, RohanDharmakumarPhD, MichaelJerosch-HeroldPhD,T1 Mapping: Basic Techniques and Clinical Applications. JACC Cardiovasc Imaging. 2016 Jan; 9(1):67-81.

Limitation of the MOLLI technique is the challenge of procuring data over 17 heartbeats and also the complete recovery of magnetization can be affected if adequate time is unavailable, as it can be dependent on the heart rate (25).

c. The latest sequences are shortened MOLLI (ShMOLLI), saturation recovery single shot acquisition (SASHA) and saturation pulse prepared heart rate independent inversion recovery (SAPHIRE) (27).

The shortened MOLLI (ShMOLLI) sequence is a modification of the modified Look Locker technique, with a faster acquisition time in a brief breath hold and nine

heartbeats(24). It is dependent on the conditional fitting. Conditional means that the data from previous two cycles are exclusively used if T1 is short enough to grant complete magnetization recovery after any of the previous cycles(25).

Saturation recovery is used as a substitute for inversion recovery lately. This makes the wait for T1 recovery between saturation pulses is unnecessary and therefore the heart rate dependence is excluded (25). Saturation recovery single shot acquisition technique (SASHA) comprises the procurement of balanced steady state free precession images over consecutive heartbeats in a single shot. The first image is procured without saturation preparation, using equilibrium magnetization and the subsequent ten images are procured using a saturation pulse with varied lag over the RR interval. It is exceptionally accurate, however, is sensitive to noise.

The final T1 parametric map or colour map [figure 14] is generated based on the T1 relaxation time (in milliseconds) for each voxel and motion correction (MOCO) is applied. It can be assessed qualitatively (visually) and also quantitatively by drawing regions of interest on the myocardium. The respiratory motion during MOLLI causes artefacts, in spite of breath hold. If it's not corrected, can lead to flaws in T1 pixel estimation, which deteriorates the image quality. Additionally, there are also challenges with image registration due to different tissue characteristics like fat, blood, myocardium, etc. which null at different timings. Hence, motion correction is important and it is done using an iterative approach and multiple motion free images

are created for different inversion time with MOLLI generated images.

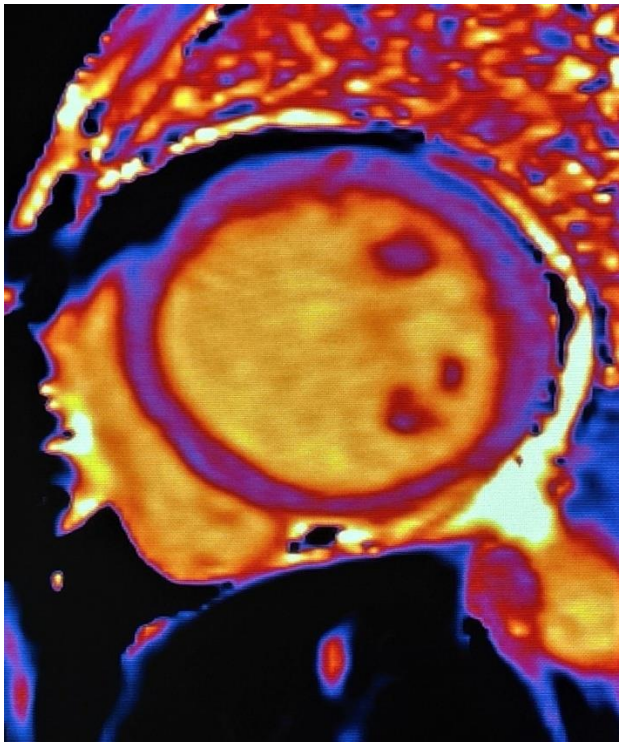


Figure 14. Normal T1 parametric map at mid cavity level

Contrast enhanced T1 mapping:

Post contrast T1 mapping and native T1 mapping are helpful in calculation of the extracellular volume fraction. Gadolinium contrast is dispersed in the extracellular space of the myocardium, which shortens the T1 relaxation time. The regions of myocardial scar and fibrosis show lessened post contrast T1 relaxation time (26).

This can be part of the routine protocol without additional increase in time of the study. There are multiple confounding factors for post contrast T1 such as heart rate, physiological factors which influence contrast administration like glomerular filtration rate, body fat, contrast dispersion time, etc. Contrast dispersion is also dependent on the extracellular water content. However, in patients with estimated glomerular filtration rate less than 30 mL/min/1.73 m^2. These factors have to be considered prior

to contrast enhanced T1 mapping and can be analysed with linear regression preceding analysis (26).Gadolinium contrast of 0.1 – 0.2 mmol/kg is used. The acquisition of contrast enhanced T1 map has to be done within 10 – 30 min after administration of the contrast(23).Normal values of contrast enhanced T1 relaxation time is 504 ± 34 ms in 1.5T scanner. There is significant correlation between global myocardial contrast enhanced T1 relaxation time and myocardial fibrosis (28).The T1 mapping post contrast or contrast enhanced T1 mapping is also acquired using MOLLI technique. ShMOLLI, SASHA and SAPHIRE techniques can also be used to acquire contrast enhanced T1 maps. Contrast enhanced T1 maps are generated similar to the native T1 maps, with motion correction and contrast enhanced T1 relaxation time for each voxel [figure 15]. These colour maps are then contoured for quantitative assessment.

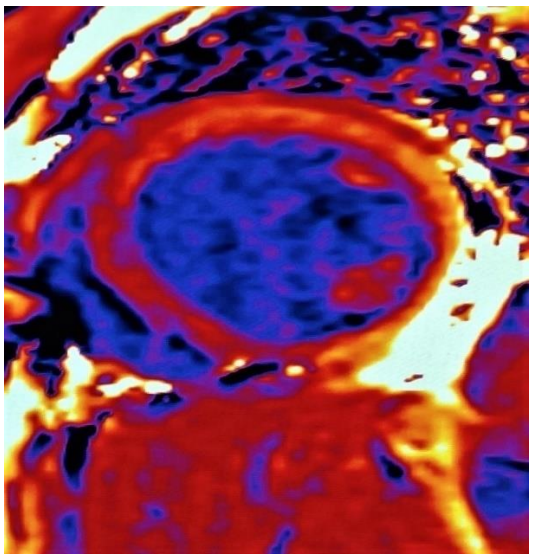


Figure 15. Normal contrast enhanced T1 parametric map at mid cavity level

T2 mapping:

T2 relaxation time, also known as spin-spin or transverse relaxation time is also a tissue-specific time constant. The excess of water content in the myocardial tissues (myocardial edema) is responsible for longer T2 relaxation time. T2 mapping sequences are commonly used to detect myocardial edema in conditions like myocarditis, cardiac allograft rejection, stress cardiomyopathy, sarcoidosis and acute myocardial infarction. Myocardial T2 values are acquired by steady-state free precession (SSFP) MR sequence. Normal myocardial T2 relaxation time is 50±4 - 55.5±2.3 msec at 1.5Tesla and 48±17 msec at 3Tesla [figure 16] (4). T2 values increases with subacute inflammation, acute inflammation, acute ischemia, necrosis and decreases with iron and haemorrhage (29).

Magnet	Technique	No. of Subjects*	Age (y)	Native T2 (msec)	Authors	Year
1.5 T	SSFP multipoint IR	19 (13)	38 ± 17	50 ± 4	Blume et al (16)	2009
1.5 T	Spiral interleaved T2	10 (5)	36 ± 7	54 ± 6.8	Sparrow et al (17)	2009
1.5 T	SSFP	14 (NR)	NR	52.18 ± 3.4	Giri et al (15)	2009
1.5 T	SSFP	21 (13)	28 ± 7	55.5 ± 2.3	Verhaert et al (33)	2011
1.5 T	SSFP	10 (NR)	NR	53.4 ± 6.1	Giri et al (44)	2012
1.5 T	SSFP	14 (NR)	NR	51.5 ± 2.0	Crouser et al (35)	2014
3 T	SSFP	60 (30)	48 ± 17	45.1 (mean)	Von Knobelsdorff-Brenkenhoff et al (43)	2013

Figure 16. Normal myocardial T2 relaxation time

Hamlin SA[1], Henry TS, Little BP, Lerakis S, Stillman AE. Mapping the future of cardiac MR imaging: case-based review of T1 and T2 mapping techniques.Radiographics. 2014 Oct; 34(6):1594-611. doi: 10.1148/rg.346140030.

Dark blood turbo spin echo and bright blood T2 preparation pulse sequences are used as T2 mapping sequences in cardiac MR imaging. T2 preparation pulse based sequence is applied followed by a readout using a steady-state free precession (SSFP) sequence and a T2 decay curve is calculated, following which T2 parametric maps are obtained (4).

Techniques of T2 mapping:

T2 mapping is an additional technique for tissue characterization. It is ruled by rapid decay of transverse magnetization. The sequences used for T2 mapping are bright blood sequence and dark blood turbo spin echo sequence. The bright blood T2 preparation pulse sequence is better than dark blood sequences as the blood flow artefacts which show a bright subendocardial rim are lesser with bright blood sequences. T2 preparation time is adjusted using a T2 decay curve.T2 decay curve is created in two steps, a T2 preparation protocol and quick imaging sequences like balanced steady state free precision or a gradient echo sequence. The T2 preparation protocol constitutes 90° and 180° pulses between two 90° pulses to generate spin-spin relaxation [figure 17]. Following which, the degree of T2 decay revolves around the degree of the longitudinal magnetization. The transverse relaxation is built over 7 RR intervals, which is seven seconds. The T2 decay can be altered by fluctuating the extent of theT2 preparation protocol. The balanced steady state free precision or gradient echo sequence is done promptly after T2 preparation. T2 map is developed through a two parameter fitting model(24).

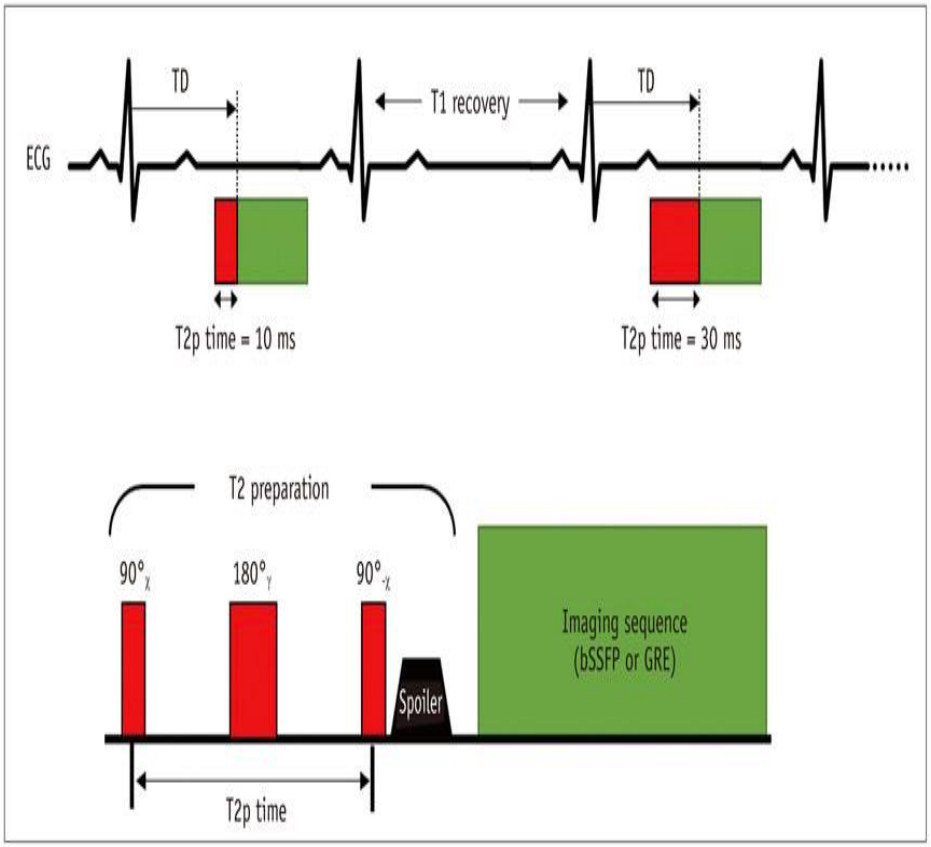


Figure 17. T2 mapping technique

Hamlin SA, Henry TS, Little BP, Lerakis S, Stillman AE. Mapping the future of cardiac MR imaging: case-based review of T1 and T2 mapping techniques.Radiographics. 2014 Oct;34(6):1594-611.

Originally, T2 mapping was established on dark blood turbo spin echo sequences. However, these sequences are sensitive to blood flow artefacts. T2 mapping is dependent on the heart rate and is prospectively ECG triggered. Presently, the normal values of T2 relaxation fluctuate between each individual study in comparison with T1 relaxation time. However, it is important in disease detection, specifically myocardial oedema which is not reliably detected with T1 mapping (28).

Similar to the T1 mapping, T2 parametric map is also a colour map [figure 18] which is generated based on the T2 relaxation time, in milliseconds, for each voxel and with

motion correction. It can be also be assessed visually and also quantitatively by drawing regions of interest on the myocardium(30).The T2 parametric mapping is advantageous as it is more reliable than the T2 weighted images in distinguishing myocardial oedema. It is considered exceptionally higher than T1 mapping and extracellular volume fraction in detecting myocarditis. It is also considered as a novel tool in monitoring the cardiac transplant patients (30).

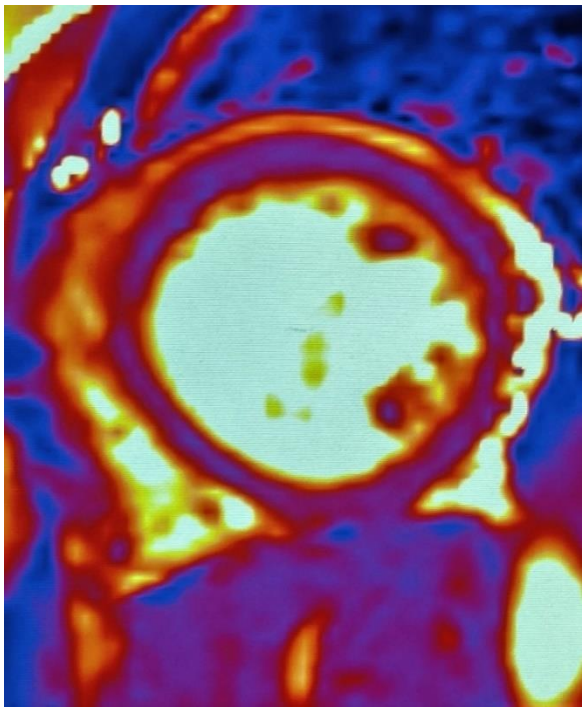


Figure 18. Normal T2 parametric map at mid cavity level

Extracellular volume fraction (ECV):

The extracellular volume manifests the extracellular space in the myocardium, where contrast uptake into the cells is absent. It is a method used to evaluate the myocardial extracellular distribution volume, which is helpful in detection of myocardial fibrosis.

It is calculated by using the hematocrit at the time of study; native T1 and post contrast relaxation time of the myocardium and the blood pool using the formula given below [refer to figure 19]. It acts as an addition to the late gadolinium enhancement for detection of myocardial fibrosis (31).

$$ECV = (1 - hematocrit)\frac{\left(\frac{1}{T1_{myo\ post}} - \frac{1}{T1_{myo\ pre}}\right)}{\left(\frac{1}{T1_{blood\ post}} - \frac{1}{T1_{blood\ pre}}\right)}$$

Figure 19. ECV formula.

Peter Kellman, Joel R Wilson, Hui Xue, Martin Ugander, Andrew E Arai. Extracellular volume fraction mapping in the myocardium, part 1: evaluation of an automated method, Journal of Cardiovascular Magnetic Resonance 2012, 14:63

Hematocrit can be measured from the venous blood sample taken prior to the cardiac MRI if achievable, else in24 hours of the scan. It complements the late gadolinium enhancement pattern. Achieving a dynamic steady state using a bolus intravenous infusion is important to estimate the ECV precisely. ECV can quantitatively distinguish and identify the myocardial abnormalities that are not clinically evident. Direct calculation of extracellular volume was originally created for quantifying the extracellular fractional distribution volume and has been recommended as a medium to identify and measure diffuse myocardial fibrosis.

Pixel wise mapping of ECV [figure 20] is cumbersome requiring extensive post processing and correction of respiratory motion. Co-registration is method to produce ECV maps by eliminating artefacts in native T1 and contrast enhanced T1 maps and produce a better quality ECV maps without mis-registration. The ECV fraction for a normal subject using pixel mapping and MOCO and co-registration is $25.4 \pm 2.5\%$,

measured in the mid wall, the range being 20.4-30.4% in 1.5 T (31).The ECV fraction for normal healthy myocardium in 3 T is 27-29%. It is observed to be marginally higher in women as compared to men.ECV values can be elevated in myocardial oedema, myocardial fibrosis, hypertrophic cardiomyopathy, dilated cardiomyopathy, cardiac amyloidosis, etc.(32).

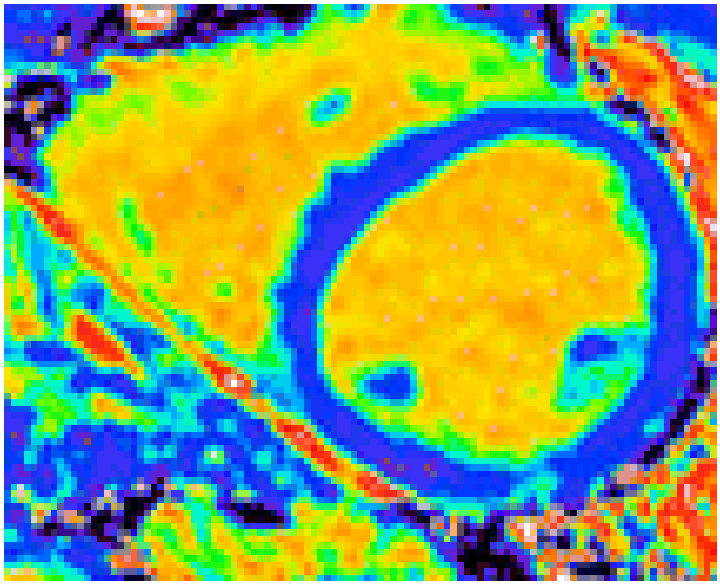


Figure 20. Normal ECV map

Scully PR, Bastarrika G, Moon JC, Treibel TAMyocardial Extracellular Volume Quantification by Cardiovascular Magnetic Resonance and Computed Tomography.Curr Cardiol Rep. 2018 Mar 6; 20(3):15

It has an improved concurrence with collage volume histologically than contrast enhanced T1 (26). This is significant as endomyocardial biopsy which was the gold standard for detection of myocardial fibrosis can be replaced with non-invasive cardiac MRI with late gadolinium enhancement and parametric mapping. ECV is better than late gadolinium enhancement as it can help in early detection of fibrosis(32). ECV fraction can be of prognostic significance as comparable to left ventricular ejection fraction in varied cardiac diseases (33).ECV can be elevated in segments where late gadolinium enhancement is present or abnormal, whereas can be

normal in the normal appearing myocardium. It also increases with the age in normal subjects with no comorbidities. This can be explained on the basis of loss of myocytes or absent collagen degradation in the myocardium with age(32). ECV fraction can also be used to detect myocardial remodelling post infarct which might not be apparent on late gadolinium enhanced images(34).

Cardiac MRI protocol and quantification of parametric mapping:

The general protocol used for parametric mapping for myocardial characterization is cine imaging, STIR sequences, native T1 mapping, native T2 mapping, T2* mapping, post contrast T1 mapping and late gadolinium enhancement. ECV mapping is done in few centres. However, hematocrit has to be done prior to the cardiac MRI or within 24 hours of the study and ECV fraction values are then calculated (23).

The protocols used for parametric mapping can vary according to the disease processes, as follows (23):

* If it's a dispersed disease process- short axis view at basal and mid cavity level has to be procured alongside a long axis map optionally with an optional single long axis map.

*If it's a scattered disease process- basal and mid cavity short axis view along with four chamber view or three chamber view, depending on whether it is amyloidosis or Anderson Fabry disease.

* If it's a focal disease process- the short axis views depending on the involved region has to be procured.

The recommended protocol for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume is given by Society for Cardiovascular Magnetic Resonance (SCMR) which is endorsed by the European Association for Cardiovascular Imaging as given in figure 21.

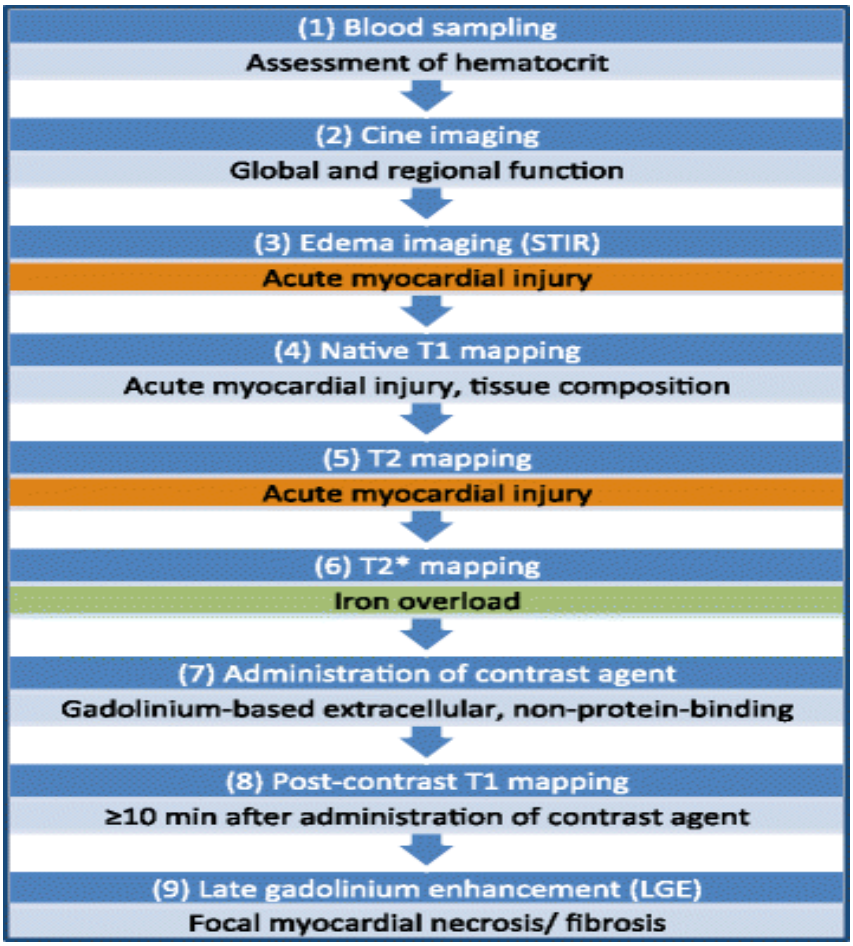


Figure 24. The recommended protocol for cardiac MRI and parametric mapping
Messroghli DR, Moon JC, Ferreira VM, Grosse-Wortmann L, He T, Kellman P. Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI).J Cardiovasc Magn Reson. 2017 Oct 9;19(1):75.

These parametric maps are quantified by drawing or contouring the myocardial segments at basal, mid cavity, apical and apex levels according to the 17 segment model of the American heart association. However, care should be taken that only the myocardium is contoured sparing the blood pool, lung, liver, etc.

The segmental measurement of each segment is not practised in many centres and so a mid cavity single segment of interest that is expected to be the epitome of the entire myocardium is quantified. This is also practised as there can be problems related to artefacts in measuring each segments and hence give a false value (35).Region of interest is drawn on the septum of mid cavity for a diffuse disease process and in focal disease process, additional region of interest has to be drawn in abnormal areas. Region of interest can also be created automatically. The values of parametric mapping are displayed as numerical value with standard deviation(23).

Clinical applications of parametric mapping in non-ischemic cardiomyopathy:

The T1 mapping enables to study the relaxation time of the myocardium which further is depictive of the tissue characteristic. It depends on the intracellular, extracellular and interstitial changes in the myocardium. Hence, it can be used to determine various pathologies and point towards early diagnosis of many diseases affecting the myocardium. T1 mapping could imply subclinical myocardial disease and hence can be used to differentiate between healthy and diseased myocardium. The T1 mapping has a diagnostic accuracy of 98% when compared between those with non-ischemic cardiomyopathy and healthy myocardium (25).

a. Dilated cardiomyopathy (DCM):

Dilated cardiomyopathy is a disease process that is described by dilated ventricles and systolic dysfunction due to an unexplained cause. Pathologically, there is profuse myocardial fibrosis and the extent of myocardial fibrosis is an indicator of systolic dysfunction. Late gadolinium enhancement, typically mid myocardial pattern, is used

to predict the myocardial fibrosis in DCM. Nevertheless, lately native T1 values and ECV fraction values are gaining popularity as they can predict fibrosis, as they will be elevated, even in the absence of late gadolinium enhancement. Hence, these parameters are considered as prognostic factors for clinical outcome. They are also shown to have correlation with the left ventricular ejection fraction. T2 values are also elevated in these patients, likely due to the myocardial edema. Contrast enhanced T1 values on the other hand are lower in dilated cardiomyopathy(36). Among the parametric mapping, the native T1 values had the greater diagnostic accuracy of 98%(25).

b. Hypertrophic cardiomyopathy (HCM):

Hypertrophic cardiomyopathy is characterized by hypertrophied left ventricle with no dilatation and with no other cause for the hypertrophy. Similar to the dilated cardiomyopathy, myocardial fibrosis is an important prognosticator of systolic function in hypertrophic cardiomyopathy too. Hence, in this disease process as well native T1 and ECV fraction values are higher and contrast enhanced T1 values are lower as compared to the normal(23).Further, native T1 values are correlated with the severity of the disease and the increasing wall thickness in hypertrophic cardiomyopathy. Contrast enhanced T1 values are also correlated with the diastolic dysfunction. ECV can also be used as a biomarker for groups with and without sarcomere gene related hypertrophic cardiomyopathy (24).

c. Amyloidosis:

Amyloidosis is defined by the deposition of the beta sheet structure misfolded protein in the myocardium. The commonest types of amyloidosis that involves the heart are light-chain (AL) amyloidosis and transthyretin (ATTR) amyloidosis, which is again divided intovariant ATTR amyloidosis and senile systemic amyloidosis. The cardiac deposition of light chain amyloidosis and transthyretin has poor prognosis. These proteins expand the interstitial space and infiltrate it. Endomyocardial biopsy is a gold standard for diagnosing amyloidosis. Late gadolinium enhancement pattern is subendocardial with distribution in the non-coronary territory. As these changes do not appear until late in the disease, parametric mapping is of significance for early detection of the disease. Native T1 relaxation values and ECV are elevated. Native T1 also enables to measure the disease progression and severity. ECV is also a potentially useful parameter that enables direct measurement of the amyloid burden and serves as an early marker for diagnosis, disease monitoring, and prognosis. Banypersad et al. showed that if native T1 relaxation values are above 1044 milliseconds and ECV above 45%, there is higher risk and poor prognosis. Hence, these are also used for risk stratification. Nevertheless, T2 relaxation values are not affected in cardiac amyloidosis (24). Additionally, ECV fraction is helpful to follow up patients on therapy and assess their disease progression and regression(23). Hence, ECV is used to measure the disease burden and therapy monitoring (26). Native T1 mapping alone is also advantageous in patients with renal failure, secondary to amyloidosis, as gadolinium is contraindicated and late gadolinium enhancement and ECV calculations are not done(37).

d. Myocarditis:

Myocarditis is inflammation of the myocardium. 12% of all sudden cardiac deaths are due to myocarditis. The symptoms are similar to myocardial infarction and difficult to diagnose clinically. Cardiac MRI is helpful in diagnosing myocarditis as the enhancement pattern is subepicardial and mid myocardial on delayed enhancement images. Predominantly, the lateral and inferior walls of the myocardium are affected. Biopsy from these areas of enhancement have shown to be lymphocytes adhered to the myocardial cells (25). Native T1 relaxation time and ECV fraction are elevated in myocarditis due to the inflammation and edema(24). Extracellular volume fraction has the best diagnostic accuracy for myocarditis as compared to the other parameters in a study by Radunski et al (38). Native T2 relaxation time was found to be more advantageous than native T1 relaxation time and ECV fraction in discriminating acute myocarditis and new onset heart failure(39).The diagnostic performance of parametric mapping is higher than T2 weighted imaging and delayed enhancement. Native T1 relaxation time greater than 990 millisecond with standard deviation greater than 2 is documented as elevated values for myocarditis (40). Native T1 mapping is observed to have greater diagnostic performance than T2 mapping for diagnosing myocarditis(41).Endomyocardial biopsy is the gold standard for the diagnosis of acute myocarditis. T2 values were observed to be greater than 59 milliseconds in patients who are clinically suspected to have acute myocarditis and were greater than 60 milliseconds in biopsy proven acute myocarditis (42).

e. Sarcoidosis:

Sarcoidosis is an inflammatory disease that is characterized by non-caseating granulomatous tissue infiltration. Involvement of lungs are the commonest manifestation of Sarcoidosis and cardiac involvement is rare. Cardiac manifestations will be arrhythmias or heart failures. Cardiac involvement can also lead to sudden death, however, diagnosis of cardiac sarcoidosis is often challenging. Cardiac MRI has high diagnostic accuracy as it helps in tissue characterization and assessment of the functional parameters of the heart. Myocardial scarring can be detected using late gadolinium enhancement and is useful for prognostication. In addition, quantitative characterization of myocardium is possible by parametric mapping. The native T1 mapping, T2 mapping and ECV fractions will be elevated in cardiac sarcoidosis, independent of LGE. Sarcoidosis diagnosis can be a challenge in tuberculosis endemic countries as their imaging findings overlap.

f. Anderson Fabry Disease:

Anderson Fabry disease is a storage disease of X-linked glycosphingolipid caused by mutation of the alpha galactosidase gene. Left ventricular hypertrophy is a common manifestation with this condition. The other associated cardiac disorders are valvular disorders and conduction related disorders. Late gadolinium enhancement is frequently seen in the inferolateral wall in this condition. Native T1 relaxation time will be decreased in this disease and predominantly seen in the septum (24). T1 mapping is advantageous as there will be changes in the T1 relaxation time even before the manifestation of left ventricular hypertrophy. Hence, early diagnosis of Anderson Fabry is possible, which is important in early treatment (23).There are 4

phases for Anderson Fabry disease, phase 1 is normal, phase 2 is low native T1 relaxation time, phase 3 is left ventricular hypertrophy and phase 4 is heart failure with pseudo-normal value of native T1 relaxation time (43). Native T1 relaxation time has greater sensitivity and specificity in diagnosis of Anderson Fabry disease regardless of the gender and left ventricular function(44).

f. Iron overload disease:

Iron deposition in the myocardium is due to iron overload secondary to recurrent blood transfusions for sickle cell anaemia, thalassemia, myelodysplastic disease etc and extensive intestinal absorption of iron in hereditary hemochromatosis. T2* mapping is the gold standard test for diagnosis of iron deposition in the myocardium. Latest studies observed that T1 mapping is better than T2* for reproducibility. The native T1 mapping requires validation. It is important to detect it early as it can lead to arrhythmias and heart failure. T2* enables to quantify iron deposition in the myocardium accurately and is more reliable. It is also useful is monitoring disease progression. Native T1 values will be lower in conditions of iron deposition in the myocardium. However, ECV fraction will be elevated in these patients (23).

Nevertheless, non-contrast T1 mapping is helpful in early detection of iron deposition, even in minimal quantity and is considered as a adjunct to T2* mapping (37).

g. Takotsubo cardiomyopathy:

Takotsubo cardiomyopathy is caused by secondary to stress. It is a reversible condition, which leads too heart failure. T2 mapping values are seen to be higher in this condition, greater than 65 ± 6 ms, in affected segments of the heart (23).

Hence, the parametric mapping values in each condition are varied. Prolonged native myocardial T1 signal and extracellular fraction volume is seen in diseases causing edema or fibrosis, and amyloid deposition. Shortening of the T1 signal is common iniron deposition, Anderson-Fabry disease and fat deposition (4). However, the native T2 values are elevated in myocardial edema in myocarditis, Takotsubo cardiomyopathy, etc. [figure 22, 23, 24].

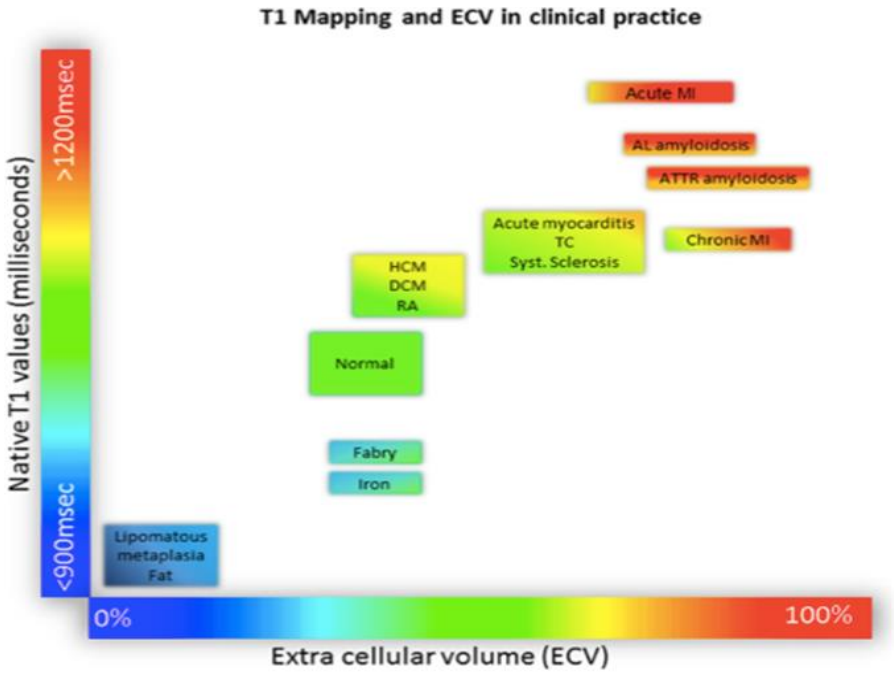


Figure 22. Native T1 and ECV fraction in different pathologies.

Philip Haaf, Pankaj Garg, Daniel R. Messroghli, David A. Broadbent, John P. Greenwood, Sven Plein Cardiac T1 Mapping and Extracellular Volume (ECV) in clinical practice: a comprehensive review. Journal of Cardiovascular Magnetic Resonance (2016) 18:89-90.

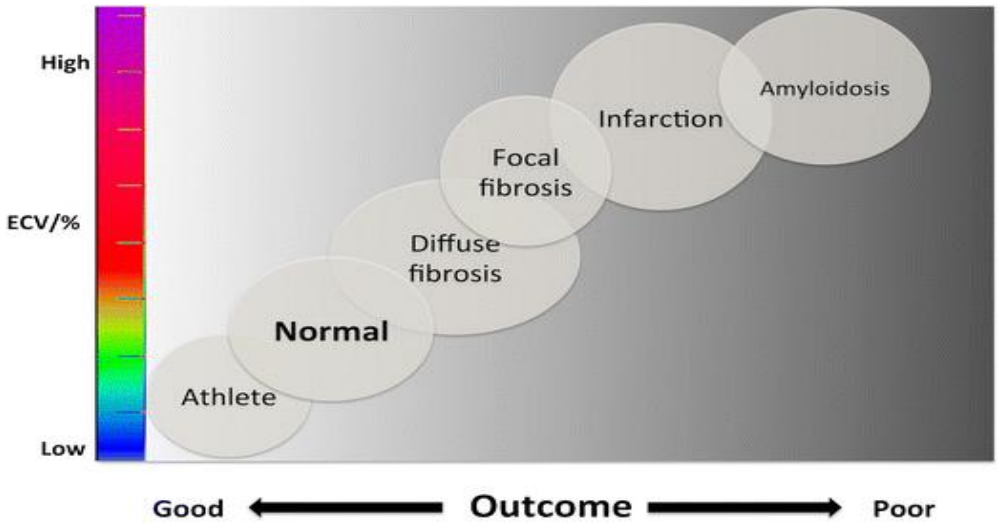
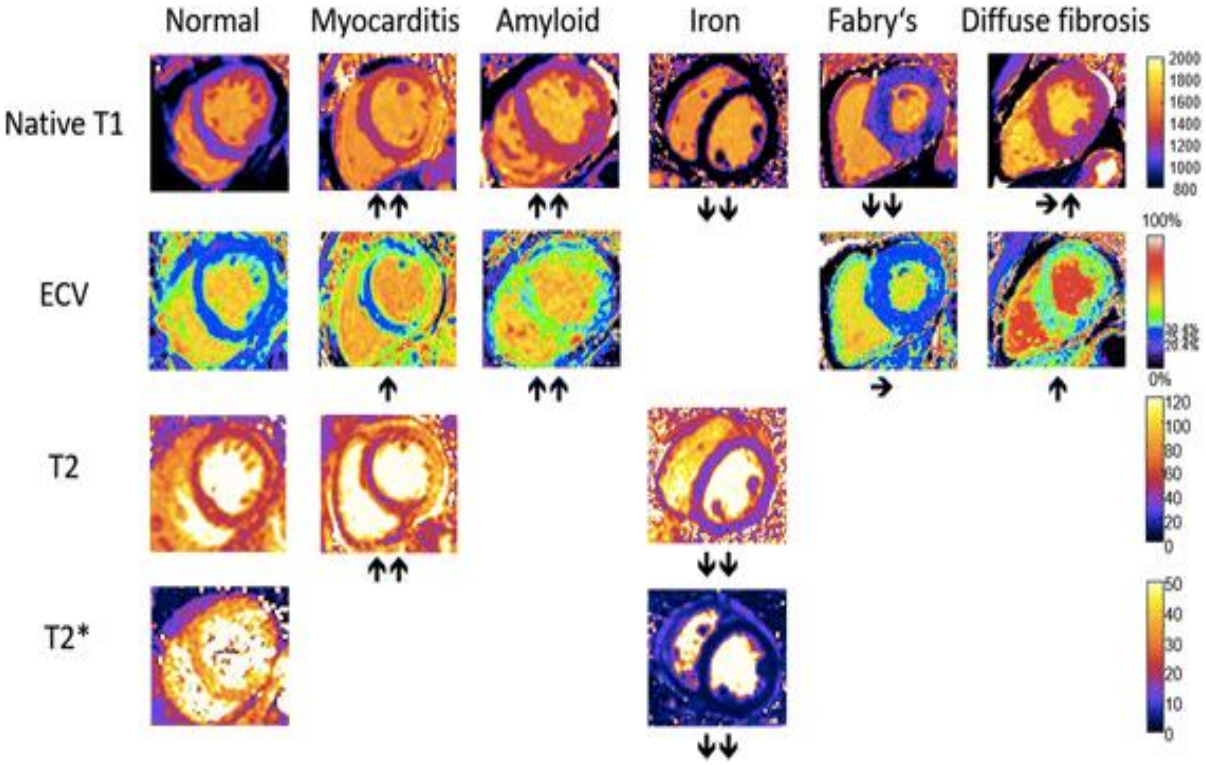


Figure23. ECV fraction in different disease condition

Scully PR, Bastarrika G, Moon JC, Treibel TA Myocardial Extracellular Volume Quantification by Cardiovascular Magnetic Resonance and Computed Tomography. Curr Cardiol Rep. 2018 Mar 6;20(3):15

Figure 24. Native T1, ECV, T2 and T2* maps in various myocardial diseases



Messroghli DR, Moon JC, Ferreira VM, Grosse-Wortmann L, He T, Kellman P. Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI).J Cardiovasc Magn Reson. 2017 Oct 9;19(1):75.

Parametric mapping can identify the appropriate site for biopsy, if biopsy is required. The proven and potential clinical utility of parametric mapping is summarised in the Table 2(23).

Table 2: Proven and potential clinical utility of parametric mapping

Proven clinical utility	Iron deposition Amyloid disease Anderson-Fabry disease Myocarditis
Potential clinical utility	Cardiomyopathy Heart failure Congenital heart disease Acute/chronic myocardial infarction Myocardial ischaemia Susected transplant rejection Athlete's heart (Para-)cardiac masses

Messroghli DR, Moon JC, Ferreira VM, Grosse-Wortmann L, He T, Kellman P. Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI).J Cardiovasc Magn Reson. 2017 Oct 9;19(1):75.

Ify et al (45) evaluated native T1 and T2 mapping in 58 middle aged men with dilated cardiomyopathy and compared it with controls and with aerobic exercisers in this age group and the found that there was significant difference between the segmental native T1 values, T2 values and ECV between dilated cardiomyopathy cases and exerciser's myocardium, measured in the septum of the basal and mid cavity section (T1 values in exercisers was 957 ± 32 ms and in dilated cardiomyopathy was 1017 ± 42 ms, T2 values were 52.8 ± 3.2 ms and 55.9 ± 4.4 ms and extracellular fraction volume were 26.3 ± 3.6% and 31.2 ± 4.1% respectively).In the study by by Puntmann et al (46) on the native T1-Mapping in non-ischemic dilated cardiomyopathy (NIDCM) and their

outcomes assessed in 637 cases (395 men) observed the native T1 segmental septal value were 997 ms and 1113 ms in 1.5T and 3T, the global mean T1 value was 962 ms and 1058 ms in 1.5T and 3T and the post contrast T1 values were 439 ms and 441 ms, in 1.5T and 3T respectively. He also found that the values of native T1 mapping in septal segment and global mean values and ECV in 1.5T and 3T were significantly higher (1069 ms, 999 ms, 30% in 1.5 T and 1183 ms, 1094 ms and 31% in 3T respectively) in the patients who died due to heart failure.

The role of native T1 and T2 mapping for early detection of sarcoidosis in 53 subjects by Puntmann et al (47), demonstrated that the native T1 mapping, native T2 mapping and ECV values from the septal segment of mid cavity were significantly higher in cases with sarcoidosis (1139 ms, 54 ms and 28 %) as compared to the controls (1052 ms, 45 ms and 25%). Puntmann et al (48) also observed that the presence and absence of late gadolinium enhancement had no significant difference in the mean T1 in his study on T1 mapping in normal myocardium, dilated and hypertrophic cardiomyopathy. However, T1 mapping was considered superior to late gadolinium enhancement in distinguishing normal and abnormal myocardium (HCM: 1241 ± 51 ms and 1234 ± 71 ms, NIDCM: 1290 ± 52 ms and 1301 ± 49 ms).

Siepen et al (49) observed that the native T1 values and ECV values were significantly higher in dilated cardiomyopathy (1056 ± 62 ms and 27 ± 4 % respectively) as compared to the controls (1020 ± 40 ms and 23 ± 3 % respectively) in his study on native T1 mapping in dilated cardiomyopathy and comparing the myocardial fibrosis with endomyocardial biopsy. He also found no significant difference in the post contrast T1 values between dilated cardiomyopathy and controls. Karur et al (50)

examined 30 cases (11 men) with Anderson Fabry disease (AFD) and 30 cases (17 men) with HCM in 3T and discovered that the segmental septal native T1 values and global mean of T1 values were significantly different between Anderson Fabry disease and HCM (1161 ± 47 ms and 1192 ± 52 ms, respectively in AFD and 1296 ± 55 ms and 1268 ± 55 ms, respectively in HCM). The native T1 values in both segmental and global were also found to be significantly lower in AFD in both 1.5 T and 3 T.

In a study by Nakamori et al (51), on native T1 mapping in non-ischemic dilated cardiomyopathy with arrhythmia, the mid myocardial enhancement pattern was the commonest. There was no difference in native T1 mapping in non-ischemic dilated cardiomyopathy cases with and without late gadolinium enhancement (1121 ± 39 and 1117 ± 48 respectively). Spieker et al (52) studied in 46 cases (33 men) with suspected acute myocarditis and correlated it withT2 mapping correlation for worse outcomes and detected that the global T2 mapping was significantly higher in cases with suspected acute myocarditis as compared to the controls **(**68.1 ± 5.8 msec vs 60 ± 4.2 msec), which was demonstrated as useful in prognostication and risk stratification in this study.

Ridouani et al (53) detected that native T2 mapping demonstrated to have greater diagnostic accuracy than native T1 mapping in differentiating the AL and ATTR amyloidosis as the native T2 mapping was significantly greater in light chain amyloidosis (AL) as compared to transthyretin amyloidosis (ATTR) (63.2 ± 4.7 ms vs 56.2 ± 3.1 ms). It was also observed that ECV was an outstanding predictor of the outcome of amyloidosis. Mayr et al (54) demonstrated that T2 mapping was higher in

cases with segments showing late gadolinium enhancement as compared to absent late gadolinium enhancement segments (65 msec and 60 msec) in the study on relationship of T2 mapping and delayed contrast enhancement on acute myocarditis.

These above studies confirm the significance of parametric mapping in non-ischemic cardiomyopathy which can be even used as a prognostic indicator of outcomes.

MATERIALS AND METHODOLOGY

Study design: It was a prospective cross-sectional descriptive study.

Study period: The study was conducted in the department of Radio diagnosis from November 2017 to August 2018 for a period of 9 months, after obtaining approval from institutional review board (IRB Min No 10933 [OBSERVE] dated 07.11.2017).

Participants:

Inclusion criteria-

Cases

- All adult patients (>18 years) referred for clinical cardiac MRI for non-ischemic cardiomyopathy between November 2017- August 2018
- GFR- >30 ml/min/1.73 m2
- Patients who could hold breathe for 15 seconds for at least 8 times
- Patients who gave consent for the study
- Patients who had negative coronary angiogram

Controls

Patients who were referred for MRI of other body parts who were normotensive, non-diabetic and who did not have any cardiac risk factors and who gave consent

for performing the study were included as normal subjects.

The status “normal subject” was based on:

i) No cardiac related medical history

ii) Absence of any symptoms indicating cardiovascular dysfunction

iii) Normal cardiac dimensions and function proven by cine CMR

The study for normal subjects was done using the fluid research grant fund, an institutional grant for the research project.

Exclusion criteria:

- GFR <30ml/min/1.73m2
- Pregnant patients
- Patients with contraindications for MRI

Sample size:

The calculations were made for 5% error and 90% power. The mean and standard deviation for native T1 and T2 mapping for normal cases was taken from a recent study in our department and using the formula for two means comparison, a sample size of minimum 55 cases were calculated. However we included 73 subjects in the study. In the control group we included 58 subjects. Formula used was:

$$n = \frac{2s_p{}^2\left[z_{1-\alpha/2} + z_{1-\beta}\right]^2}{\mu_d^2}$$

$$s_p^2 = \frac{s_1^2 + s_2^2}{2}$$

Where,

s_1^2 : Standard deviation in the first group

s_2^2 : Standard deviation in the second group

μ_d^2 : Mean difference between the samples

α : Significance level

1- β : Power

Cardiac MR Protocol:

Cardiac MRI scan was performed in the 1.5-T Siemens Magnetom Avanto fit, Erlangen, Germany.

Technical details of the MRI machine:

System length: 160 cm, Bore size: 60cm, system weight 5.3 tons, RF Tim:204x48, Gradient strength: SQ Gradients (45mT/m@200T/m/s), Helium composition: zero helium boil-off technology. Total imaging matrix (TIM) – integrated coil technology, provides up to 204 coil elements and 48 channels. Dot Go- an MRI exam software helps in streamlining the protocols. It is powered by new syngo MR E11 software – platform.

In addition to the routine cardiac MR protocol for non ischemic cardiomyopathy, parametric mapping was also done.

Parametric Mapping

T1 mapping:

T1 mapping was done using Modified Look-Locker inversion recovery sequence (MOLLI) FOV of 320 × 320; TR/TE/flip-angle: 3.3 ms/1.57 ms/50°, interpolated voxel size of 0.9 × 0.9 × 8 mm, phase encoding steps of n = 166, HR adapted trigger delay, with 11 (3-3-5) phase sampling arrangements.

T2 mapping:

T2 parametric maps were obtained by a similar principle to that used in T1 mapping, where series of images were generated to calculate a T2 decay curve. A T2 preparation pulse was applied to convey T2 signal contrast, and a consequent readout was performed by using a steady-state free precession (SSFP) sequence that had decreased sensitivity to turbo spin-echo artefacts. For T2 mapping, 3 SSFP images were collected at end-diastole within one breath-hold.

Calculation of ECV:

ECV was calculated manually using the formula, ECV= (1-hematocrit) (1/T1 myocardium post contrast- 1/native T1 myocardium)/ (1/T1 blood pool post contrast- 1/T1 blood pool pre contrast).

The parametric maps were generated at three levels- basal, mid cavity, apical and apex in short axis view. The myocardium was then contoured according to the 17 segment model of the American heart association which were basal anterior, basal anteroseptal, basal inferoseptal, basal inferior, basal inferolateral, basal anterolateral, mid cavity

anterior, mid cavity anteroseptal, mid cavity inferoseptal, mid cavity inferior, mid cavity inferolateral, mid cavity anterolateral, apical anterior, apical septal, apical inferior, apical lateral and apex [figure 24] (55).

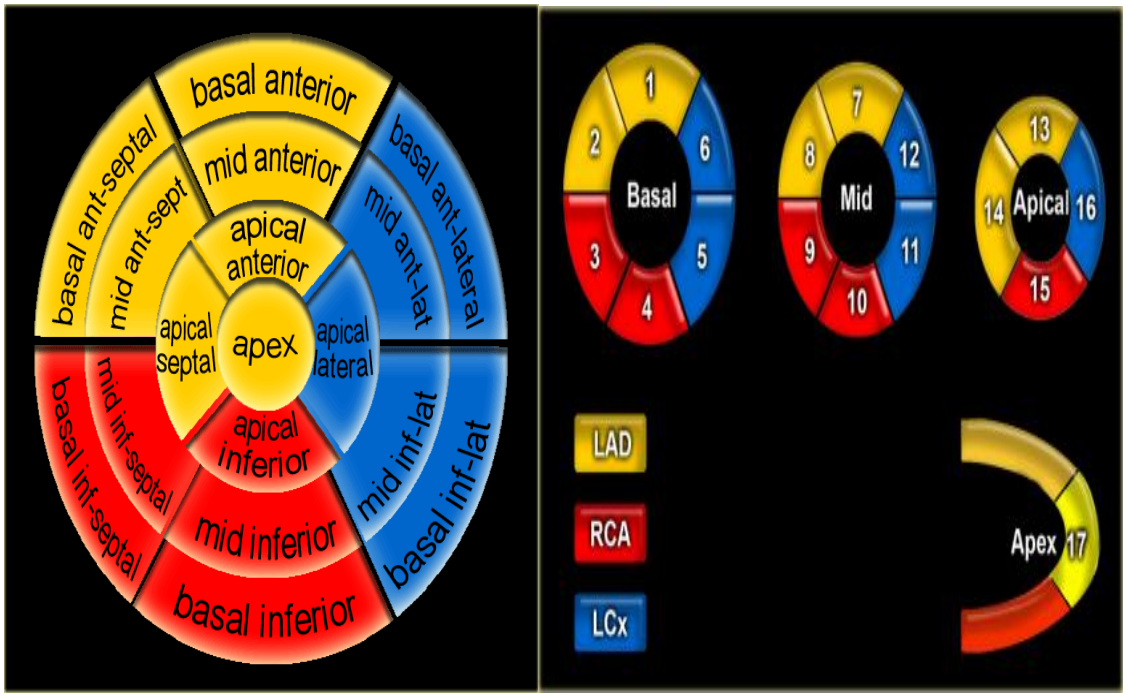


Figure 24. American heart association 17 segment model

Image source- Radiology assistant ischemic and non-ischemic cardiomyopathy

Hematocrit assessment was done prior to the cardiac MRI within 24 hours. The parametric maps were quantified by manually drawing or contouring the myocardial segments at basal, mid cavity, apical and apex levels according to the 17 segment model of the American heart association. However, care was taken that only the myocardium was contoured sparing the blood pool, lung, liver, etc. The segmental measurement of each segment was taken. The values of parametric mapping were displayed as numerical value with standard deviation (23).The ECV value were calculated manually using the established formula.

The cardiac MRI protocol used in the study is demonstrated in Figure 25.

Cardiac MRI protocol for non-ischemic cardiomyopathy
Blood sample for assessment of hematocrit
Cine Imaging (global and regional function)
Edema Imaging (STIR)
Native T1 mapping
Native T2 mapping
Administration of contrast agent (Gadolinium based contrast)
Post contrast T1 mapping
Late Gadolinium enhancement

Figure 25. Cardiac MRI protocol for non-ischemic cardiomyopathy

Variables:

Categorical variables

1. Sex
2. Presence or absence of late gadolinium enhancement
3. Late Gadolinium enhancement patterns
4. Diagnosis based on cardiac MRI

Continuous variables

1. Age

2. Hematocrit

3. Cardiac MR parameters - Ejection fraction (EF), absolute and indexed end diastolic volume (EDV), end systolic volume (ESV), myocardial mass and stroke volume

4. Native T1 mapping (milliseconds) - 17 segments

5. Post contrast T1mapping (milliseconds) - 17 segments

6. Native T2 mapping (milliseconds) - 17 segments

7. ECV- 17 segments

Potential confounders:

1. Physical or biological confounders- T1 increases by ~ 1% for every 1 °C increase in body temperature and T2 shortens with the increasing temperature

2. Methodological confounders- acquisition and processing errors of the parametric maps and ECV calculation

Data collection:

Patient's demographic details were obtained from the clinical workstation and recorded by the principal investigator

Interpretation of cardiac MRI:

MRI scan were reported in a standardized format and checked by guide / co-guides. T1 and T2 relaxation values of the myocardium for the 17 cardiac segment models as described by the American Heart Association was measured and documented by the principal investigator. The left ventricular functional parameters were obtained by contouring the left ventricular myocardium using the established methods.

Native T1, post Gadolinium T1 mapping and T2 mapping of myocardium was obtained by drawing region of interest in each of the 17 segments in the respective maps by the principal investigator under the supervision of the guide. Myocardial enhancement in the late gadolinium enhancement (LGE) were also documented in all the 17 cardiac segments and these findings were compared to the T1, post contrast T1, T2 relaxation times and ECV.

Statistical analysis

The data was analysed for normality of distribution and screened for outliers and extreme values using Box-Cox plot and histogram (for shape of the distribution). All continuous variables were described using mean (SD) and also using median and IQR whenever required. The categorical variable demonstrated as frequency (%). Independent T test anode way ANOVAs was used to determine the difference in the mean of continuous variable between the groups. Area under the curve derived from ROC curve was used to determine the threshold for abnormal T1 relaxometric values. A p value of less than 0.05 is considered statistically significant. All the statistical analysis was performed using SPSS 16.0(SPSS, Chicago,Il).

RESULTS

1. Demographic Characteristics:

77 cases who were diagnosed clinically as non-ischemic cardiomyopathy and planned for cardiac MRI were considered as cases in our study. Four of them were excluded as they were not willing to participate in the study. Thus 73 cases with non-ischemic cardiomyopathy were included as cases who underwent cardiac MRI according to the study protocol.58 subjects having normal cardiac MRI were included as controls in our study as shown in the figure 26 below.

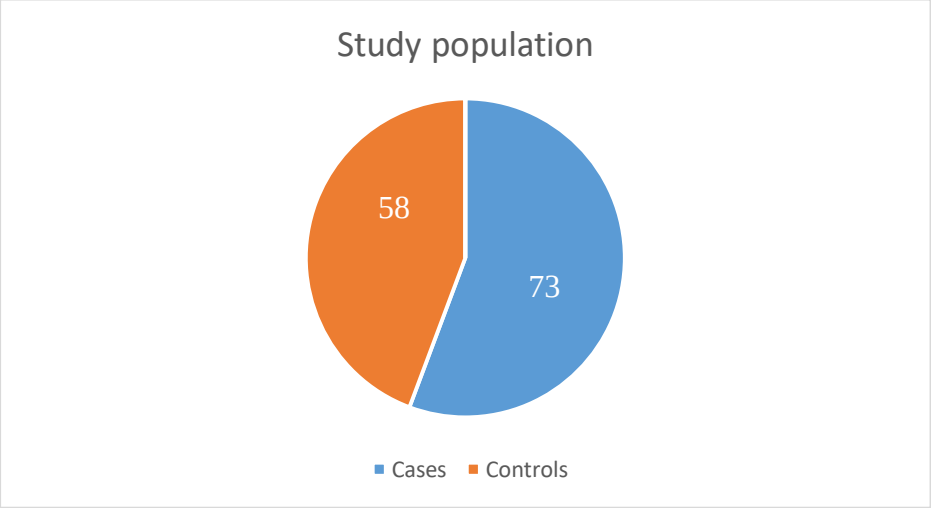


Figure 26- Cases and controls in the study population

The mean age among the cases was 47±12.94 and the mean age among the controls was 45±11.27 as shown in figure 27. No significant difference in the mean age between the cases and control. Out of 131 subjects, 64% (n=84) were males, among cases 74% (n=54) and among controls, 52% (n=30) as shown in figure 28 a and b.

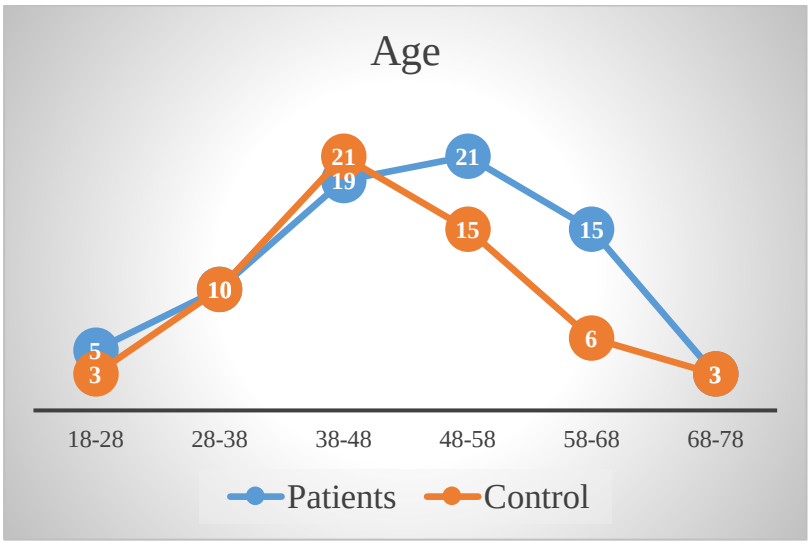


Figure 27- Age distribution in the study population

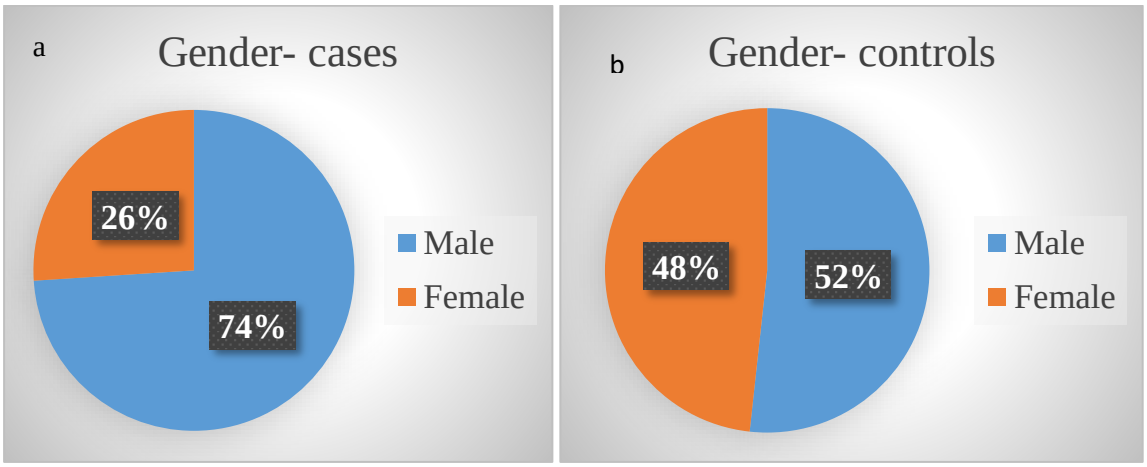


Figure 28 a and b- Gender distribution in the study population

2. Characteristics of Cardiac MRI including parametric mapping:

a. The distribution of non-ischemic cardiomyopathy

Out of the 73 cases clinically diagnosed as non-ischemic cardiomyopathy, following the cardiac MRI, 55% (n=40) were diagnosed as dilated cardiomyopathy, 26% (n=19) were diagnosed as HCM, 12% (n=9) were diagnosed as restrictive cardiomyopathy (RCM) and 7% (n=5) were diagnosed as myocarditis as shown in figure 29. We did not have RV cardiomyopathy or ARVC in our study sample.

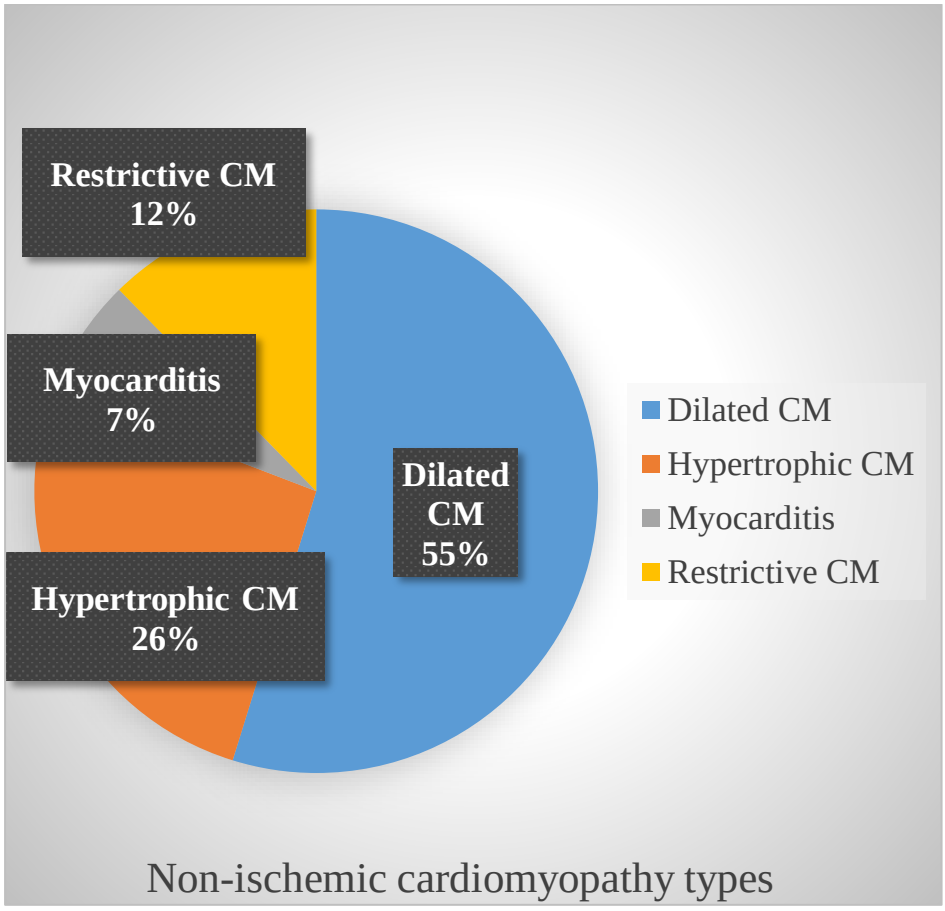


Figure 29- Distribution of non-ischemic cardiomyopathy

b. Patterns of late gadolinium enhancement

The patterns of late gadolinium enhancement observed in our study cases were mid myocardial, transmural, subepicardial and subendocardial in location. The frequency distribution of various late gadolinium enhancement patterns is shown in figure 30. Mid myocardial pattern was seen in 59 % cases (n= 23), transmural pattern was seen in 26 % cases (n=10), subepicardial in 13% (n=5) and subendocardial in 2% (n=1).

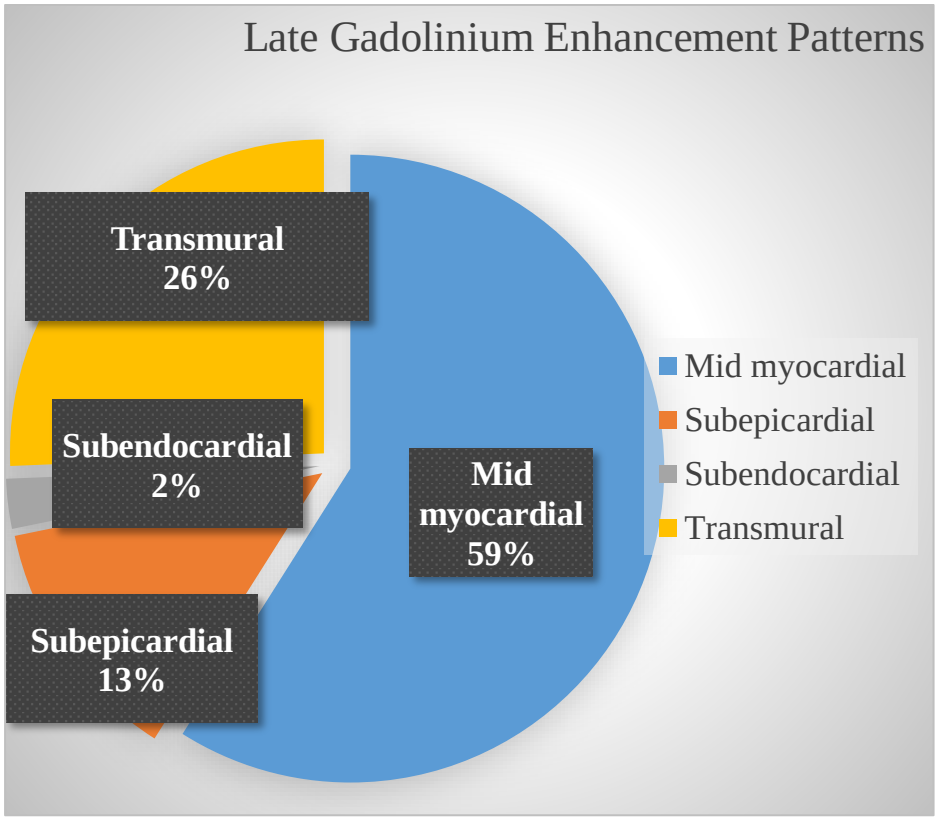


Figure 30- Patterns of late gadolinium enhancement

c. Segmental distribution of late gadolinium enhancement:

The distribution of presence and absence of late gadolinium enhancement (LGE) in 17 segments of the heart in cases as shown in figure 31 and table 3.

Table 3: Segmental distribution of late gadolinium enhancement

Segments	**LGE absent n (%)**	**LGE present n (%)**
Basal anterior	57 (78.1)	16 (21.9)
Basal anteroseptal	50 (68.5)	23 (31.5)
Basal inferoseptal	55 (75.3)	18 (24.7)
Basal inferior	61 (83.6)	12 (16.4)
Basal inferolateral	60 (82.2)	13 (17.8)
Basal anterolateral	59 (80.8)	14 (19.2)
Mid cavity anterior	55 (75.3)	18 (24.6)
Mid cavity anteroseptal	51 (69.9)	22 (30.1)
Mid cavity inferoseptal	53 (72.6)	20 (27.4)
Mid cavity inferior	59 (80.8)	14 (19.2)
Mid cavity inferolateral	60 (82.2)	13 (17.8)
Mid cavity anterolateral	58 (79.5)	15 (20.5)
Apical anterior	57 (78.1)	16 (21.9)
Apical septal	57 (78.1)	16 (21.9)
Apical inferior	60 (82.2)	13 (17.8)
Apical lateral	58 (79.5)	15 (20.5)
Apex	59 (80.8)	14 (19.4)

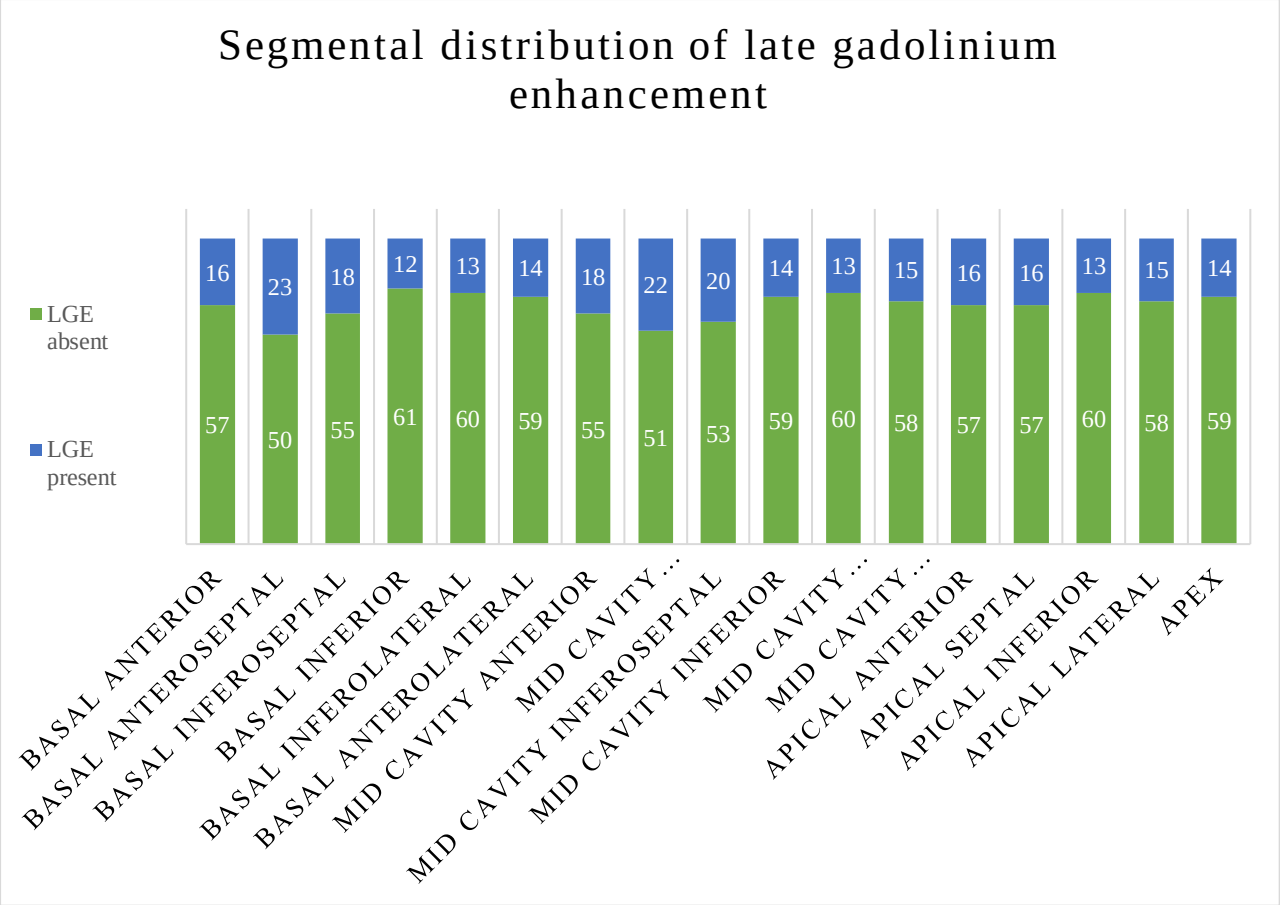


Figure 31- Segmental distribution of late gadolinium enhancement

d. <u>Global and segmental analysis of the parametric mapping in cases and controls:</u>

We have analysed the native T1, native T2, post Gadolinium T1 and ECV measurements of all the 17 individual segments for each of the subjects and these were considered as segmental measurements. We have also calculated the mean average of the segmental parametric measurements of native T1, native T2, post Gadolinium T1 and ECV for each patient which were considered as global measurement.

Using Independent T test, the mean segmental values of each of the parametric measurements between cases and controls were compared and the results are demonstrated in tables 4-7.

Table 4: Comparison of mean segmental values of native T1 mapping

Parametric map **Segments**	**Native T1 (ms) cases**	**Native T1 (ms) controls**	**p value**
Basal anterior	1067.75 ± 79.59	1025.21 ± 77.64	0.002
Basal anteroseptal	1088.04 ± 77.61	1061.89 ± 65.21	0.041
Basal inferoseptal	1079.25 ± 71.31	1060.69 ± 72.79	0.036
Basal inferior	1097.67 ± 70.24	1058.05 ± 74.03	0.002
Basal inferolateral	1066.37 ± 63.67	1032.36 ± 78.69	0.145
Basal anterolateral	1047.53 ± 62.70	1022.86 ± 71.1	0.007
Mid cavity anterior	1044.50 ± 73.25	1017.72 ± 62.04	0.028
Mid cavity anteroseptal	1072.30 ± 70.64	1051.02 ± 54.69	0.061
Mid cavity inferoseptal	1079.89 ± 63.83	1055.24 ± 54.41	0.009
Mid cavity inferior	1086.39 ± 69.38	1057.23 ± 64.49	0.015
Mid cavity inferolateral	1059.42 ± 63.50	1039.44 ± 61.35	0.021
Mid cavity anterolateral	1051.11 ± 64.03	1022.47 ± 58.7	0.071
Apical anterior	1058.43 ± 85.19	1025.87 ± 74.48	0.023
Apical septal	1078.66 ± 79.63	1049.67 ± 63.59	0.025
Apical inferior	1086.76 + 83.56	1045.28 ± 62.78	0.024
Apical lateral	1074.11 + 78.39	1044.34 + 68.99	0.002
Apex	1096.04 + 77.91	1068.05 + 60.71	0.026

There was significant difference between the cases and control in the mean of segmental T1 parametric relaxation times in most of the segments except in basal inferolateral, mid cavity anteroseptal and mid cavity anterolateral.

Table 5: Comparison of mean segmental values of native T2 mapping

Parametric map **Segments**	**Native T2 (ms) cases**	**Native T2 (ms) controls**	**p value**
Basal anterior	50.4 ± 5.16	49.93 ± 4.20	0.579
Basal anteroseptal	49.92 ± 4.71	50.92 ± 3.72	0.190
Basal inferoseptal	48.79 ± 4.94	49.3 ± 4.45	0.719
Basal inferior	50.13 ± 4.44	50.06 ± 4.51	0.935
Basal inferolateral	50.1 ± 5.03	50.65 ± 5.32	0.545
Basal anterolateral	49.98 + 4.65	49.68 ± 4.84	0.546
Mid cavity anterior	50.57 ± 4.60	51.61 ± 3.98	0.176
Mid cavity anteroseptal	50.89 ± 5.51	51.84 ± 5.30	0.320
Mid cavity inferoseptal	50.16 ± 4.98	50.34 ± 3.48	0.542
Mid cavity inferior	49.89 ± 3.70	50.28 ± 3.58	0.544
Mid cavity inferolateral	50.65 ± 5.20	50.73 ± 4.29	0.820
Mid cavity anterolateral	51 ± 4.15	50.59 ± 3.17	0.929
Apical anterior	52.97 ± 5.25	52.6 ± 4.46	0.292
Apical septal	51.96 ± 5.29	52.37 ± 4.52	0.637
Apical inferior	50.55 ± 5.10	50.25 ± 4.63	0.568
Apical lateral	52.70 ± 5.02	52.21 ± 4.76	0.728
Apex	52.62 ± 7.34	55.13 ± 8.11	0.065

There was no significant difference in the native T2 values between cases and controls. This could be because most of the non-ischemic cardiomyopathy cases in our cohort didn't have myocardial edema and hence the native T2 values were within normal limits. As the number of myocarditis cases were smaller in number (n=5), the myocardial edema related changes in the native T2 is not reflected in the average native T2 of the cases.

Table 6: Comparison of mean segmental values of post contrast T1 mapping

Parametric map **Segments**	**T1 post gadolinium (ms) cases**	**T1 post gadolinium (ms) controls**	**p value**
Basal anterior	451.32 ± 97.15	487.01 ± 81.88	0.042
Basal anteroseptal	436.85 ± 96.03	470.84 ± 83.63	0.052
Basal inferoseptal	442.56 ± 98.34	480 ± 79.33	0.053
Basal inferior	442.92 ± 99.44	474.51 ± 80.93	0.074
Basal inferolateral	443.56 ± 85.62	473.52 ± 81.58	0.033
Basal anterolateral	447.85 ± 86.71	480.19 ± 86.45	0.064
Mid cavity anterior	448.06 + 97.72	481.85 ± 82.57	0.054
Mid cavity anteroseptal	444.96 ± 102.75	476.22 ± 83.70	0.085
Mid cavity inferoseptal	451.95 ± 101.41	481.56 ± 90.17	0.050
Mid cavity inferior	450.56 ± 99.02	480.53 ± 87.02	0.606
Mid cavity inferolateral	452.63 ± 88.74	484.10 ± 86.53	0.109
Mid cavity anterolateral	451.55 ± 88.60	483.59 ± 8.92	0.061
Apical anterior	438.86 ± 92.40	466.21 ± 78.30	0.098
Apical septal	448.30 ± 95.97	476.57 ± 82.54	0.102
Apical inferior	449.32 ± 95.64	477.87 ± 84.69	0.103
Apical lateral	444.94 ± 90.78	472.12 ± 82.15	0.101
Apex	445.05 ± 97.02	451.33 ± 81.02	0.715

There was significant difference between the patient and control in the mean of segmental T1 post gadolinium parametric relaxation times, in some of the segments at basal and midcavity level. None of the apical segments showed statistically significant difference in the measurements of post gadolinium T1 between cases and controls. This could be because most of the cases had negligible amount of scar in the apical region.

Table 7: Comparison of mean segmental values of extracellular volume (ECV) fraction

Parametric map **Segments**	**ECV (%) patient**	**ECV (%) control**	**p value**
Basal anterior	28 ± 5	27 ± 5	0.365
Basal anteroseptal	30 ± 6	30 ± 8	0.909
Basal inferoseptal	29 ± 6	29 ± 6	0.444
Basal inferior	30 ± 5	29 ± 6	0.397
Basal inferolateral	30 ± 6	29 ± 6	0.659
Basal anterolateral	29 ± 5	29 ± 6	0.838
Mid cavity anterior	29 ± 5	28 ± 4	0.389
Mid cavity anteroseptal	30 ± 6	29 ± 4	0.634
Mid cavity inferoseptal	28 ± 5	29 ± 4	0.201
Mid cavity inferior	30 ± 7	29 ± 4	0.721
Mid cavity inferolateral	29 ± 5	29 ± 4	0.423
Mid cavity anterolateral	30 ± 5	28 ± 4	0.570
Apical anterior	33 ± 12	31 ± 6	0.654
Apical septal	32 ± 13	30 ± 4	0.479
Apical inferior	32 ± 13	30 ± 5	0.660
Apical lateral	32 ± 9	31 ± 5	0.426
Apex	-	-	-

There was no significant difference between the patient and control in the mean of the segmental ECV.

e. Global parametric mapping measurements in cases and controls:

The various descriptive statistics of global relaxometry of cases and controls is demonstrated in table 8. Using Independent T test, the mean global relaxometric values of native T1, native T2, post Gadolinium T1 and calculated ECV of cases and controls and between males and females were compared to look for any statistically significant difference, as shown in table 9.

Table 8: Descriptive statistics of global relaxometry values

Descriptive statistics	Native T1 (ms)		Native T2 (ms)		Post gadolinium T1 (ms)		ECV (%)	
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Mean	1072.66 ± 46.23	1043.68 ± 41.38	50.59 ± 2.98	50.98 ± 3.41	446.52 ± 90.39	489.83 ± 49.08	29.5 ± 4	29.3 ± 4
Median	1069.18	1044.46	50.70	50.69	450.35	471.93	29.5	28.2
Interquartile range	1041.54-1105.81	1006.66-1070.81	47.92-52.62	48.33-53.36	383.69-517.27	452.10-526.68	26-33	26-32

Table 9: Comparison of mean of the global relaxometry between cases and controls and with gender

Mean global relaxometry	Native T1 relaxation (ms)	Native T2 relaxation (ms)	Post gadolinium T1 (ms)	ECV (%)
Cases (Total)	1072.66 ± 46.23	50.59 ± 2.98	446.52 ± 90.39	29.5 ± 4
Cases (Males)	1062.27 ± 55.83	50.56 ± 3.52	457.68 ± 96.7	29.6 ± 5
Cases (Females)	1101.86 ± 39.69	51.86 ± 3.03	413.03 ±58.2	31.79 ± 3
Controls (Total)	1043.68 ± 41.38	50.98 ± 3.41	489.83 ± 49.08	29.3 ± 4
Controls (Males)	1031.37 ±41.93	50.38 ± 3.27	504.54 ± 68.84	28.3 ± 4
Controls (Females)	1056.19 ±36.68	51.72 ± 3.5	453.16 ±77.1	30 ± 3
p value (cases &controls)	<0.001	0.504	0.002	0.870
p value (M & F cases)	0.02	0.138	0.032	0.152
p value (M & F controls)	0.02	0.14	0.019	0.303

There was significant difference between the cases and controls in the global mean of native and post gadolinium T1 relaxation time. No significant difference was found in the other parameters. There was also significant difference in the native and post contrast T1 relaxometry values between males and females among the cases as well as in the controls. Box plot of the descriptive statistics between cases and controls are shown in figures 32 -35.

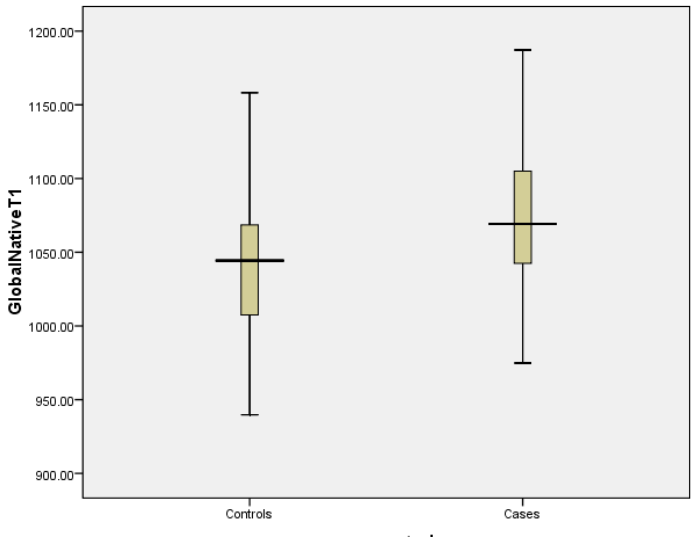


Figure 32 Global native T1 mapping in the study population

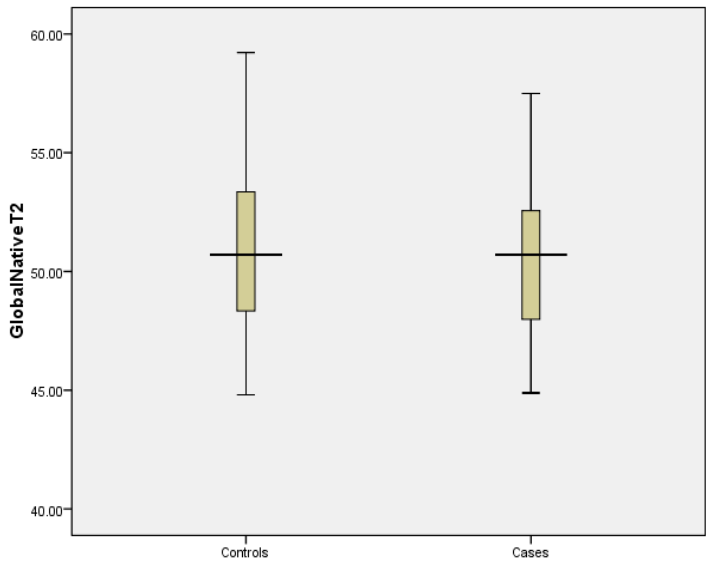


Figure 32 Global native T2 mapping in the study population

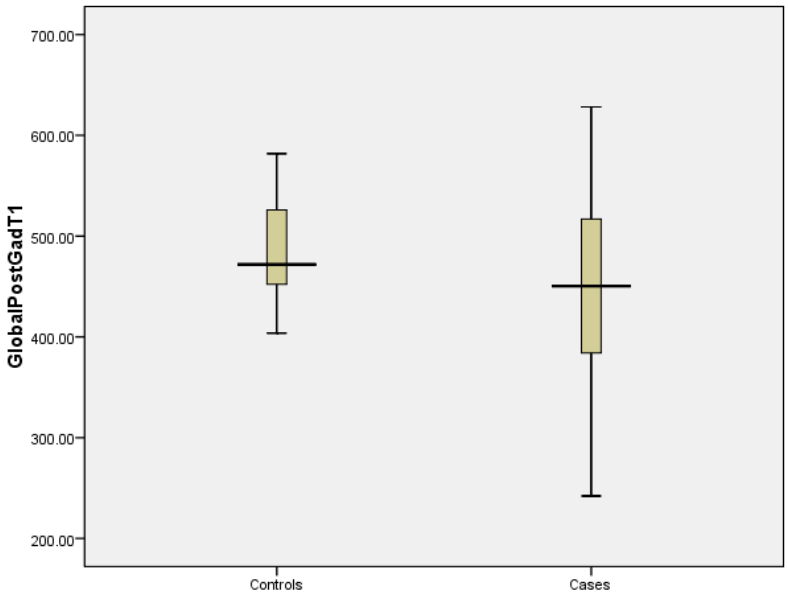


Figure 34. Global post contrast T1 mapping in the study population

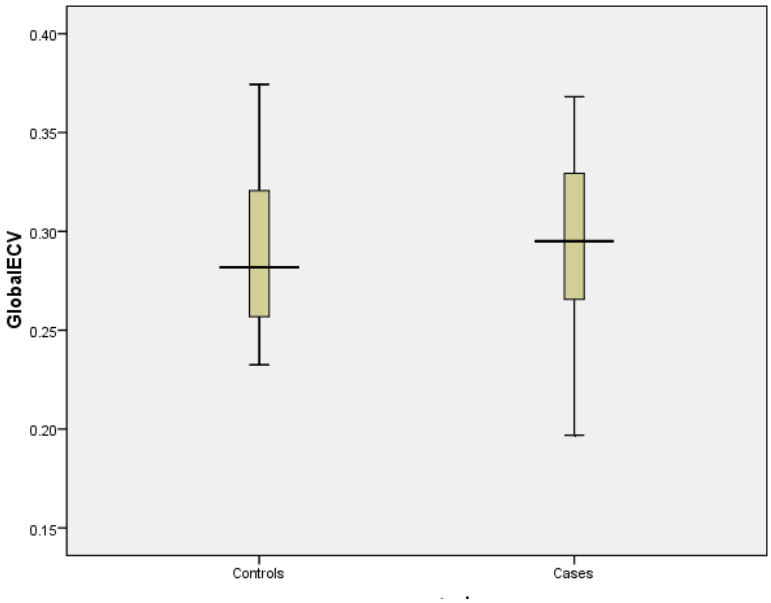


Figure 35. Global mean of ECV in the study population

f. Global parametric mapping in different types of non-ischemic cardiomyopathy:

The descriptive statistics of global parametric values for the different types of non-ischemic cardiomyopathy is given in table 10 and as box plots in figure 36-39.

Table 10: Descriptive statistics of global mean of relaxometry in different types of non-ischemic cardiomyopathies (NICM)

	NICM	**Mean**	Median	IQR
Native T1 (ms)	**DCM**	1069.75	1072.21	1042.31- 1103.83
	HCM	1070.31	1062.91	1041.56- 1100.04
	Myocarditis	1057.95	1037.61	1013.94- 1112.13
	RCM	1098.03	1104.24	1068.96- 1151.82
Native T2 (ms)	**DCM**	50.47	50.22	47.82-52.43
	HCM	52.02	52.45	50.50- 53.58
	Myocarditis	50.24	48.30	47.27- 54.19
	RCM	50.79	51.08	46.84- 54.23
Post contrast T1 (ms)	**DCM**	435.46	445.38	354.30- 516.47
	HCM	463.66	462	401.16- 529.80
	Myocarditis	453.30	415.55	353.33- 572.13
	RCM	451.30	490.79	383.41- 508.76
ECV	**DCM**	30.3	30	26.5- 33.5
	HCM	29.3	29.5	26.4- 32.5
	Myocarditis	24.3	24.4	21-27.4
	RCM	35.2	31.9	28.5-45.1

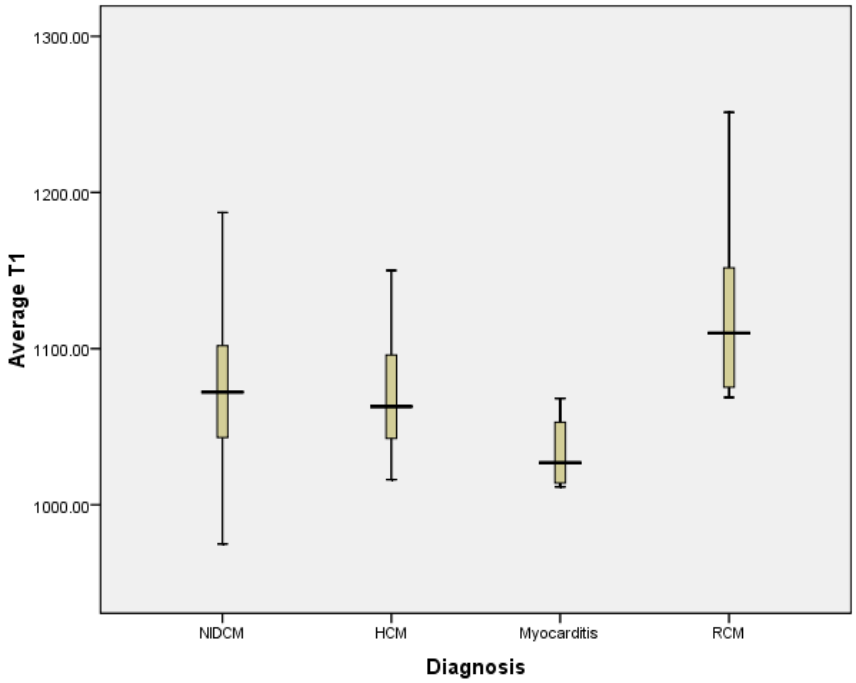


Figure 36- Box plot of global native T1 mapping in different types of NICM

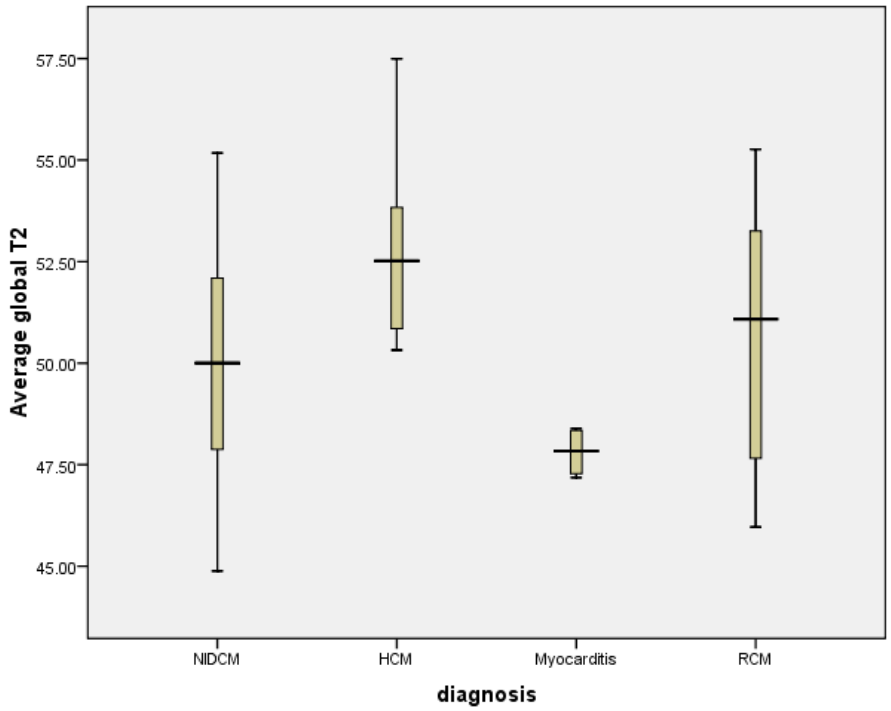


Figure 37- Box plot of global native T2 mapping in different types of NICM

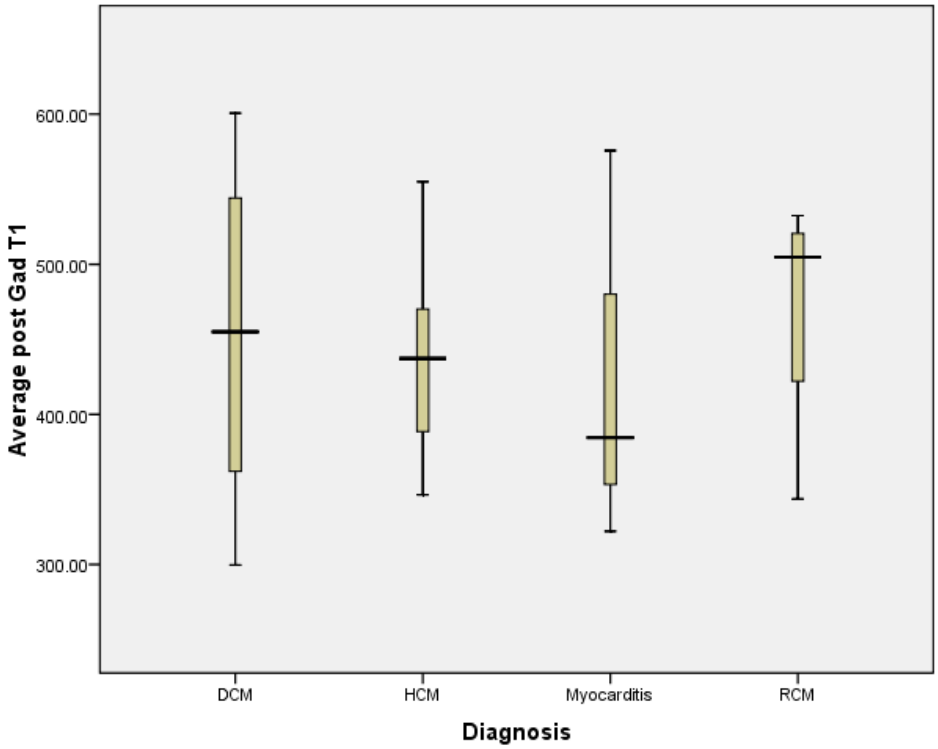


Figure 38- Box plot of global post contrast T1 mapping in different types of NICM

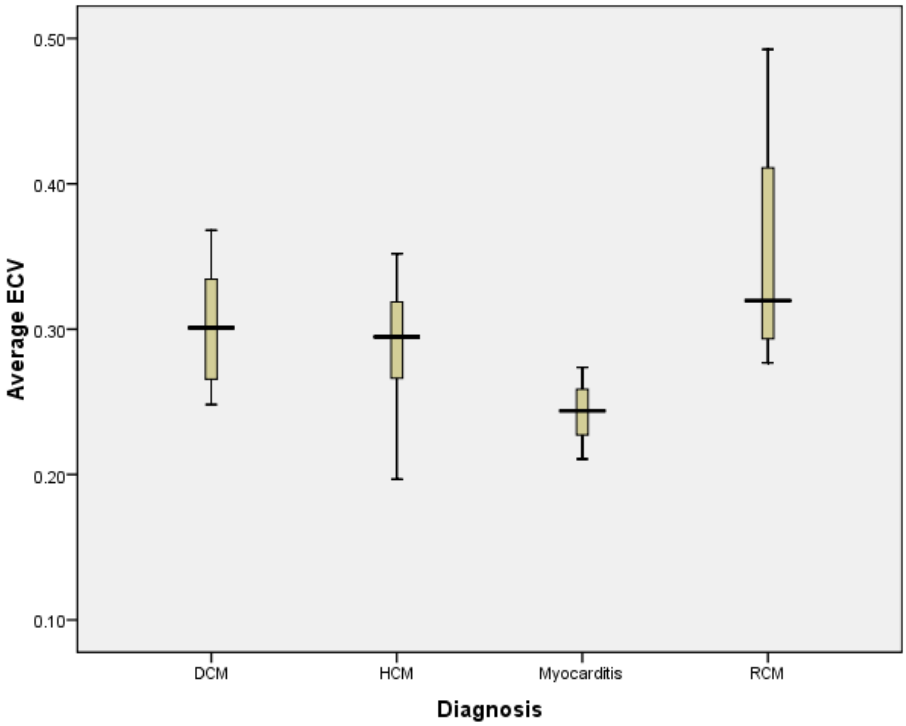


Figure 39-Box plot of global mean of ECV in different types of NICM

Comparison of the global relaxometry between different types of non-ischemic cardiomyopathy was performed using one way Anova as given in table 11. There was significant difference between the ECVs in the different types of non-ischemic cardiomyopathy (NICM) with p value = 0.042. Post HOC analysis (using Bon Ferroni test) showed there was significant difference in the ECV values between HCM and RCM (p=0.045) and between myocarditis and RCM (p=0.006).

Table 11: Comparison of global mean of relaxometry in different types of non-ischemic cardiomyopathies (NICM)

Diagnosis **Parametric mapping**	**DCM (n=40) Mean ±SD**	**HCM (n=19) Mean ±SD**	**Myocarditis (n=5) Mean ±SD**	**RCM (n=9) Mean ±SD**	**p value**
GlobalT1 (ms)	1069.8 ± 49.08	1070.3 ± 35.80	1057.9 ± 59.3	1098.03 ± 98.25	0.494
Global T2 (ms)	50.47 ± 3.35	52.02 ± 2.88	50.24 ± 5.47	50.79 ± 3.61	0.446
Post Gadolinium T1 (ms)	435.46 ± 97.35	463.66 ± 79.61	453.3 ± 113.6	451.3 ± 73.88	0.761
ECV (%)	30 ± 3	29 ± 4	24 ± 3	35 ± 9	0.042*
* Post HOC analysis: HCM vs RCM p=0.045 and Myocarditis vs RCM p=0.006					

g. Comparison of global and segmental relaxometry with respect to late gadolinium enhancement:

We have analysed the global relaxometric values with respect to LGE and found that there was no significant difference in the relaxometric values between those with and without LGE. We have also separately analysed statistically significant difference in the various parametric values between those with late gadolinium enhancement versus

those without late gadolinium enhancement in each of the segments, using student's independent T test as demonstrated in tables 12-15.

Table 12: Comparison of segmental T1 relaxometry with respect to LGE

Segments	**T1 relaxation time (ms)**		
	LGE absent (mean ± SD)	**LGE present (mean ± SD)**	**p value**
Apex	1080.19 ± 73.9	1114.76 ± 46.2	0.087
Apical Anterior	1037.48 ± 78.01	1090.94 ± 96.27	0.013
Apical septal	1060.05 ± 70.68	1109.4 ± 86.60	0.011
Apical inferior	1062.17 ± 75.06	1128.17 ± 79.66	0.003
Apical lateral	1053.61 ± 71.31	1121.51 ± 83.24	0.0008
Mid cavity Anterior	1104.09 ± 850	1090.47 ± 64.13	0.946
Mid cavity Anteroseptal	1055.94 ± 62.02	1097.78 ± 69.16	0.042
Mid cavity Inferoseptal	1152.30 ± 937.8	1104.62 ± 58.09	0.821
Mid cavity inferior	1067.88 ± 67.01	1112.79 ± 67.70	0.019
Mid cavity Inferolateral	1045.07 ± 57.73	1106.38 ± 81.85	0.0007
Mid cavity anterolateral	1031.35 ± 56.85	1095.57 ± 79.66	0.0001
Basal Anterior	1038.94 ± 75.82	1118.54 ± 89.10	0.0001
Basal Anteroseptal	1068.60 ± 68.55	1110.41 ± 86.18	0.012
Basal Inferoseptal	1076.41 ± 73.13	1087.92 ± 66.66	0.555
Basal inferior	1075.04 ± 73.02	1116.82 ± 67.26	0.059
Basal Inferolateral	1049.22 ± 67.74	1067.38 ±109.82	0.394
Basal anterolateral	1030.26 ± 62.54	1088.86 ± 86.91	0.001

There was significant difference in the segmental T1 relaxometric values in those with and without LGE in most of the segments except apex, mid cavity anterior and inferoseptal segments and basal inferoseptal and inferolateral segments. There was significant difference in the T1 relaxometry with respect to LGE in all the apical segments. The global T1 relaxometric values for those with and without LGE were 1076.33±60 versus 1068.92 ± 48 (p =0.567).

Table 13: Comparison of segmental T2 relaxometry with respect to LGE

Segments	T2 relaxation time (ms)		
	LGE absent (mean ± SD)	LGE present (mean ± SD)	p value
Apex	53.69 ± 7.94	54.14 ± 6.71	0.835
Apical Anterior	52.07 ± 4.37	56.14 ± 7.02	0.001
Apical septal	51.93 ± 4.80	53.4 ± 5.98	0.253
Apical inferior	50.23 ± 4.50	51.96 ± 7.73	0.229
Apical lateral	52.21 ± 4.62	54.61 ± 6.57	0.075
Mid cavity Anterior	50.7 ± 4.06	52.81 ± 5.71	0.059
Mid cavity Anteroseptal	51.16 ± 5.24	52.01 ± 6.42	0.255
Mid cavity Inferoseptal	49.79 ± 3.63	52.73 ± 6.86	0.005
Mid cavity inferior	49.82 ± 3.65	52.06 ± 3.13	0.029
Mid cavity Inferolateral	50.46 ± 4.33	52.78 ± 7.99	0.100
Mid cavity anterolateral	50.55 ± 3.47	52.69 ± 5.18	0.036
Basal Anterior	49.8 ± 4.68	53.09 ± 4.48	0.009
Basal Anteroseptal	50.16 ± 4.29	51.32 ± 4.47	0.243
Basal Inferoseptal	48.59 ± 4.89	49.42 ± 5.15	0.537
Basal inferior	49.92 ± 4.48	51.98 ± 4	0.128
Basal Inferolateral	50.34 ± 5.16	50.67 ± 5.21	0.828
Basal anterolateral	49.79 ± 4.85	50.33 ± 3.79	0.691

There was significant difference in the segmental T2 relaxometric values in those with and without LGE in apical anterior and lateral, mid cavity anterior, anterolateral and inferoseptal segments. The global T2 relaxometric values for those with and without LGE were 51.16±4 versus 50.63 ± 3 (p =0.515).

Table 14: Comparison of segmental post contrast T1 relaxometry with respect to LGE

Segments	T1 post gadolinium relaxation time (ms)		
	LGE absent (mean ± SD)	LGE present (mean ± SD)	p value
Apex	445.69 ± 91.39	444.19 ± 126.08	0.962
Apical Anterior	456.35 ± 82.66	410.89 ± 110.28	0.067
Apical septal	467.91 ± 88.31	403.96 ± 95.14	0.013
Apical inferior	467.96 ± 87.24	400.15 ± 115.98	0.019
Apical lateral	458.27 ± 88.65	440.37 ± 84.76	0.493
Mid cavity Anterior	472.93 ± 91.01	397.51 ± 78.18	0.022
Mid cavity Anteroseptal	471.12 ± 90.57	397.51 ± 99.84	0.011
Mid cavity Inferoseptal	477.11 ± 93.41	396.81 ± 93.68	0.001
Mid cavity inferior	467.22 ± 96.76	845.98 ± 1473.45	0.010
Mid cavity Inferolateral	469.31 ± 91.20	437.31 ± 64.04	0.260
Mid cavity anterolateral	472.66 ± 86.59	408.72 ± 67.73	0.011
Basal Anterior	470.87 ± 91.55	430.66 ± 92.86	0.127
Basal Anteroseptal	458.98 ± 90.44	414.69 ± 92.66	0.046
Basal Inferoseptal	456.21 ± 101.83	403.06 ± 82.33	0.063
Basal inferior	457.88 ± 94.69	432.14 ± 71.07	0.405
Basal Inferolateral	441.61 ± 88.98	454.10 ± 67.42	0.929
Basal anterolateral	463.59 ± 87.90	434.91 ± 79.26	0.283

There was significant difference in the segmental post contrast T1 relaxometric values in those with and without LGE in most of the segments. The global post contrast relaxometric values for those with and without LGE were 444.54± 84 versus 448.62 ± 97 (p =0.858).

Table 15: Comparison of segmental ECV with respect to LGE

Segments	ECV (%)		
	LGE absent (mean ± SD)	LGE present (mean ± SD)	p value
Apex	-	-	-
Apical Anterior	32 ± 9	39 ± 15	0.081
Apical septal	31 ± 11	31 ± 1	0.929
Apical inferior	31 ± 10	41 ± 19	0.079
Apical lateral	31 ± 7	34 ± 5	0.501
Mid cavity Anterior	29 ± 4	31 ± 6	0.173
Mid cavity Anteroseptal	30 ± 5	31 ± 7	0.494
Mid cavity Inferoseptal	29 ± 5	28 ± 5	0.663
Mid cavity inferior	30 ± 6	31 ± 5	0.732
Mid cavity Inferolateral	29 ± 5	31 ± 5	0.299
Mid cavity anterolateral	29 ± 4	32 ± 6	0.072
Basal Anterior	27 ± 5	31 ± 8	0.101
Basal Anteroseptal	30 ± 7	28 ± 7	0.458
Basal Inferoseptal	29 ± 6	27 ± 6	0.300
Basal inferior	30 ± 5	31 ± 10	0.702
Basal Inferolateral	30 ± 6	28 ± 9	0.644
Basal anterolateral	28 ± 5	29 ± 8	0.882

The significant difference in the segmental ECV fraction in those with and without LGE was found only in mid cavity anterolateral segment. The global ECV fraction for those with and without LGE were 29.3 ± 4 versus 30.6 ± 5 (p =0.472).

h. Determination of threshold for native T1 values using ROC curve:

Receiving operating characteristic curve (ROC curve) was derived for each of the segmental parametric analysis measurement which showed significant difference between the cases and controls on comparison. This was done to assess if any of the segment is specific as a representative to assess the parametric mapping. Area under the curve (AUC) was used to assess how well the segmental analysis can distinguish between cases and controls.

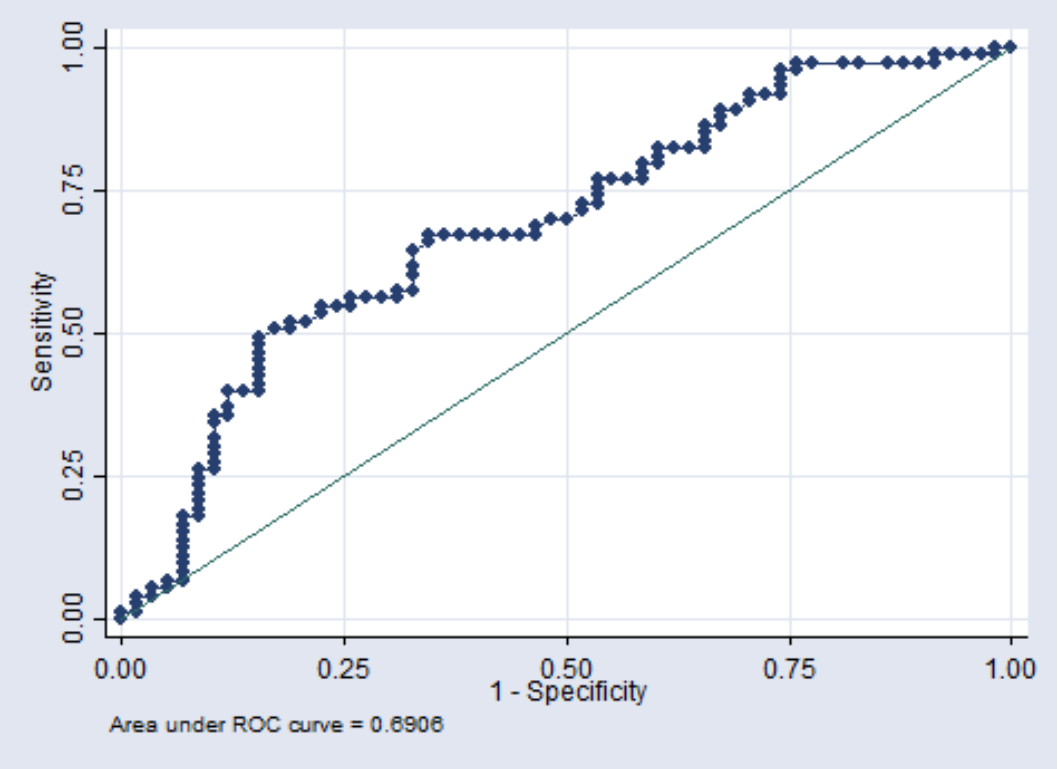


Figure 40- ROC curve of native T1 mapping of basal inferior segment

Table 16: Sensitivity, specificity and area under the curve (AUC) of native T1 mapping

Native T1 mapping of basal inferior segment	
Sensitivity	64 %
Specificity	67 %
AUC	0.6906
Cut off native T1 value	1074 msec

Based on the derived area under the curve values of T1 relaxometry, done for each of the 17 segments, only the basal inferior segment showed sensitivity and specificity reasonable for diagnostic purpose (sensitivity 64%, specificity 67%, AOC 0.69)for T1 relaxometric value of 1074 msec as shown in figure 40 and table 16.

When the sensitivity of mid cavity anteroseptal segment is 90.41 % (for native T1 relaxometry of 1007 msec), corresponding specificity is only 20.69 %. Similarly, when the sensitivity of mid cavity inferoseptal is 90.41 % (for T1 relaxometry of 1007 msec), the corresponding specificity is only 12.07 %. Hence, a single representative mid cavity septal segment measurement for parametric mapping which is practised in many centres, may not be representative of relaxometric values of all 17 segments as the diagnostic accuracy of septal segments are poor as demonstrated in the present study.

Based on the derived AOC curves of post Gadolinium T1 relaxometry of each of the 17 segments, none of the individual segments proved to have diagnostic accuracy in terms of sensitivity and specificity.

i. Cases:

1. Figure 41. 56 year old lady with dilated cardiomyopathy with mid myocardial pattern of enhancement in the midcavity antero-septal and infero-septal segments and corresponding elevated native T1 values, normal native T2 values and low post contrast T1 values in these segments.

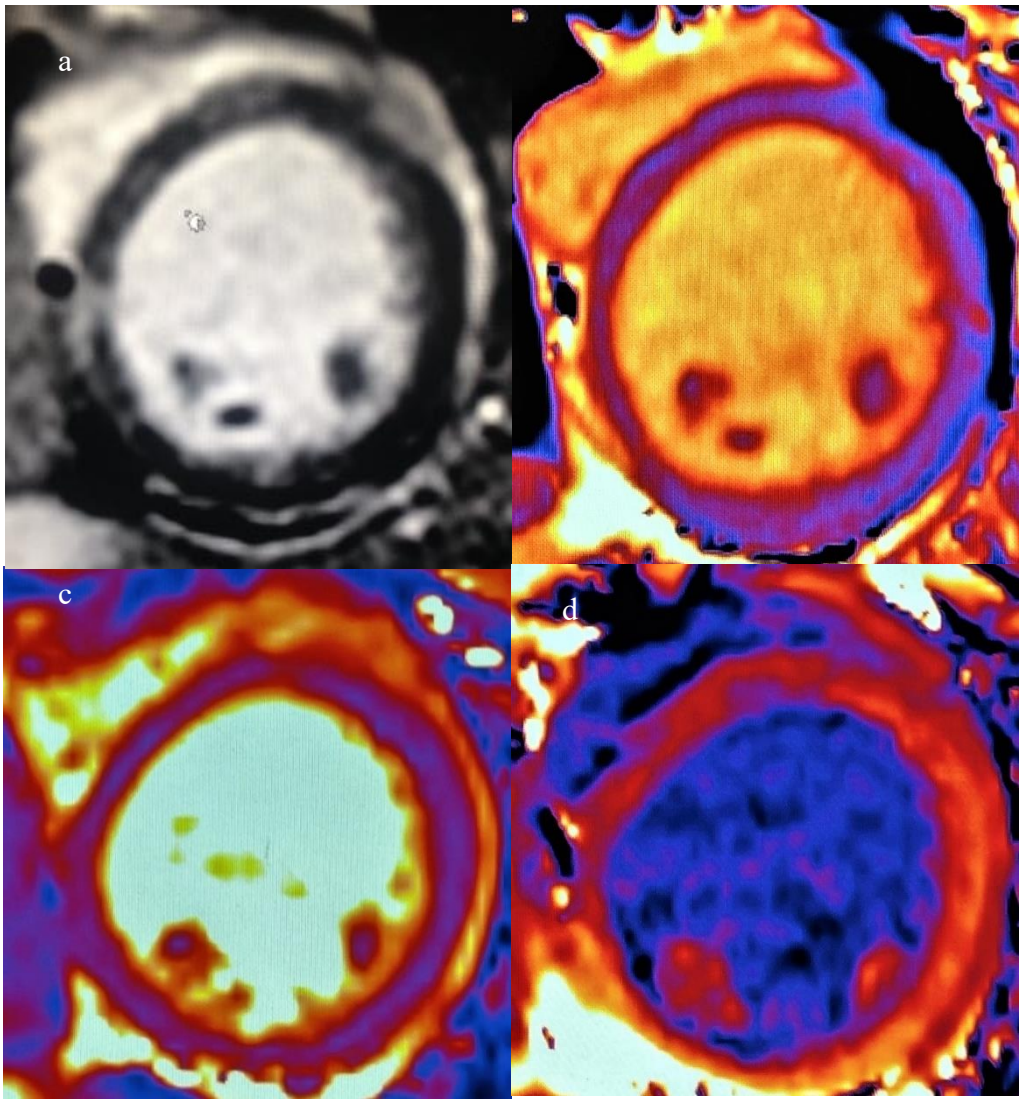


Figure 41
a- Late gadolinium in midcavity antero-septal and infero-enhancement- mid myocardial pattern septal segments

b- Native T1 midcavity
Antero-septal- 1068.1 ± 54 ms
Infero-septal- 1098.6 ± 18 ms

c - Native T2 midcavity
Antero-septal- 50.8 ± 4 ms
Infero-septal- 50.1 ± 4 ms

d- T1 post gadolinium midcavity
Antero-septal- 246.8 ± 25 ms
Infero-septal- 257 ± 16 ms

2. Figure 42. 71 year old man with hypertrophic cardiomyopathywith normal native T1, elevated native T2 and post contrast T1 values in the apical septal segment.

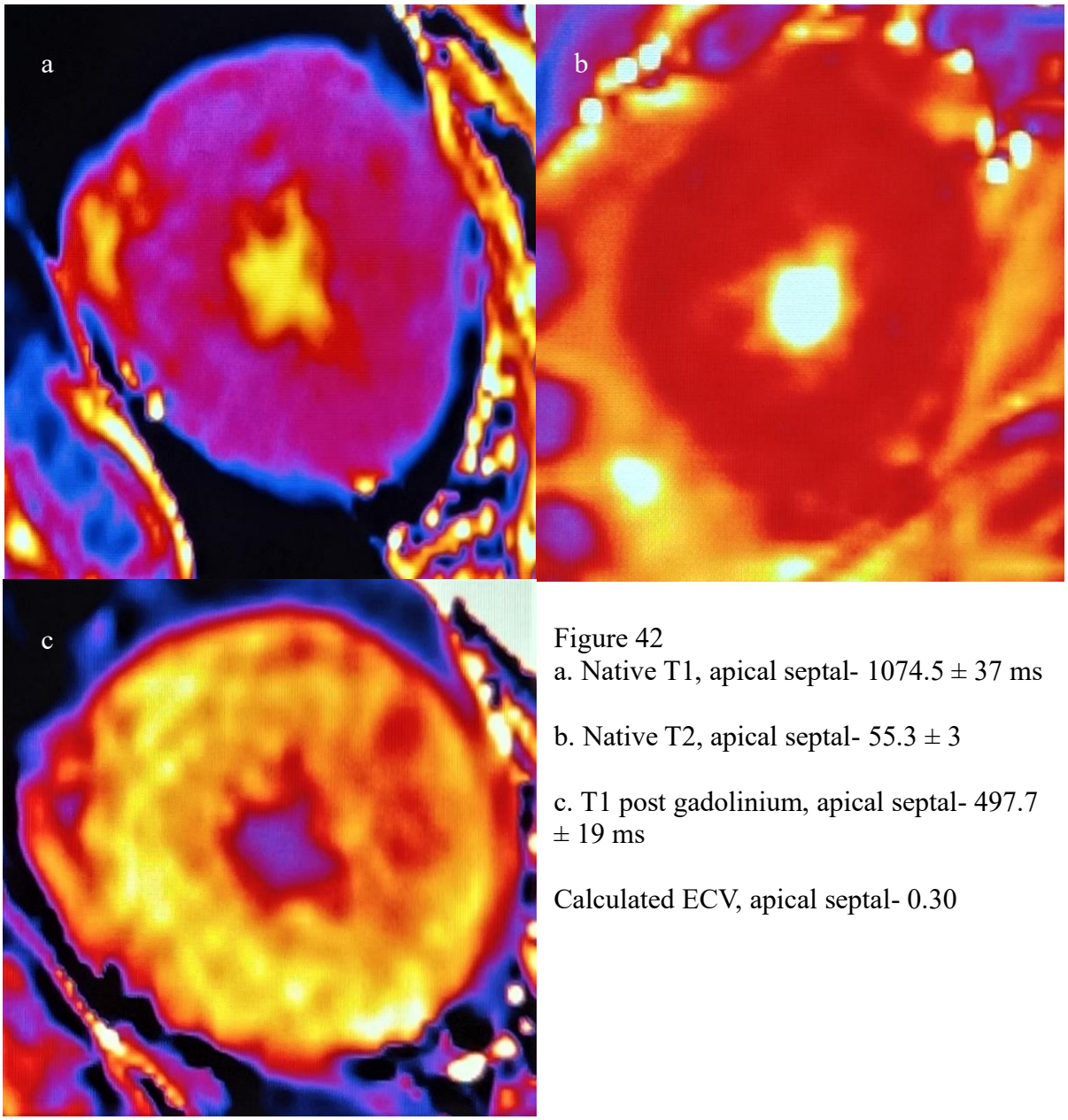


Figure 42
a. Native T1, apical septal- 1074.5 ± 37 ms

b. Native T2, apical septal- 55.3 ± 3

c. T1 post gadolinium, apical septal- 497.7 ± 19 ms

Calculated ECV, apical septal- 0.30

3. Figure 43. 66 year old man with cardiac amyloidosis with transmural enhancement in basal antero-septal and infero-septal segments and elevated native T1 values in these segments

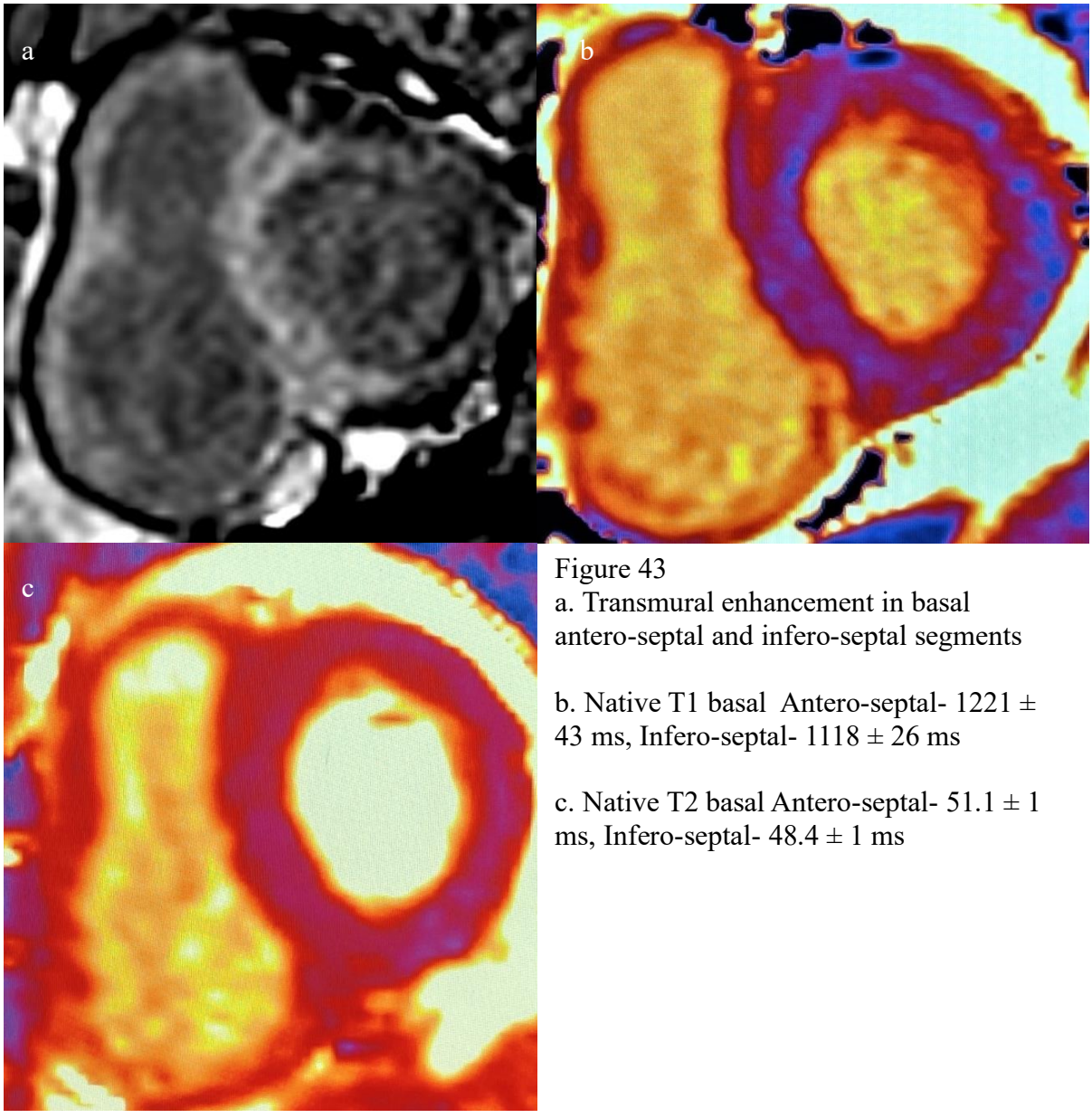


Figure 43
a. Transmural enhancement in basal antero-septal and infero-septal segments

b. Native T1 basal Antero-septal- 1221 ± 43 ms, Infero-septal- 1118 ± 26 ms

c. Native T2 basal Antero-septal- 51.1 ± 1 ms, Infero-septal- 48.4 ± 1 ms

4. Figure 44. 47 year old lady with myocarditis with STIR hyperintensity in the mid cavity septum and anterior wall, mid myocardial enhancement in the midcavity antero-septal and infero-septal segments, elevated native T2 values and native T1 values with lower post contrast T1 values.

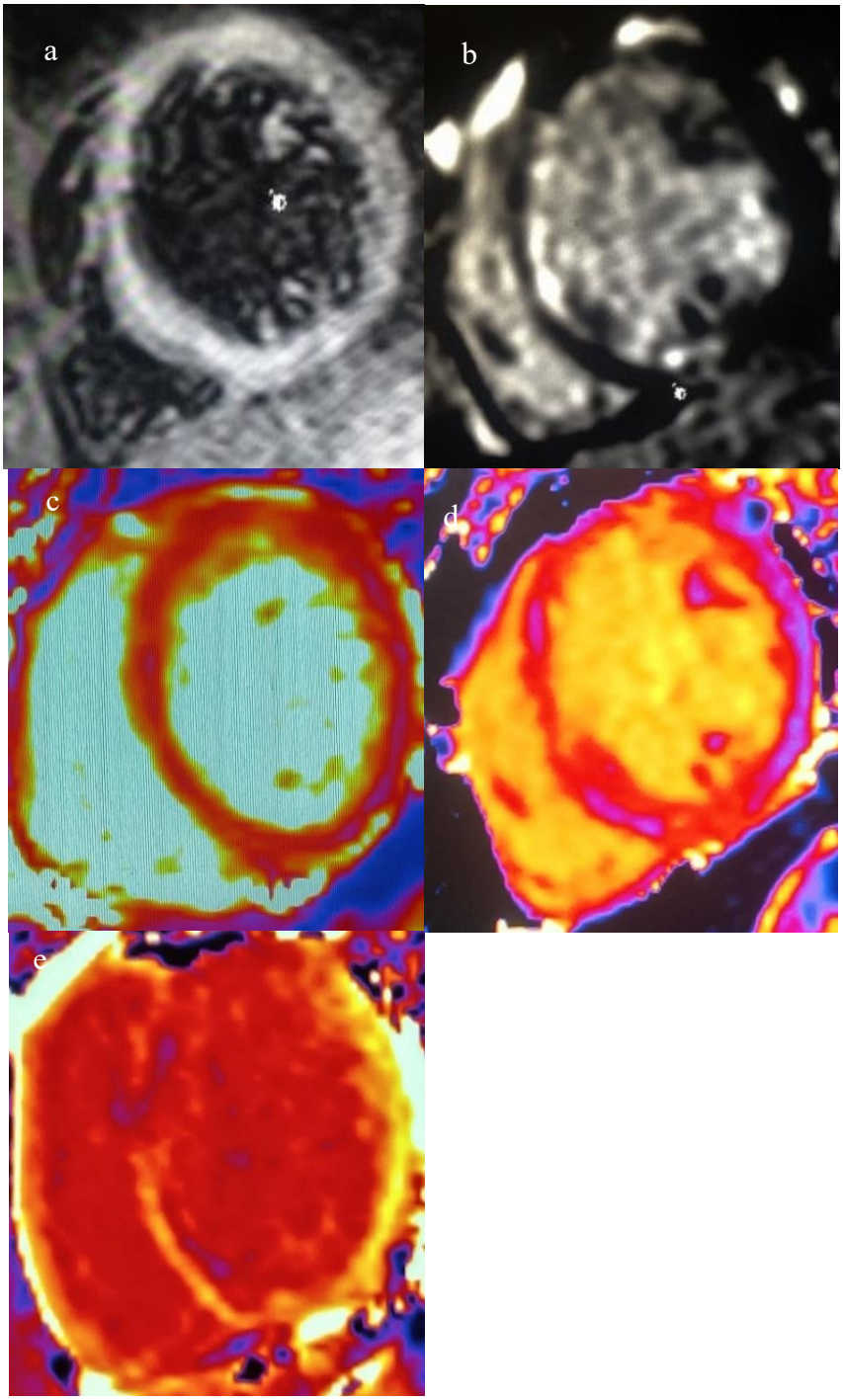


Figure 44
a. STIR hyperintensity in the midcavity septum and anterior wall

b. Mid myocardial enhancement in the midcavity antero-septal and infero-septal segments

c. Native T2 midcavity Antero-septal- 60.2 ± 8 ms, Anterior- 65.8 ± 5.7 ms, Infero-septal – 59.4 ± 6 ms

d. Native T1midcavity Antero-septal- 1177 ± 62 ms, Anterior- 1153.5 ± 98 ms, Infero-septal- 1161 ± 73 ms

e. T1 post gadolinium midcavity, Antero-septal – 388.2 ± 29 ms, Infero-septal – 411.6 ± 28 ms

DISCUSSION

We have studied 73 cases with non-ischemic cardiomyopathy and 58 controls. As there is paucity of established literature in Indian cohort regarding parametric mapping values in different types on non-ischemic cardiomyopathy, our objective was to derive at reference values for non-ischemic cardiomyopathy in the Indian cohort. No prior literature is available, which has evaluated the global and segmental parametric values separately for native T1, native T2 and post Gadolinium T1 and ECV values in non-ischemic cardiomyopathy.

a. Demographic characteristics:

The demographic characteristics of our study population are similar to those in the published literature as given in table 17.

74 % of cases and 52% of controls were males in our study population. There was no statistical significant difference in the age distribution between cases and controls in our study.

Ify et al (45) evaluated native T1 and T2 mapping in 58 middle aged male subjects with dilated cardiomyopathy compared with controls and the mean age was 47.9 ± 14.5 years. While in the study done by Maceira et al analysing the T2 mapping in normal myocardium in 32 healthy subjects, the mean age distribution was 57 ± 12 years and 62.5% were men.

Puntmann et al (46) assessed native T1-Mapping in non-ischemic dilated cardiomyopathy (NIDCM) and their outcomes in 637 cases (395 men) who had mean

age of 50 years with no significant change in native T1 values with gender. In another study by Puntmann et al on the role of native T1 and T2 mapping for early detection of sarcoidosis, the median age was 45 years in 53 (21) subjects.

Dabir et al (56) estimated native T1 mapping values in 102 adults (53 men) with normal myocardium and mean age was found to be 41 ± 17 years with no significant change in T1 mapping values with gender distribution. However, Roy et al (24) in his study on native T1, T2 mapping and ECV on healthy myocardium of 75 adults (41 men) and mean age of 56 ± 19 years observed higher ECV values in females. Liu et al (57) also showed that females had higher native T_1 values, post contrast T1 values and ECV values compared to men in his study in 1231 (606 men) healthy adults for evaluation of age related myocardial fibrosis with post contrast T1 mapping. In a study by Parekh et al (58) on native T1 mapping in young adults less than 25 years and children with hypertrophic cardiomyopathy, the mean age was 14.1 ± 4.6 years and in controls was 15.7 ± 5.7 years, studied in 21 subjects, 15 men, there was significant difference with gender distribution, native T1 was higher in females with hypertrophic cardiomyopathy.

Siepen et al (49) detected native T1 mapping in dilated cardiomyopathy and compared the myocardial fibrosis with endomyocardial biopsy in 74 subjects with DCM (47 men) with mean age of 52 ± 9 years in healthy subjects, 55 ± 16 years in early dilated cardiomyopathy and 58 ± 12 years in dilated cardiomyopathy.

Karur et al (50) evaluated native T1 mapping in 3 T to discriminate Anderson Fabry disease and hypertrophic cardiomyopathy with 30 subjects in each group (11 men in AFD and 17 men in HCM) with mean age of45 ± 14.1 years in Anderson Fabry

disease and 49.3± 13.5 years in HCM. Ismail et al evaluated native T1 and T2 mapping to assess the myocardial fibrosis in HCM as compared to the controls in20 cases with HCM (15 men) and the mean age was 59.9±9.1.In a study by Spieker et al (52), on T2 mapping correlation with worse outcomes in suspected acute myocarditis subjects, the mean age was 41±16 years, studied in 46 cases (33 men).

Ridouani et al (53) assessednative T2 mapping to differentiate between the light chain (AL) and transthyretin cardiac amyloidosis (ATTR) to determine the prognosis in 24 (14 men) and 20subjects (17 men) with AL and ATTR respectively and the mean age was 65 ± 12 years in AL and 73± 15 years in ATTR.

Table 17: Comparison of demographic characteristics in normal subjects and cases with published literature

Authors	**Sample size (normal subjects)**	**Age (years) / Male (n)**	**Cohort**
Present study	58	45/30	Normal subjects
Dabir et al	102	41± 17/ 53	Normal healthy subjects
Roy et al	75	56 ± 19/ 41	Normal healthy subjects

Authors	Sample size (cases)	Mean Age (years) ; Male (n)	Cohort
Present study	73	47; 54	Non-ischemic cardiomyopathy
Ify et al	58	47.9± 14.5; 58	NIDCM
Puntmann et al	637	50; 395	NIDCM
Puntmann et al	53	45; 21	Sarcoidosis
Siepen et al	74	55 ± 16.9(early DCM), 58 ± 12(DCM); 47	Early DCM and DCM
Karur et al	30(AFD), 30 (HCM)	45± 14; 11 49.3± 14; 17	AFD and HCM
Parekh et al	21	14.1± 4.6;15	HCM
Ismail et al	20	59.9± 9.1; 15	HCM
Spieker et al	46	41±16 ;33	Suspected acute myocarditis
Ridouani et al	24(AL), 20(ATTR)	65 ± 12; 14 (AL) 73± 15;17 (ATTR)	AL and ATTR amyloidosis

b. <u>Mean segmental and mean global parametric mapping values:</u>

1. <u>Native and post Gadolinium T1 mapping, ECV</u>

In our study population we did segmental analysis of each of the 17 segments of the heart and mean value of each segment was obtained. There was significant difference in the segmental mean native T1 and post contrast T1 relaxation times between the non-ischemic cardiomyopathy cases and control group in most of the segments. This is similar to the published studies in literature as described below and demonstrated in table 18 and 19. However, no difference was observed in the segmental mean ECV between the two groups.

The global mean of the parametric mapping in our study showed significant difference between the non-ischemic cardiomyopathy cases and controls in native T1 mapping

and post contrast T1 mapping. Native T2 mapping and ECV fraction did not show any significant difference between the cases and controls. This is also comparable to the studies published in the literature. There was significant difference in the mean of global native T1 [1062.27 (males) versus 1101(females); p=0.002] and post contrast T1[457.69 (males) versus 413(females); p=0.032] with gender, among the NIDCM cases.

While analysing the global mean of parametric mapping in various types of non-ischemic cardiomyopathy like hypertrophic cardiomyopathy, dilated cardiomyopathy, restrictive cardiomyopathy and myocarditis, only ECV showed significant difference between the different types of NICM.

Ify et al (45) evaluated native T1 and T2 mapping in 58 middle aged male subjects with dilated cardiomyopathy compared with controls and aerobic exercisers in this age group and demonstrated significant difference between the segmental native T1 values and ECV between dilated cardiomyopathy subjects and exerciser's myocardium, measured in the septum of the basal and mid cavity section(T1 values in exercisers was 957 ± 32 ms and in dilated cardiomyopathy was 1017 ± 42 ms and extracellular fraction volume was 26.3 ± 3.6%and 31.2 ± 4.1% respectively).

Puntmann et al (46), when he evaluated the native T1 mapping in NIDCM subjects, the native T1 segmental septal value was 997 ms in 1.5T and 1113 ms in 3T and the global mean T1 value was 962 ms in 1.5T and 1058 ms, evaluated in 3T scanner, in non-ischemic dilated cardiomyopathy subjects. The post contrast T1 values were 439 ms and 441 ms, in 1.5T and 3Tscanners respectively. He also found that the values of native T1 mapping in septal segment and global mean values and ECV in 1.5T and 3T

scanners were significantly higher (1069 ms, 999 ms, 30% in 1.5 T and 1183 ms, 1094 ms and 31% in 3T respectively) in the patients who died due to heart failure. In this study, they noticed that septal segmental measurement of native T1 value had greater accuracy than the whole short axis values of all the segments of the myocardium as there is no degradation by blood pool or the lateral segments. No significant difference is observed with post contrast T1 mapping between NIDCM cases and controls. Puntmann et al (47) in another study on the role of native T1 and T2 mapping for early detection of sarcoidosis showed that the native T1 mapping and ECV values from the septal segment of mid cavity were significantly higher in subjects with sarcoidosis (1139 ms, and 28 %) as compared to the controls (1052 ms and 25%).

Karur et al (50) assessed native T1 mapping to differentiate Anderson Fabry disease and hypertrophic cardiomyopathy in 3T scanner and observed that the segmental septal native T1 value and global mean of T1 value were significantly higher in both AFD and HCM (1161 ± 47 ms and 1192 ± 52 ms, respectively in AFD and 1296 ± 55 ms and 1268 ± 55 ms, respectively in HCM). The native T1 values both segmental and global were significantly lower in AFD in both 1.5 T and 3 T scanners. Global mean of native T1 values and ECV values were significantly greater in contrast to segmental septal native T1 values and ECV values measured in this study, in Anderson Fabry disease, as the fibrosis in septum will be lower in these patients. However, septal segmental values were preferred in subjects with Anderson Fabry disease as it was easier to measure and had better distinction. This study also showed that 3T scanner measurement of native T1 was better. When native T1 mapping acquired in MOLLI sequence, a cut off value of 1220 ms or lower was considered as

useful to differentiate between AFD and HCM in 3T when septal measurement of left ventricle is done.

Kato et al (59) studied the native T1 mapping in hypertrophic cardiomyopathy and showed that the native T1 values were significantly higher in hypertrophic cardiomyopathy cases than controls. Native T1 values were also elevated in areas without late gadolinium enhancement, suggesting early detection of diffuse myocardial disease. In this study global mean of the native T1 values of the segments were taken. Siepen et al (49) evaluated native T1 mapping in dilated cardiomyopathy and compared the myocardial fibrosis with endomyocardial biopsy and found that the native T1 values, post contrast T1 values and ECV values were significantly higher in dilated cardiomyopathy (1056 ± 62 ms, 420 ± 45 ms and 27 ± 4 % respectively) as compared to the controls (1020 ± 40 ms, 442 ± 43 ms and 23 ± 3 % respectively). Average mean of mid cavity segments were taken as global native T1 value in this study. No significant difference is observed with post contrast T1 mapping between DCM cases and controls. Ridouani et al (53) assessed native T2 mapping to differentiate between the light chain and transthyretin cardiac amyloidosis to determine the prognosis and demonstrated thatthe native T2 mapping had greater diagnostic accuracy than native T1 mapping in differentiating the AL and ATTR amyloidosis. In this study it was also observed that ECV was outstanding predictor of the outcome. No significant difference was observed with post contrast T1 mapping between AL and ATTR.

Table 19: Comparison of mean of segmental and global native T1 and ECV values with published literature

Authors	Sample size	Clinical diagnosis	Native T1 (ms)			ECV (%)			Study centre
			Segmental	Global	p value	Segmental	Global	p value	
Present study	73 (NIDCM); 58 (controls)	NICM; Controls (1.5T)	Refer to table 4	1073 ± 46; 1044 ± 41	<0.001	Refer to table 7	29.5 ± 4; 29.3 ± 4	0.476	Vellore, India
Ify et al	16 21 21	DCM; Exercisers; Controls	1017 ± 42; 957 ± 32; 952 ± 31	-	<0.001	31.2 ± 4; 26.3 ± 4; 26.2 ± 3	-	<0.001	UK
Puntman et al	637 609 28	DCM (total); Survived; Died (1.5T)	997; 994; 1069	962; 951; 999	Segmental-<0.001 Global-0.01 (1.5 T) 0.02 (3T)	26; 26; 30	-	0.03	UK
Karur et al	30 (AFD); 30 (HCM)	AFD; HCM (3T)	1161 ± 47; 1296 ± 55	1192 ± 52; 1268 ± 55	<0.001	24.6 ± 3; 26.2 ± 4	25.5 ± 2; 25.6 ± 3	0.07; 0.95	Canada
Kato et al	29; 15	HCM; Controls (1.5 T)	-	1117 ± 55; 1065 ± 35	<0.001	-	-	-	USA
Siepen et al	29 (DCM); 45 (early DCM); 56 (controls)	DCM; Early DCM; Controls (1.5 T)		1056 ± 62; 1019 ± 47; 1020 ± 40	0.01		27 ± 4; 25 ± 4; 23 ± 3	0.0001	Germany
Puntman et al	53; 36	Sarcoidosis; Controls (1.5 T)	1139; 1052	-	<0.001	28; 25	-	0.015	UK
Ridouani et al	24 (AL); 20 (ATTR); 40 (controls)	Amyl. AL; Am.ATTR; Controls (1.5 T)	1104 ± 54; 1066 ± 42; 975 ± 26		0.01	53 ± 17; 46 ± 11;		0.2	France

Table 20: Comparison of mean of segmental and global post contrast T1 values with published literature

Authors	Sample size	Clinical diagnosis	Post contrast T1 (msec)			Study centre
			Segmental	Global	p value	
Present study	73 (NICM); 58 (Controls)	NICM; Controls (1.5T)	Refer to table 6	446.52 ± 90; 489.83 ± 49	0.002	Vellore, India
Puntman et al	637; 609; 28	DCM (total); Survived; Died (1.5 T)		439; 439; 435	0.58	UK
Siepen et al	29 (DCM); 45 (early DCM); 56 controls)	DCM; Early DCM; Controls (1.5 T)		420 ± 45; 431 ± 40; 442 ± 43	0.03	Germany
Ridouani et al	24 (AL); 20 (ATTR)	Amy AL; Amy.ATTR (1.5 T)	-	378 ± 73; 363 ± 69	0.9	France

2. T2 mapping

In our study population there was no significant difference in the segmental mean and global mean of T2 mapping between the cases and controls contrary to the published literature as shown below and in table 20. In this study, there was no significant difference in the native T2 values with gender.

Puntmann et al (47) evaluated the role of native T1 and T2 mapping for early detection of sarcoidosis and demonstrated that native T2 mapping from the septal segment of mid cavity were significantly higher in subjects with sarcoidosis (54 ms) as compared to the controls (45 ms).Spieker et al (52) in the study on T2 mapping correlation with worse outcomes in suspected acute myocarditis subjects showed that

the global T2 mapping was significantly higher in subjects with suspected acute myocarditis as compared to the controls (68.1 ± 5.8 msec vs 60 ± 4.2 msec), which was demonstrated as useful in prognostication and risk stratification in this study. Ify et al (45) evaluated middle aged subjects with early non-ischemic dilated cardiomyopathy and compared with controls and aerobic exerciser's in this age group and found that there was significant difference between the segmental native T2 values between dilated cardiomyopathy subjects and exerciser's myocardium, measured in the septum of the basal and mid cavity section (T2 values in exercisers was 52.8 ± 3.2 ms and in dilated cardiomyopathy was 55.9 ± 4.4 ms).Ridouani et al (53) assessed native T2 mapping to differentiate between the light-chain and transthyretin cardiac amyloidosis to determine the prognosis and demonstrated that the native T2 mapping was significantly greater in light chain amyloidosis (AL) as compared to transthyretin amyloidosis (ATTR) (63.2 ± 4.7 ms vs 56.2 ± 3.1 ms). The average mean of mid ventricular segment was taken as native T1 and T2 values. The native T2 mapping was demonstrated to have greater diagnostic accuracy than native T1 mapping in differentiating the AL and ATTR amyloidosis.

Table 20: Comparison of mean of segmental and global native T2 values with published literature

Authors	Sample size	Clinical diagnosis	Native T2 (msec)			Study centre
			Segmental	Global	p value	
Present study	73 (NICM); 58 (controls)	NICM; Controls (1.5 T)	Refer to table 5	50.59 ± 3; 50.98 ± 3	0.639	Vellore, India
Ify et al	16; 21; 21	NIDCM; Exercisers; Controls	55.9 ± 4.4; 52.8 ± 3.2; 52.9 ± 3.3	-	0.024	UK
Puntmann et al	53; 36	Sarcoidosis; Controls (1.5 T)	54; 45	-	<0.001	UK
Ridouani et al	24 (AL); 20 (ATTR); 40 (controls)	Amy. AL; Amy.ATTR; Controls (1.5 T)	63.2 ± 4.7; 56.2 ± 3.1; 51.1 ± 3.1		0.0001	France
Spieker et al	46; 60	Acute myoacarditis; Controls	-	68.1 ± 5.8; 60 ± 4.2	<0.001	Germany

c. <u>Late gadolinium enhancement pattern and significance:</u>

1. <u>Native T1 mapping:</u>

There was significant difference in the segmental native T1 and post contrast T1 values in most segments between cases with and without late gadolinium enhancement similar to few published literature as shown in table 21. There was no significant difference in the global relaxometric values with respect to LGE. Mid myocardial pattern was the most prominent pattern observed in our study followed by transmural.

Kato et al (59) demonstrated that among subjects with hypertrophic cardiomyopathy, segments with and without late gadolinium enhancement, the native T1 relaxation time was high in both groups (LGE absent- mean native T1- 1114 ± 56 msec, LGE present- mean native T1- 1141 ± 46 msec). However, LGE positive subjects had higher values than LGE negative subjects suggestive of myocardial fibrosis burden, even in the absence of late gadolinium enhancement. Nakamori et al (51) in his study on native T1 mapping in non-ischemic dilated cardiomyopathy with arrhythmia found that the mid myocardial enhancement pattern was the commonest and the native T1 mapping cannot replace late gadolinium enhancement, though it provides additional information. However, there was no difference in native T1 mapping in non-ischemic dilated cardiomyopathy cases with and without late gadolinium enhancement (1121 ± 39 and 1117 ± 48 respectively).

Puntmann et al (48) evaluated native T1 mapping in normal myocardium, dilated and hypertrophic cardiomyopathy and showed that the presence and absence of late gadolinium enhancement had no significant difference in the mean T1. T1 mapping was considered superior to late gadolinium enhancement in distinguishing normal and abnormal myocardium (HCM: 1241 ± 51 ms and 1234 ± 71 ms, NIDCM: 1290 ± 52 ms and 1301 ± 49 ms).Malek et al (60) evaluated native T1-mapping as compared to late gadolinium enhancement for assessment of myocardial fibrosis in hypertrophic cardiomyopathy and showed that the native T1 mapping is superior to late gadolinium enhancement in assessing myocardial fibrosis.

Ferreira et al (61) assessed T1 mapping in acute myocarditis and showed that the late gadolinium enhancement combined with T1 mapping did not improve the diagnosis of acute myocarditis(presence of LGE, native T1 value 1045 ± 66 msec and LGE absent native T1 value 978 ± 45 msec). The T1 and LGE combination did not improve diagnostic accuracy, rather reduced the T1 mapping diagnostic accuracy also, as T1 cannot help in differentiating edema and myocyte necrosis.

Table 21: Comparison of native T1 values with respect to LGE in the published literature

Authors	**Sample size (cases)**	**Clinical diagnosis**	**Native T1 (msec)**			**Study centre**
			LGE present	**LGE absent**	**p value**	
Present study	73	NICM	Segmental: Refer to table 12			Vellore, India
			1076.33±60	1068.92 ± 48	0.567.	
Kato et al	29	HCM	1141 ± 46	1114 ± 56	<0.001	USA
Nakamori et al	50	NIDCM	1121 ± 39	1117 ± 48	0.68	USA
Puntmann et al	25 (HCM); 27 (DCM)	HCM; NIDCM	1241 ± 51; 1290 ± 52	1234 ± 71; 1301 ± 49	0.88; 0.58	UK
Malek et al	25	HCM	1060	-	0.62	Poland
Ferreira et al	50	Acute myocarditis	1045 ± 66	978 ± 45	<0.001	UK

2. Native T2 mapping:

There was significant difference in the segmental native T2 values of cases with respect to LGE in a few of the segments. No significant difference was found in the global native T2 values of cases with respect to LGE This could be because the

number of myocarditis cases, where we expected to have elevated native T2 mapping was significantly less in our cohort .Mayr et al (54) studied the relationship of T2 mapping and delayed contrast enhancement on acute myocarditis, which demonstrated that the T2 mapping was higher in cases with segments showing late gadolinium enhancement as compared to absent late gadolinium enhancement segments (65 msec and 60 msec) as shown in the table 22. High native T2 values even in the absence of late gadolinium enhancement, was suggestive of myocardial inflammation.

Table 22: Comparison of native T2 values with respect to LGE in the published literature

Authors	**Sample size**	**Clinical diagnosis**	**Native T2 (msec)**			**Study centre**
			LGE present	**LGE absent**	**p value**	
Present study	73	NICM (myocarditis =5)	Segmental: Refer to table 13			Vellore, India
			51.16 ± 4	50.63 ± 3	0.515	
Mayr et al	39	Myocarditis	65	60	<0.001	USA

CONCLUSIONS

These are the conclusions from our study of parametric mapping in non-ischemic cardiomyopathy versus controls in 1.5 Tesla:

1. We studied the segmental and global nativeT1, T2, post contrast T1 and extracellular volume in non-ischemic cardiomyopathy patients in the Indian cohort that was presented to our department for cardiac MRI and the descriptive statistics and its relationship with late gadolinium enhancement was analysed

2. Statistically significant difference was found in the following:

- Segmental native T1 relaxation time and post contrast T1 relaxation time (in most of the segments) of non-ischemic cardiomyopathy subjects as compared to control.

- Global native T1 relaxation and post contrast T1 relaxation time in non-ischemic cardiomyopathy subjects as compared to control.

- Global ECV between different types of non-ischemic cardiomyopathy

- Segmental native T1, segmental post contrast T1 mapping with respect to presence and absence of LGE in the cases. Only some of the segments showed significant difference in segmental T2 relaxometry with and without LGE.

3. Segmental and global T1, post contrast T1 relaxometry in NIDCM in the present study were comparable with the published literature.

LIMITATIONS

The limitations in our study were:

1. Single centre study

2. Due to non-availability of software for automatic contouring of parametric mapping, manual contouring of region of interest was done in all the 17 segments by the investigators, which was time consuming.

3. Packed cell volume was required for calculation of ECV, some of the samples clotted and few subjects gave no consent for the same, limiting the ECV calculation

4. As there was strong interobserver correlation noticed while contouring separately in a few of the cases, ICC was not assessed for the entire cohort.

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ANNEXURES

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

March 01, 2018

Dr. Linu Oommen Varghese,
PG Registrar,
Department of Radiology,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant: New Proposal:**
Parametric mapping and myocardial extracellular volume measurement for non-ischaemic cardiomyopathy in Indian cohort
Dr. Linu Oommen Varghese PG registrar, MD Radiodiagnosis, Dr. Leena R.V, Employment Number:28374, Radiology, Dr. Hannah.L Khiangte Assistant Professor, Employment No: 29027 Department of Radiology, Dr. Roshan Samuel Livingstone, Professor, Employment No: 30596, Department of Radiology, Dr. Viji Samuel Thomson, Professor, Employment number: 28037, Cardiology, Dr. Elizabeth Joseph Professor Employment Number: 20071, Radiology, Dr. Aparna I, Professor, Employment number: 28382, Radiology, Dr. Binita Riya Chacko, Employment Number: 31893, Radiology.

Ref: IRB Min. No. 10933 [OBSERVE] dated 07.11.2017

Dear Dr. Linu Oommen Varghese,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Leena R.V, Dept. of Radiology, CMC, Vellore

1 of 4

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

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Ref: IRB Min. No. 10933 [OBSERVE] dated 07.11.2017

Dear Dr. Linu Oommen Varghese,

The Institutional Review Board **(Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Parametric mapping and myocardial extracellular volume measurement for non-ischaemic cardiomyopathy in Indian cohort" on November 07th 2017.

The Committee reviewed the following documents:

1. IRB application format
2. Proforma
3. Information Sheet and Consent Form (English, Tamil, Hindi, Telugu and Bengali)
4. Proforma
5. Cvs of Drs. Leena, Linu, binitha, Riya, Aparna, Elizabeth, Hannah, Roshan and Viji.
6. No. of documents 1- 5.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

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Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on November 07th 2017 in the BRTC Conference Hall, Biostatistics Building, Christian Medical College, Vellore 632 004.

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA (Theology), Dr. Min (Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Dr. RatnaPrabha	MBBS, MD (Pharma)	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Dr. SowmyaSathyendra	MBBS, MD (Gen. Medicine)	Professor, Medicine III, CMC, Vellore	Internal, Clinician
Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Sathish Kumar	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist &Epidemiologist
Dr. Asha Solomon	MSc Nursing	Associate Professor, Medical SurgicalNursing, CMC, Vellore	Internal, Nurse
Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
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Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. John Antony Jude Prakash	MBBS, MD	Professor, Clinical Microbiology, CMC, Vellore.	Internal, Clinician.
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician
Dr. Mathew Joseph	MBBS, MCH	Professor, Neurosurgery, CMC, Vellore	Internal, Clinician
Dr. RekhaPai	BSc, MSc, PhD	Associate Professor, Pathology, CMC, Vellore	Internal, Basic Medical Scientist
Ms. Grace Rebekah	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of Withdrawals for the study entitled: "Parametric mapping and myocardial extracellular volume measurement for non-ischaemic cardiomyopathy in Indian cohort" on a monthly basis. Please sendcopies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:

A sum of 21,200/- INR (Rupees Twenty one Thousand Two hundred Only) will be granted for 10 Months.

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

IRB Min. No. 10933 [OBSERVE] dated 07.11.2017

DATA COLLECTION PROFORMA

Serial number- Date of collection:

Name- Hospital number-

Age- Sex-

Indication for referral-

ECG finding-

Echocardiogram finding-

17 segments of heart- T1, post contrast T1, T2 and ECV values for each segment

Apex-Ap, Apical- septal(As), inferior(Ai), lateral(Al) and anterior(Aa), Mid cavity- inferoseptal(Mis), inferior(Mi), inferolateral(Mil), anterolateral(Mal), anterior(Ma), anteroseptal(Mas), Basal- inferoseptal(Bis), inferior(Bi), inferolateral(Bil), anterolateral(Bal), anterior(Ba), anteroseptal(Bas)

Parameters	Ap	As	Ai	Al	Aa	Mis	Mi	Mil	Mal	Ma	Mas	Bis	Bi	Bil	Bal	Ba	Bas
Native T1																	
T1 post contrast																	
Native T2																	
ECV																	
LGE																	
0- absent	1- present																
	a-midmyocardial					b-subepicardial						c-diffuse					

Radiological diagnosis and functional parameters-

Absolute LVEDV	Indexed LVEDV	Absolute LVESV	Indexed LVESV	LVEF	Absolute LV mass	Indexed LV mass

WRITTEN INFORMED CONSENT FORM

Date:

Hospital number:

Study title: Parametric mapping and myocardial ECV measurement for nonischaemic cardiomyopathy in Indian cohort

It has been explained to me by the investigator in the language that I understand that this study is being carried out as an extra sequence to the regular cardiac MRI. A bloodsample of 3 ml will also be collected as a part of the study. T1 mapping promises todetect early disease, quantify disease severity and provide prognostic insights intocertain conditions of heart. It has been explained to me that no extra drugs/ extracharge and there is no risk involved in this study. It has also been explained that I amfree to withdraw from the study any time I want and this will not in any way compromisemy treatment. I understand that my identity and participation will not be revealed in anyinformation released to third parties.

No Extra Charges

Subjects' Name

Date of Birth/ Age:

• I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions

• I understand my participation is purely voluntary and that I can withdraw from the

study anytime, without any reason, without my medical care being affected.

• I understand that my identity will not be revealed in any information.

iv) I agree to take part in the above study.

Signature of subject Thumb impression

Date

Name of the subject

Signature of the investigator

Date

Name of the investigator

Signature of the witness Thumb impression

Date

Name of the witness

PATIENT INFORMATION SHEET

Study title: Parametric mapping and myocardial ECV measurement for non-ischemic cardiomyopathy in Indian cohort

The following information is provided to inform you about this study and your participation in it. Please read the information carefully and you are free to ask any questions regarding the study and the information given. The participation in this study is purely voluntary and you are free to withdraw from the study anytime.

Purpose of the study:

A cardiac MRI T1 and T2 myocardial mapping technique is a non –invasive study, enabling direct visualization of properties and healthiness of heart muscle. By this technique, we are trying to study two properties of heart muscle called T1 and T2 relaxation times, by doing some extra imaging, in addition to the regular MRI that you will be undergoing. A blood sample of 3 ml will be collected as a part of this study. T1 and T2 mapping promises to detect early disease and to know the amount of disease in the heart

No extra money will be charged for T1 and T2 mapping of the myocardium

Method to be followed:

Patient is to arrive at MRI Room 8, one hour prior to the scheduled test time.

Patient will be asked to change into a hospital gown and remove all jewelry, dentures and hearing aids.

Intravenous (IV) cannula (usually 20G) will be placed and 3 ml blood sample withdrawn.

Baseline blood pressure will be checked.

During the test:

Standard MRI sequences including post Gadolinium studies will be obtained as requested by your treating doctor.

In addition, extra sequences will be done including native T1 and T2 mapping and postcontrast T1 mapping of myocardium is done which takes additional 8-10 minutes minute

Confidentiality:

The participation in the study will remain confidential and shall be known only to the investigators.

Withdrawal from the study:

Participation in this study is purely voluntary and you can withdraw from the study anytime without any reason. It will not compromise your treatment in any way. There are no potential risks involved in this study and you need not pay any extra money for the test.

Detailed information about the Procedure

What is cardiac MRI T1 and T2 mapping technique?

The magnetic resonance imaging (MRI) machine is a tube with a centre opening that isabout three feet wide.

A table slides into the central opening and the patient lies on the table. Pictures of the heart are created using a magnetic field, radio waves and computers.

No X-rays are used to create the images.

The images made by the MRI will allow your doctor to look at the anatomy and functioning of your heart.

In addition, by using doing T1 and T2 mapping of the heart, we will try to see the abnormality of the heart muscle from another perspective.

What are the benefits and risks of the test?

There is absolutely no risk involved in the study. You will just have to be within the scanner for an additional 8-10 minutes or so.

This test can potentially help us to detect the disease earlier.

It can also help us to know amount of disease in the heart.

Before the test:

• You cannot have anything to eat or drink for 4 hours before your test.

• Take your medications as instructed by your doctor

On day of the test

Patient is to arrive at MRI Room 8, one hour prior to the scheduled test time.

Patient will be asked to change into a hospital gown and remove all jewelry, dentures and hearing aids.

A needle {Intravenous (IV) cannula (usually 20G)} will be placed in your hand or elbow

region and a blood sample of 3 ml will be withdrawn.

Baseline blood pressure will be checked.

• Before the test starts, you will be asked questions about your medical history and the medication(s) you are taking and to make sure it is safe for you to have an MRI scan.

During the test:

Standard MRI sequences including post Gadolinium studies are obtained.

Native T1 and T2 mapping and post contrast T1 mapping of myocardium is done which takes additional 8-10 minutes.

• During the test, you will hear knocking sounds as the machine takes the pictures. We will also prompt you with instructions. For example, we may ask you to hold your breath for 8 to 10 seconds

• It is important for you to stay as still as possible because movements can create glitches in the pictures.

• At the end of the procedure, your IV canula (needle) will be removed.

After the test

• You may resume your normal activity unless your doctor tells you differently.

• Take your regular medications as directed unless your doctor tells you differently.

• By the following day, the test results will be sent to the doctor who ordered the test. You will need to contact your doctor to discuss the results of your test.

• Keep any scheduled follow-up appointments with your primary doctor

DATA SHEET

sno	hospno	name	age	sex	t1ap	t1apsd	t2ap	t2apsd	t1gap	t1gapsd	aplge	t1aa	t1aasd	t2aa	t2aasd	t1gaa	t1gaasd	aaecv	aalge	t1as	t1assd	t2as	t2assd	t1gas
1	943814G	Supriya Ghosh	22	2	1257	97.5	85.3	10.2	327.4	24.5	0	1153	90.6	49.7	8.3	398.1	31.2		0	1165	76.9	52.7	10.9	390.1
2	135145F	Sivananam R.	43	1	1127.4	137.9	55.3	5	683.3	23.4	1	936.9	102.3	38.6	6.2	506.7	34.7		0	1015	47	42.8	7.3	529.1
3	835046F	Sulochanamma P.	46	2	1202.9	102	57.9	6.2			0	1161	163.2	59.2	6.1				0	1123	73.4	53.3	6.2	
4	910564C	Suresh C	37	1	1120.2	170.2	68.7	19.1	444.6	64.1	0	1024	69.9	57.3	6.1	491.2	22.2		0	1030	74.2	57.5	10.9	490.1
5	002248H	Mohammed Ziaur Rahman	36	1	1206	99.4	66.6	16.9	488.3	24	1	1269	49.5	56.6	5	469.4	9.6		1	1279	71.4	55.8	5.3	473.7
6	985248g	Venkateswaralu B	56	1	1285.4	136	44.4	7.8	621.1	92.4	0	1275	131.6	57.1	0.5	507.8	18.5		0	1390	35.3	69	8.1	546.7
7	809133C	Sakunthala	47	2	1155.8	91.4	66.6	6.7	433.2	25.8	0	1157	86.5	61.8	4.5	388.1	25.8		0	1169	81.1	61.1	9.1	424.1
8	002412H	Shahjan Ali	63	1	1142	145.2	54.9	3.8	419.4	27.9	0	978.3	89	53.9	4.4	451.5	24.9		0	1137	102.1	52	5.6	459.2
9	777798A	Kakali Ghosh	47	2	1137.4	117.2	44.4	8.7	379.5	36.7	0	1042	66.9	51.6	5.5	451.1	24		0	1065	53.5	52.1	7.3	428.6
10	827728g	Radhashyam Maity	32	1	1169.1	81.4	56.8	10.8			0	974.5	81.6	46.8	7.8				0	993	78.3	49.6	7.1	
11	021544H	Jadish Chandra Das	58	1	1098.3	81	48.3	5.3	439.9	28.8	0	1087	88	53	4.8	487.9	27.6		0	1093	76	52.3	7.9	463.9
12	012326H	Sokorjan Bibi	29	2	1150.1	105.7	57.3	10.1			0	962.4	99	48.6	8.6				0	1067	62.6	50.8	7.5	
13	992418G	Supriya Das	41	2	1250.4	97.7	40.8	12.6			0	1071	91.4	57	6.3				0	1122	78.6	53.4	5.4	
14	483583G	Nazma Begum	54	2	1137	74	53	4	461	30	0	1085	77	55	4	468	21		0	1117	44	51	3	484
15	046226H	Prawin Kumar Darnal	55	1	1141	87	52	4	441	22	0	1230	74	56	5	425	17		0	1034	38	57	6	437
16	047346H	Rashida Khatoon	30	2	1049	99	53	4	423	14		1187	48	59	6	313	13		1	1240	87	57	4	386
17	301727F	Sudhamoy Mandal	66	1	1097	49	43	4	415	9	1	1089	42	48	3	377	18		1	1046	14	47	4	447
18	104790H	Hevanti Devi	49	2	1034	21	43	4	455	26	0	1010	37	43	3	496.9	23.5		1	1036	31	40	2	521
19	752562D	Penuel Barkos Oflyn Warjri	61	1	1085.9	85.9	51.6	5.4	467.7	36.6	0	1014	78.6	50.5	4.9	496.9	23.5		0	1038	58.1	51.9	5.6	528.5
20	093655D	Rizwan	28	1	1075.4	107.4	53.2	3.5			0	1003	53.9	51.6	3				0	995	35.6	50.6	2.8	
21	099139H	Ranajit Jana	48	1	1098	16	48	2	549	24	0	975	59	55	3	540	32		1	1143	47	52	3	535
22	607851F	Kishore Kumar Karmakar	61	1	1126	48	57	4	292	28	1	1107	73	63	2	310	15		1	1256	37	68	7	283
23	141920H	Minakshi Sinha Mahapatra	56	2	1057	39	52	2	315	27	0	1066	32	51	2	327	25		0	1096	25	46	2	296
24	161856H	Kameshwar Sah	59	0	1021	33	40	3			0	919	25	47	4				0	1000	19	50	5	
25	175573H	Mahboob Alam	31	1	861	61	45	4	NA	NA	0	894	42	46	2				0	893	39	47	4	
26	167975H	Nima Tshering Sherpa	49	1	1065	96	53	4	435	13	0	950	63	48	1	509	37		0	990	73	44	2	538
27	245540H	Prashuram Prasad	59	1	1105	48	57	2	267	13	0	905	71.5	51	2	305.5	22.9		0	950	36	54	2	296
28	202934C	Urmila Devi	44	2	1170	24	47	2	530	11	0	1014	37.8	48.7	3.6	525.3	14.7		0	1090	31	47	2	512
29	041973H	MD Toslim Uddin	46	1	1076	20	52	3	460	24	1	1064	26	58	2	461	16		0	1014	57	61	3	454
30	211061G	Jitendra Kumar	40	1	1132.3	48	47.6	5	415.8	35	1	1078	87	51.6	5	379.5	25	0.35	1	1083	73	51	3	392.7
31	115205H	Murugesan A	38	1	1038.8	103	44.6	5	492.5	43	1	1159	101	49.8	2	511	30	0.37	0	1015	71	48.2	5	525.9
32	672032G	E.G.Balakrishnan	70	1	1088.8	84	52.2	4	496.5	33	0	996.1	96	55.6	4	444.4	31	0.34	0	1078	64	50.9	4	458.2
33	083748H	Pranab Kumar Das	53	1	1082.2	47	53.9	4	258.4	13	1	1275	116	73.9	6	242.5	17	0.65	1	1061	34	55.4	3	385.6
34	121865H	Shayam Narayan Singh	48	1	1100.4	41	54.5	4	316.5	18	0	1140	79	55.1	6	315.2	22	0.32	0	1108	45	53.7	4	303.6
35	137689H	Pankaj Priya	39	1	1071.9	105	47.6	5	485.4	32	0	1118	24	57.1	1	478.2	27	0.32	1	1047	76	51.9	3	491.3
36	274649	Mariamma	75	2	946	71	56	4	301.6	24	0	1046	55	50.6	3	322.9	27	0.31	0	1117	60	51.4	4	332.5
37	790890F	Raghunandan Barnwal	65	1	1068.4	53	54.7	4	530.4	27	0	1034	51	48	3	527	23	0.32	0	1016	42	45.9	4	558.9
38	169180H	Renukadebi Dhakal	49	1	1129.9	72	55.9	3	350.8	32	0	963.2	49	52.1	4	384.2	31	0.26	0	1026	86	49.1	4	368.9
39	046133H	Arun Kanrar	39	1	1045	29	47.1	2	572.8	51	0	1064	38	47	2	502	20	0.29	0	996	23	44.6	1	467.1
40	104549H	Abu Nayem	46	1	819	31	43	5	585	9	0	980	11	53	3	588	9	0.27	0	941	30	50	4	578
41	865493D	Suriya Begum M.	65	1	1208	63	54	5	536	30	0	1042	54	55	4	556	21	0.33	0	1119	69	51	5	580
42	597346G	Chandra Deo Pal	65	1	1031	50	50	4	413	26	0	958	76	53	2	389	30	0.23	0	1039	49	45	4	385
43	439741G	Nirmala J	61	2	1219	75	74	2	479	39	0	1218	34	56	2	538	36	0.31	0	1230	41	58	3	544
44	606688G	Kuppuswamy P	61	1	966	59	49	49	552	20	0	1163	32	52	4	361	5	0.86	0	1148	44	51	4	317
45	014901G	Birendra Nath Mahto	40	1	1177	98	60	60			1	913	92	53	2				1	1016	40	53	3	
46	210047H	Yaseera Hamed K.	22	1	1009	75	52	52	535	22	0	994	65	46	4	555	27	0.29	0	1120	61	53	3	562
47	156117H	Ram Bihari Sah	60	1	1089	48	49	49	512	21	0	1015	72	52	2	502	21	0.29	0	1095	45	45	2	506
48	118111H	Satyabrata Ganguly	71	1	1075	50	54	54	504	12	1	1140	33	57	2	466	21	0.36	1	1075	37	55	3	498
49	236288H	MD Ruhul Amin	36	1	1100	114	52	52	273	22	1	1028	79	56	6	208	27		1	1026	90	52	5	211
50	161105H	Subrata Mandal	46	1	1033	26	47	47	452	23	0	1070	33	48	3	380	18	0.21	0	1083	33	46	3	390
51	152778H	Dipak Kumar Jana	50	1	1038	24	49	49	333	32	0	1085	53	52.1	4	340.8	12	0.28	0	1102	40	49	4	328
52	248783H	Rexona Azam	44	2	1108	69	49	49	348	24	0	1034	56	50.9	1	383.2	26	0.27	0	1056	51	53	2	374
53	191312H	Tapan Ghosh	42	1	1063	50	50	50	541	24	0	1048	49	52.7	4	538.3	20	0.26	0	1030	44	52	3	538
54	237891H	Alexander R Marak	40	1	1047	85	50	50	471	22	0	1019	66	46.3	4	455.4	26	0.26	0	1040	50	47	4	456
55	244586H	Priya C	19	2	1090	54	54	54	397	11	0	1110	46	61.5	4	451.1	26	0.32	0	1138	52	56	7	419
56	602176G	Gajan Gorai	52	1	1066	31	56	56	556	22	0	1046	9	55.3	2	597.4	11	0.26	0	1008	21	52	3	609
57	241030H	Rajiv Kumar Bhagat	38	1	997	92	52	52	339	29	0	1006	44	57	6	316.6	22	0.25	0	1034	47	51	4	305
58	589361G	Thilagavathi V.	54	1	1084	82	42	42	475.4	41	0	1107	65	46.9	4	387	14		0	1092	55	47.8	4	453.8
59	408743D	Amrik Singh	64	1	1105	61	59	59			1	1075	99	56.4	3				1	1162	48	54.4	4	
60	229890H	Santosh Kumar Mehta	24	1	1122	70	54	54	498	31	0	1094	73	52.2	2	550.7	15	0.31	0	1121	65	51	2	576
61	143256H	Dhaneswari Devi	56	2	1148	54	52	52	331	26	0	1005	66	49.4	6	343.5	26		0	1013	79	50	4	355
62	684638D	Sarat Sharma	51	1	1071	68	54	54	259	23	0	1059	35	53.3	2	284	29		0	1064	62	52	4	280
63	876100B	Rabindranath Manna	53	1	1176	57	50	50	588	21	1	1064	47	54.9	2	581.4	35		1	1055	44	52	4	589
64	233876H	Uday Chandra Laskar	58	1	1088	47	63	63	460	22	1	1100	37	63.7	3	435.5	24		1	1131	49	63	6	461
65	903651G	Sourav Mukherjee	23	1	1115	75	48	48	570	24	0	1108	42	52.4	3	561.7	45	0.31	0	1040	73	48	5	600

t1gassd	asecv	aslge	t1ai	t1aisd	t2ai	t2aisd	t1gai	tigaisd	aiecv	ailge	t1al	t1alsd	t2al	t2alsd	t1gal	t1galsd	alecv	allge	t1mas	t1massd	t2mas	t2massd	t1gmas	t1gmassd	masecv
32		0	1188	76.1	47.9	6.4	381.9	25		0	1138.1	101	49	8	397.8	33		0	1112.8	64	49.7	8	358.6	19	
25.9		0	1041.6	59.9	39.8	4.8	559.2	49		1	1011.2	72	47.1	7	659.8	285		0	1032.4	45	49.2	8	563.3	37	
		0	1100.9	83.8	49.5	5.7				0	1167.6	91	58.4	9				0	1109	113	48.9	8			
33.9		0	988.3	57.8	50.8	6.5	525.9	22		0	1020.3	73	52.1	4	499.9	24		0	1073.8	90	54.6	7	478	33	
9.5		1	1302.8	35	52.3	3.9	472.8	10		1	1250	67	55	5	480.9	12		1	1218.5	66	53.4	5	515	10	
23.6		0	1440.5	148	45.5	10	550.6	26		0	1225.4	141	61.4	10	529.7	28		0	1165.5	71	63.8	7	529	17	
33		0	1123.2	75.2	53.8	5.7	431	30		0	1094	91	59.8	10	454	25		0	1177	62	66.7	4	387.6	23	
51		0	1145.2	76.2	49.2	7.2	464.2	30		0	1044.2	87	49.2	5	464.7	23		0	1061.4	89	55.7	9	446.4	27	
26.8		0	1116.8	65.8	52.8	8.4	438.5	28		0	1074.6	93	50.4	8	430.5	46		0	1060.4	88	50.7	7	438.1	34	
		0	1010.1	63.9	45.7	5.1				0	978.3	55	50	6				0	970.1	72	51.6	10			
24		0	1118.5	65.4	49.8	4.7	441.9	28		0	1134.7	90	50.2	7	476.6	32		0	1135	49	51.6	4	483.1	19	
		0	1085.9	57	49.7	6.4				0	1114.6	90	51.7	6				0	1027.7	87	49.4	8			
		0	1062.1	71.9	52.8	4.1				0	1043.6	49	54.6	7				0	1161.8	58	52.5	7			
29		0	1108	48	51	5	452	27		0	1100	52	50	3	477	31		0	1262	99	51	5	501	26	
23		0	1153	8	44	3	389	13		1	1244	64	58	1	379	8		1	1009	38	53	5	451	20	
18		1	1117	73	54	5	432	8		0	1093	50	49	3	273	4		1	1022	51	50	4	425	29	
11		1	1085	14	47	3	393	9		1	1138	39	46	3	457	10		1	1117	37	48	3	338	25	
17		0	1072	36	42	1	507	15		0	1079	47	43	2	487	23		1	1054	22	44	3	481	24	
25.8		0	1063.8	72	50.5	4.8	502.7	28		0	1016	86	55	5	526.3	40		0	1044.4	69	41.1	4	504.4	34	
		0	989.6	51.9	49.9	2.5				0	949	49	53	5				0	1033.7	43	48.8	2			
27		1	1054	48	51	2	546	26		0	1049	33	52	2	525	24		1	1053	42	51	3	525	20	
9		1	1215	47	58	5	302	12		1	1100	78	66	3	319	14		1	1239	73	67	7	316	20	
12		1	1095	16	46	2	353	20		0	1036	19	48	3	331	10		0	1027	19	51	4	247	25	
		0	1030	36	48	1				0	934	21	49	2				0	953	26	44	3			
		0	887	31	47	4				0	889.4	29	46	3				0	904	27	44	3			
29		0	984	39	50	3	533	40		0	1032	80	57	5	531	37		0	948	58	46	3	512	27	
21		0	901.8	69	55.9	5	294.3	19		0	932	59	56	1	301	17		0	1013	41	67	6	256	21	
16		0	1089.3	69	45.8	4	479.4	26		0	1135	27	46	1	478	31		0	1155	72	49	5	468	18	
15		0	1046	42	60	3	445	20		0	1032	21	59	3	443	16		0	1090	49	50	4	424	21	
38	0.33	1	1064.7	87	52.4	4	389.4	37	0.34	1	1046.7	92	50.7	5	354.8	33	0.38	1	1068.7	39	51	3	373.9	28	0.34
24	0.31	0	1167.5	72	46.9	4	545	34	0.33	0	1184.9	104	48.6	3	509.1	35	0.38	0	1098.1	67	46.5	4	532.5	24	0.32
29	0.34	0	1159.5	55	50.3	5	492.2	31	0.32	0	1090.7	93	50.9	4	458.9	21	0.34	0	1111	63	57.1	6	451.4	28	0.34
16	0.32	1	1226.9	56	66.4	4	229.1	12	0.69	1	1063.8	48	52.2	4	425	20	0.27	0	1205.5	86	52.6	4	289.2	10	0.48
21	0.34	0	1191.1	73	46.5	5	317.4	31	0.32	0	1183.7	77	54.9	6	325.9	20	0.31	0	1090.6	60	44.4	5	305.4	17	0.31
27	0.29	1	1079.5	71	54	3	497.8	29	0.29	1	1223.2	38	57.1	3	470.1	30	0.35	1	1067.8	59	51.7	4	447.8	29	0.31
29	0.3	0	1037.9	66	47.2	4	361.1	35	0.26	0	1027.8	50	49.5	3	349.3	24	0.27	0	1141.1	61	46.5	5	339	24	0.31
18	0.28	0	1005.9	40	50.7	4	547.1	22	0.29	0	1064.4	96	49.9	5	514.9	18	0.35	0	1012.6	55	51	5	592.5	20	0.25
4	0.29	0	1013.2	64	45.3	4	380.7	25	0.28	0	1060.5	95	48.5	4	386.2	32	0.28	0	906.6	72	47	5	314.1	24	0.34
6	0.31	1	1059.8	18	46.5	2	509	10	0.28	0	1046.2	41	46.7	2	522.7	37	0.26	0	974	26	40.2	3	493.8	14	0.29
7	0.27	0	931	21	56	3	582	13	0.26	0	971	14	53	3	578	19	0.28	0	972	44	51	4	634	13	0.22
21	0.32	0	1127	62	50	5	571	25	0.34	0	1053	71	56	4	549	26	0.34	0	1112	62	48	5	569	29	0.34
26	0.25	0	957	79	48	3	380	21	0.24	0	950	58	52	3	380	19	0.24	0	1036	56	51	5	373	31	0.26
24	0.31	0	1253	68	59	4	491	22	0.37	0	1249	99	61	3	496	40	0.36	0	1141	57	59	4	507	25	0.32
23	1.03	0	1128	27	52	4	349	25	0.9	0	1046	17	54	3	382	21	0.75	0	1074	71	56	3	548	17	0.36
		1	1061	22	51	5				1	946	87	60	2				1	1048	38	45	3			
22	0.32	0	1103	39	49	3	560	26	0.32	0	977	15	52	4	505	22	0.34	0	1026	59	46	5	576	17	0.27
17	0.31	0	1084	64	44	2	503	22	0.31	0	989	89	53	2	505	25	0.28	0	1033	74	46	2	518	32	0.28
19	0.3	1	1113	40	57	4	511	10	0.3	1	1149	24	56	3	465	31	0.36	1	1085	39	57	2	472	29	0.33
23		1	1045	70	42	6	201	19		1	1044	88	48	4	201	23		0	1146	63	43	4	206	18	
16	0.21	0	1084	44	47	4	409	22	0.19	0	1080	31	48	2	390	21	0.21	0	1058	28	46	2	382	15	0.22
15	0.3	1	1075.3	87	50.5	3	352.8	20	0.27	0	1022	97	52	5	347	21	0.27	0	1068	42	52	4	323	26	0.25
32	0.28	0	1066.7	74	50.5	3	373	29	0.28	0	1101	82	51	2	357	18	0.31	0	1053	37	49	3	350	29	0.27
14	0.25	0	1045.8	38	51.9	4	542	19	0.26	0	1045	36	49	5	530	21	0.27	1	1042	37	52	4	530	14	0.26
21	0.27	0	1116.3	67	44.7	4	489.4	32	0.25	0	1016	94	47	2	469	33	0.25	0	1063	37	48	3	462	24	0.27
20	0.37	0	1161.2	44	60.7	5	429.6	16	0.36	0	1162	74	60	4	441	21	0.35	0	1095	46	52	5	367	18	0.43
11	0.24	0	1062.8	35	51.5	2	658.1	21	0.21	0	1092	13	52	2	613	17	0.26	0	1182	37	51	2	571	13	0.33
22	0.27	0	1006.2	78	43.5	5	338.3	20	0.23	0	1048	79	41	3	322	20	0.25	0	1016	50	46	5	324	14	0.21
22		0	1086.5	47	46.5	2	472.6	14		0	1084.1	59	45.8	3	452	19		0	1010.8	58	43.6	2	460.4	14	
		1	1133	37	49.6	3				1	1171.7	71	55.3	3				1	1137.7	47	52.7	4			
19	0.29	0	1089.2	37	53.8	4	551.1	26	0.31	0	1080	55	53	3	549	23	0.3	0	1079	27	50	3	577	15	0.28
34		0	1027.2	74	47.3	4	400	22		0	1003	65	50	5	375	38		0	1022	61	48	4	336	29	
27		0	1070.1	50	47.4	4	304.7	28		0	1096	58	54	6	291	19		0	1007	59	48	2	268	17	
30		0	1094.9	93	52.1	4	544.9	24		0	1142	48	56	3	548	32		1	1085	53	52	2	607	23	
21		1	1145.7	31	62	3	457.4	15		1	1146	37	66	3	436	21		1	1118	60	59	4	480	17	
26	0.25	0	1034.3	56	48.2	4	578.4	18	0.27	0	1111	59	52	3	561	29	0.31	0	1044	78	51	5	613	20	0.23

maslge	t1ma	t1masd	t2ma	t2masd	t1gma	t1gmasd	maecv	malge	t1mal	t1malsd	t2mal	t2malsd	t1gmal	t1gmalsd	malecv	mallge	t1mil	t1milsd	t2mil	t2milsd	t1gmil	t1gmilsd	milecv	millge	t1mi
0	1106.4	95	49.4	10	391.3	38		0	1139.4	108	50.6	9	397.3	27		0	1038.5	95	50.3	10	406.2	35		0	1111.2
0	930.6	220	45.1	6	668.3	107		0	1042.7	78	44.6	5	597.6	49		0	1030.9	77	47.9	8	565.3	47		0	1176
0	1014.6	130	50.6	8				0	1190.8	104	50.8	6				0	1201	75	53.6	7				0	1163.7
0	1052.5	91	52.3	7	502	27		0	1023	65	51.7	9	513.4	25		0	1025.2	57	54.7	9	504.1	27		0	1070.8
1	1250.3	78	55.9	6	506	12		1	1236.7	75	53.1	4	505	13		1	1224.6	63	51.7	4	507	14		1	1237.5
0	1064.5	179	61.8	8	534.9	37		0	1088.2	122	60.9	10	538	20		0	1117.7	135	67.3	10	572.6	45		0	1189.9
1	1153.5	98	65.6	5	328	19		1	1078.2	74	56.6	7	465.5	34		0	1058.3	75	57.5	13	461.5	29		0	1192.8
0	898.2	120	55.6	4	457.4	31		0	969.8	121	51.8	4	459.8	33		0	1116.4	90	49.1	5	469.1	29		0	1224.2
0	1036.3	53	46.8	4	461.8	36		0	1049.4	71	52.3	6	436.6	28		0	1048.3	68	54.5	7	409.9	39		0	1091.3
0	985.5	91	51.4	8				0	982.3	65	53.2	7				0	964.9	81	48.6	6				0	1004.9
0	1109.6	72	52.4	4	521.7	38		0	1083.8	57	51.4	4	522.6	32		0	1126.3	55	50.1	4	535.1	23		0	1132.8
0	1017.5	46	48.6	9				0	1001.5	80	47.1	5				0	1085.9	68	49.3	7				0	1056.2
0	1074.7	68	55.2	6				0	1058.3	61	54.7	6				0	1062.1	52.4	53.6	6				0	1200.6
0	1099	49	52	5	508	30		0	1093	58	50	4	496	21		0	1068	54	53	4	471	22		0	1088
0	1236	68	54.1	4	385	5		0	1286	36	62.6	6	364	7		1	1294	75	77.6	7	380	13		1	1147
1	1024	72	50	5	306	32		1	1013	52	52	4	397	33		1	1044	50	48	3	411	23		1	1073
1	1083	43	47	4	368	33		1	1147	45	48	4	358	28		1	1103	35	48	3	360	21		1	1208
0	1020	40	42±1.3	1	488.8	14		1	1055	33	43	2	481	17		1	1034	30	42	2	507	22		0	1069
0	1023.4	57	44.9	3	527.6	29		0	979.2	63	48.8	5	518.7	25		0	1066	84	49.7	4	514	29		0	1041.7
0	1027.2	37	49.3	4				0	1014.6	27	50.9	3				0	1042.1	68	49.6	4				0	1016.2
1	1030	59	50	2	525	35		1	1012	47	50	3	555	22		0	1010	70	52	3	530	26		0	1079
1	1164	31	53	3	316.4	12		1	1083	57	52	5	389	24		1	1094	48	51	4	419	20		1	1183
1	1035	28	46	4	292	13		0	1043	10	47	4	313	22		0	1095	60	48	3	328	21		0	1091
0	949	22	49	3				0	1022	48	50	2				0	988	27	45	2				0	1108
0	881	29	43	3				0	898	30	46	2				0	883	32	44	2				0	883
0	929	42	44	2	540	27		0	947	55	50	2	535	31		0	999	47	53	3	543	36		0	998
0	937	63	53	4	279	19		0	996	77	54	3	288	23		0	997	67	50	6	266	27		0	1059
0	986	46	46	1	512	23		0	1092	74	45	3	504	18		0	1081	59	46	2	449	13		0	1024
0	1023	82	46	4	447	26		0	991	37	49	3	436	30		0	1011	25	47	4	437	24		0	1046
1	1084.6	59	53.5	3	332	30	0.41	1	1060.6	64	54.4	6	353.2	28	0.37	1	1045.6	79	50.8	6	381.7	38	0.33	1	1058.4
0	1042.8	80	47.3	4	532.7	34	0.31	0	1106.7	87	48.5	3	550.7	36	0.3	0	1133.5	79	45.3	4	509.5	24	0.36	0	1102
0	1015.8	66	52.9	3	459.1	24	0.31	0	1037.5	55	56.5	5	459.2	20	0.31	0	1072.5	73	55.7	6	468.2	29	0.31	0	1013.1
1	1053.1	35	54	3	390	22	0.29	1	1059	60	51.2	4	437	26	0.25	0	1073.4	43	50.8	4	439.6	26	0.24	0	1220.8
0	1024	44	46.3	3	321	16	0.28	0	1038.5	45	47.9	3	323.3	18	0.28	0	1071.7	53	46.4	4	328.8	23	0.28	0	1150.9
1	1195.5	42	51.6	3	463.9	21	0.31	1	1054.8	81	51.2	3	445.2	42	0.31	1	1033.2	68	50.3	4	443.7	35	0.31	1	1071.6
0	1105.6	72	43.7	3	367.4	28	0.27	0	1050.1	34	48.8	5	378.2	19	0.25	0	1063.9	37	51	5	362.3	29	0.27	0	1072.4
0	1048	91	50.3	5	574.5	25	0.28	0	1058.4	72	55.5	3	559.2	29	0.3	0	1038.1	77	52	4	533.6	23	0.33	0	1057.2
0	859.8	75	44.4	4	306	19	0.34	0	981.6	51	45	3	299.7	21	0.38	0	993.7	43	41	3	297.4	17	0.38	0	996.8
1	945.8	32	50	1	526.3	15	0.24	0	931.4	26	51.4	2	532.4	18	0.23	0	913.4	39	49.8	2	534.8	23	0.22	0	1011
0	969	29	51	1	601	12	0.25	0	1047	25	51	4	614	25	0.27	0	1010	26	52	3	591	21	0.28	0	952
0	1030	54	51	4	574	28	0.3	0	1053	64	42	5	556	26	0.34	0	1132	37	50	4	567	37	0.35	0	1036
1	1005	74	53	3	381	36	0.25	0	985.2	49	52	4	401	21	0.22	0	995	52	46	4	400	28	0.23	0	973
0	1165	95	59	5	470.4	27	0.37	0	1148	55	59	4	518	25	0.31	0	1065	48	54	3	524	25	0.28	0	1110
0	1048	36	50	3	556	21	0.34	0	1023	56	52	3	554	18	0.35	0	1023	33	54	3	547	27	0.35	0	1248
1	1038	34	58	4				1	1009	34	57	2				1	1019	23	53	4				1	1047
0	965	79	49	2	568	21	0.26	0	1102	92	51	5	558	26	0.32	0	1080	92	45	4	569	34	0.3	0	1087
0	1003	70	50	3	484	39	0.31	0	999	54	49	2	508	23	0.28	0	1023	65	52	4	521	30	0.28	0	1047
1	1100.9	32	58	3	435	13	0.38	1	1116	30	59	3	438	28	0.38	1	1117	42	54	3	454	29	0.36	1	1075
1	1040	100	45	7	272	30		1	1046	74	48	5	298	28		1	1018	88	43	4	297	26		0	1112
1	1055	42	48	3	375	19	0.23	1	1025	30	46	3	372	19	0.23	1	1024	39	46	4	383	29	0.22	1	1045
1	985	83	49	3	349	27	0.21	0	1032	58	51	3	338	18	0.23	0	1053	55	50	3	336	30	0.23	0	1115
1	1058	54	49	3	361	20	0.26	1	1056	47	50	2	366	28	0.26	0	1061	56	55	3	317	31	0.32	0	1050
0	1016	42	51	2	530	24	0.25	0	1016	36	51	4	527	25	0.25	0	1044	39	51	3	540	29	0.25	0	1023
0	1093	79	46	3	506	26	0.23	0	1064	64	48	4	488	29	0.24	0	1038	64	48	5	497	34	0.23	0	1068
0	1117	71	52	6	450	43	0.32	0	1091	54	47	4	432	24	0.33	0	1050	41	50	4	446	25	0.31	0	1105
0	1049	32	52	2	590	14	0.27	0	1007	27	52	3	593	24	0.25	0	1089	27	52	2	618	24	0.25	0	1061
0	1024	58	46	3	325	23	0.21	0	1008	55	47	3	326	18	0.21	0	1023	50	49	5	322	25	0.21	0	997
0	1006.4	67	41	4	396.4	20		0	1000.6	70	42.1	1	427.8	9		0	996.6	63	43.7	4	417.8	14		0	1067
1	1115.6	64	52.6	5				1	1095.5	72	52.1	4				1	1110.6	78	55.7	6				1	1139.5
0	1059	42	51	2	561	23	0.29	0	1064	49	52	1	553	13	0.3	0	1075	42	54	4	560	17	0.29	0	1077
0	1056	63	51	4	348	30		0	1005	61	48	4	377	23		0	1025	53	49	5	388	36		0	1074
0	1013	62	44	4	290	27		0	1035	48	48	5	301	39		0	1055	65	49	3	267	29		0	1097
1	1182	55	54	4	551	17		0	1142	66	54	4	534	17		1	1166	59	53	4	546	17		1	1134
1	1103	34	58	3	479	17		1	1116	41	55	4	476	19		0	1114	44	51	4	483	21		0	1147
0	1034	72	51	5	603	37	0.24	0	1047	69	47	4	553	31	0.29	0	1108	84	47	5	525	25	0.34	1	1107

t1misd	t2mi	t2misd	tigmi	t1gmisd	miecv	milge	t1mis	t1missd	t2mis	t2missd	t1gmis	t1gmissd	misecv	mislge	t1bas	tibassd	t2bas	t2bassd	t1gbas	t1gbassd	basecv	baslge	t1ba	t1basd	t2ba
85	49.7	10	418	71		0	1098	71	50.3	10	389	32		0	1141.9	99	50.9	7	386.2	33.2		0	1202.2	82	50.6
121	46.9	7	563.1	32		0	1081.4	59	45.9	7	551	30		0	1030	30	50.9	9	489.8	51.4		0	1000	15	50.8
102	56.6	8				0	1157	79	51	8				0	1306.5	70	56.4	7				0	1218.1	65	56.4
66	53	8	488.8	36		0	1036.6	55	54.9	6	491	27		0	1041.9	52	52.8	6	481.2	35		0	1021	51	52.7
59	52.4	4	5519.9	16		1	1212.4	50	50.9	4	514.1	16		1	1241.2	57	56.6	13	467.7	12		1	1269.5	82	53.9
115	57.1	11	544.5	32		0	1184.3	75	59.5	8	547.7	18		0	1174.2	77	66.8	11	555.8	54		0	1048.8	156	76.6
80	60.6	12	418.4	31		0	1161	73	58.4	5	414.1	26		1	1326.7	62	60.2	8	388.2	29		1	1332.9	90	61.7
68	53.1	6	429.2	43		0	1122.8	76	53.3	5	457.5	20		0	1073.6	70	48.3	8	405.6	17		0	1050.5	62	52.2
56	51.6	7	454.3	29		0	1083.6±	66	52.6	11	425.2	27		0	1103.6	68	52.5	8	392.4	39		0	1064.6	80	51.6
92	47.1	8				0	984.4	49	48.3	7				0	1054.3	93	48.3	5				0	1096.2	82	49.4
52	49.7	4	502.6	23		0	1140.3	58	50.2	5	500.8	23		0	1166.8	57	51.9	4	472.2	22		0	1143.5	67	54.5
64	48.6	5				0	1058.2	56	47	4				0	1087.5	93	44.1	6				0	1138.6	83	47.7
100	50	4				0	1279.3	58	53.7	5				0	1125.7	86	52.4	8				0	1053.7	56	53.4
52	49	4	527	27		0	1201	98	52	5	504	26		0	1157	50	53	5	450	33		1	1105	37	51
83	47.9	3	386	10		1	1030.8	54	50	4	435	28		0	1029	47	49	4	441	21		0	925	65	48
61	55	3	401	25		1	1164	21	78	4	398	23		1	1100	59	46	2	400	17		1	1088	57	55
30	47	3	354	22		1	1136	24	48	2	338	11		1	1221	43	51	1	450	16		1	1115	53	48
33	41	1	515	15		0	1103	30	43	2	502	11		0	1045	49	42	2	401	14		0	1066	40	40
75	46.2	4	511.2	30		0	1052.1	50	46	4	497.6	29		0	1077.4	74	46.3	5	476.6	37		0	1059.9	67	49.8
59	49.8	4				0	1045.3	51	48.8	2				0	989.3	55	49.7	2				0	1199.4	92	51.1
58	51	3	535	24		0	1081	37	50	3	532	28		1	1117	45	56	3	503	21		1	1099	70	56
40	55	1	332	14		1	1134	44	55	5	267	24		1	1211	79	57	3	288	14		1	1066	43	51
39	48	3	336	27		0	1099	18	50	4	257	16		1	1104	52	55	6	284	15		1	1112	58	45
66	47	2				0	1028	15	45	1				0	1008	36	45	2				0	990	93	48
39	45	4				0	888	40	43	2				0	879	43	45	4				0	881	31	47
38	49	3	537	30		0	977	46	46	4	529	31		0	934	59	48	5	504	27		1	929	57	47
67	48	3	242	23		0	1055	47	56	6	256	20		0	984	51	51	7	246	18		0	917	63	50
66	46	2	510	30		0	1134	47	45	1	507	18		0	1087	51	56	3	496	23		0	1123	63	43
49	47	3	454	25		0	1077	29	50	3	421	22		0	1018	48	46	4	434	23		0	1028	42	50
60	52.4	5	354.6	28	0.37	1	1107.6	52	50.8	4	340.2	31	0.38	1	1140.8	81	49.4	5	349.6	29	0.37	1	1137.2	57	48.2
61	48.1	5	531.2	29	0.32	0	1054.1	42	45.8	2	540	18	0.3	0	1049	50	43.1	5	548.4	55	0.28	0	1000.1	56	44.1
99	54.8	5	469.9	38	0.3	1	10880.1	43	53.3	5	447.9	29	0.34	0	1105.4	67	56.5	7	417.2	33	0.38	0	1098.8	76	57.6
58	57.7	3	249.2	18	0.58	0	1068.4	27	52.2	3	419	20	0.26	1	1043.6	47	53	2	316	12	0.38	1	1058.1	41	52.2
87	44.5	5	292.2	30	0.33	0	1105.4	44	45.8	3	321.6	16	0.29	0	1027.3	53	44.8	5	268.2	27	0.26	0	1030.2	66	45.9
71	51.3	4	445.4	35	0.31	1	1071.5	59	51.7	4	447.8	29	0.31	1	1049.6	42	51.1	4	465.5	22	0.28	1	1219.8	55	61.4
60	50	4	373.3	30	0.26	0	1129	82	49.8	5	384.8	19	0.25	0	1136.8	83	50.8	5	323.6	33	0.29	0	1141.1	77	54.5
82	49.5	4	571.7	28	0.29	0	1022	54	48.7	4	602.3	17	0.24	0	1105.2	59	50.9	5	530	20	0.34	0	1084.1	56	51.6
42	44.2	3	354.4	35	0.29	0	997.4	55	42.9	4	335.6	24	0.32	0	1013.7	39	45.1	5	393.7	22	0.27	0	1035.2	49	43.8
24	47.9	2	549.1	8	0.24	0	967.6	20	47.4	4	541.4	28	0.23	1	1009.1	46	44.6	3	523.5	19	0.26	1	910.4	78	45.1
43	51	2	620	19	0.23	0	935	14	48	2	606	15	0.23	0	1029	51	49	3	597	28	0.28	0	1028	31	48
43	50	4	560	27	0.32	0	1111	60	52	5	549	30	0.37	0	1141	37	57	6	532	25	0.39	0	1122	68	47
78	49	4	392	32	0.23	0	1007	41	48	4	395	19	0.23	1	1099	68	53	5	384	37	0.25	1	1099	82	48
64	51	4	507	20	0.31	0	1123	37	53	3	504	25	0.32	0	1278	26	48	5	522	38	0.34	0	1035	61	50
48	50	2	548.4	27	0.41	0	1030	47	52	2	562	19	0.33	0	1052	58	47	5	533	20	0.38	0	1017	54	49
39	54	2				1	1073	24	51	4				1	1018	56	44	5				1	984	52	49
64	55	4	543	25	0.33	0	1058.3	64	45	5	582	23	0.28	0	1058	65	47	3	530	39	0.33	0	1023	47	44
51	45	3	541	26	0.26	0	1043	60	45	2	544	32	0.26	0	1004	80	41	4	530	34	0.25	0	977	53	47
44	52	4	479	30	0.32	1	1088	34	55	3	480	23	0.32	1	1183	48	50	2	477	12	0.35	1	1077	59	51
89	46	6	260	29		0	1079	82	47	5	222	24		1	1089	106	47	7	200	20		1	1162	114	49
46	46	2	370	31	0.23	1	1057	35	46	2	375	26	0.23	1	1050	36	45	3	372	22	0.17	1	1054	38	47
37	52	4	324	29	0.25	0	1121	45	52	4	320	30	0.26	1	1111	39	55	5	357	22	0.22	1	1079	96	54
56	53	4	334	27	0.29	0	1055	46	51	4	341	28	0.29	0	1043	43	49	3	346	22	0.27	0	1042	37	50
47	50	3	520	27	0.26	0	1014	30	51	2	533	16	0.25	0	1072	81	50	4	516	31	0.27	0	1087	75	48
44	45	4	468	34	0.27	0	1059	42	48	3	477	14	0.25	0	1036	57	49	4	442	24	0.29	0	1006	71	48
78	46	5	442	30	0.32	0	1085	47	45	2	413	27	0.36	0	1124	51	49	4	431	20	0.33	0	1181	115	48
78	49	3	612	30	0.25	0	1068	29	53	2	599	15	0.26	0	1153	77	55	2	546	21	0.33	0	1108	32	51
70	48	2	330	32	0.2	0	1002	32	48	2	336	18	0.2	0	1023	70	45	5	336	38	0.17	0	968	70	45
64	45.5	2	411.6	17		0	1085.4	49	42.6	2	444	7		0	1095.6	79	46.9	2	442	14		0	1081.8	64	51.2
35	51	5				1	1135.8	42	50.2	4				1	1064.5	39	50.5	5				1	1079.1	61	51
42	51	4	569	15	0.28	0	1103	29	50	3	569	18	0.29	0	1065	33	52	3	563	25	0.26	1	1059	39	55
54	51	4	369	29		0	1053	44	49	5	356	21		0	1131	98	47	5	299	28		0	1047	43	48
52	47	5	270	22		0	1077	57	49	3	266	17		0	1018	79	45	5	265	29		0	987	75	50
66	55	4	560	19		1	1098	42	52	4	607	23		0	1068	49	53	4	579	25		0	1059	46	55
54	55	3	480	17		1	1162	33	57	4	473	24		1	1134	52	56	3	503	26		1	1103	39	56
66	46	4	584	35	0.28	0	1032	50	45	3	617	18	0.22	0	1062	93	45	4	587	35	0.26	0	1050	99	44

t2basd	t1gba	t1gbasd	baecv	balge	t1bal	t1balsd	t2bal	t2balsd	t1gbal	t1gbalsd	balecv	ballge	t1bil	t1bilsd	t2bil	t2bilsd	t1gbil	t1gbilsd	bilecv	billge	t1bi	t1bisd	t2bi	t2bisd	t1gbi
11	393.9	33		0	1156.2	93	52.2	7	374.3	33		0	1177.6	97	51.7	7	367.1	22		0	1225.7	109	47.9	14	393
8	578.4	118		0	1040	40	53.4	8	521.6	91		0	1121.6	49	53.1	7	512.5	36		0	1011.3	93	47.2	5	565.1
9				0	1150.3	90	52.8	8				0	1139.1	77	53.6	6				0	1156	75	53	12	
4	501.1	36		0	1046.3	65	47.8	7	485.7	41		0	1039.5	47.3	53.5	12	479.8	32		0	1056.6	57	55.4	10	465.5
8	483.5	15		1	1272.3	102	53.5	100	478.4	16		1	1299.4	84	56.5	10	474.8	23		1	1263	67	57.2	11	484.2
14	556.8	52		0	1030.4	146	70.9	5	507.2	21		0	1173.4	79	70.5	14	481.1	21		0	1142.8	133	61.5	14	515.1
7	345	82		1	1069.9	66	56.7	9	437.3	34		0	1044.9	81	56.1	12	454.4	38		0	1138.7	103	57.3	11	422.4
7	432.2	39		0	1063.4	88	50.5	7	446.2	29		0	1084.3	62	48.6	8	443.7	24		0	1094.6	59	50.1	8	423.1
7	443.9	39		0	1042.9	51	48.9	8	423	29		0	1089.7	42	48.4	6	408	22		0	1100.9	72	49.1	6	430.6
7				0	981.6	97	46.2	7				0	983.8	61	45.1	9				0	1013.4	69	50.1	8	
4	520.7	44		0	1120.8	49	51.7	3	517.2	23		0	1154.2	62	50.9	4	520.3	24		0	1164.4	64	54.1	5	506.1
7				0	1131.6	83	52.5	6				0	1114.6	86	52.5	8				0	1092.4	70	49.5	7	
6				0	1058.7	76	53.7	6				0	1054.2	46	54.2	5				0	1096	90	50.7	5	
4	484	18		0	1133	89	47	5	481	30		1	1119	62	48	5	470	35		1	1158	65	50	4	483
5	421	22		0	1026	75	58	5	387	10		1	1070	104	58	6	388	18		1	1025	86	49	5	383
4	368	23		1	1159	76	49	4	389	14		1	1122	48	44	5	379	19		1	1139	51	55	4	409
2	450	16		1	1206	94	48	4	432	20		1	1034	60	46	4	421	14		1	1161	35	52	2	393
1	442	27		0	941	41	40	2	366	14		0	1010	9	44	2	465	30		0	1098	21	42	2	512
5	514.8	35		0	1010.2	57	48.5	5	527.2	30		0	1063.5	86	51	6	521.6	28		0	1041.7	70	45.9	4	527.2
4				0	1032.2	63	52.6	3				0	1005.3	58	52.1	3				0	1037.1	63	52	6	
3	538	24		1	1040	42	56	2	542	6		0	1040	57	56	5	523	39		0	1081	60	55	3	525
2	403	12		0	1081	48	50	2	499	24		0	1024	58	53	2	415	16		0	1373	91	58	4	240
3	265	16		0	1082	27	46	3	339	18		0	1086	39	45	3	333	17		0	1130	38	49	3	301
3				0	974	20	50	2				0	1023	38	47	2				0	1090	12	46	3	
3				0	867	30	48	3				0	949	41	55	2	NA	NA		1	887	31	46	3	
5	530	37		0	956	59	49	3	512	22		0	1004	58	48	4	511	32		0	980	47	47	4	506
4	256	17		0	990	48	55	6	263	20		0	1082	48	54	5	228	23		0	1066	46	57.5	6	236
2	424	15		0	1041	84	47	3	470	14		0	1100	59	53	3	462	19		0	1093	41	44	2	562
4	423	26		0	1002	46	47	3	426	20		0	1000	48	50	5	401	23		0	1061	70	44	3	407
4	354.2	26	0.36	1	1092.6	72	49	4	370.7	31	0.33	1	1103.2	87	47.4	5	392.1	34	0.3	0	1127.8	89	49.5	4	364.5
3	550.8	55	0.27	0	1000.4	60	44.4	4	518.5	31	0.3	0	1022.8	68	44.7	3	543.4	39	0.28	0	1023.6	86	43.6	4	548.7
6	484.1	42	0.3	0	1076.6	43	56	5	450.4	32	0.33	0	1083.6	80	60	6	448.6	23	0.34	0	1141.3	83	57	6	447.6
4	371.5	22	0.3	1	1032.5	64	46	4	412.7	35	0.23	0	1053.8	98	48.3	5	405.9	35	0.26	0	1186.5	63	54.7	4	317.4
4	276.1	29	0.25	0	1017.8	60	45.3	3	299	28	0.23	0	1054.7	63	44.9	5	289.8	28	0.24	0	1150.5	68	45.1	6	238.4
3	391	4	0.41	1	1062.2	74	53.5	4	436.8	34	0.32	1	1037.5	84	56.3	4	436.2	40	0.31	1	1136.4	87	55.2	6	409.3
5	332.8	30	0.28	0	1079	74	50.5	3	307.5	29	0.3	0	1064.1	45	51.3	4	325	27	0.28	0	1096.9	56	51.7	5	330.5
5	562.2	16	0.29	0	1015.9	55	47.9	4	535.6	27	0.3	0	1062.4	61	54.7	4	513.2	18	0.34	0	1126.5	106	55.4	5	534
4	395	27	0.27	0	1058.8	77	42.3	3	412.7	31	0.26	0	1044.7	44	44.1	4	406.3	22	0.26	0	1046.2	44	44.2	5	396.7
2	529.6	13	0.22	0	983.7	51	47.2	2	539.1	29	0.24	0	996.1	48	40.2	2	520.7	18	0.26	0	1031.5	51	49.7	2	527.2
1	610	23	0.26	0	1002	88	45	3	596	39	0.27	0	1053	69	49	4	569	38	0.32	0	1042	45	49	2	575
4	562	25	0.35	0	1083	74	51	4	529	33	0.38	0	1108	91	40	4	534	27	0.38	0	1131	34	56	5	565
5	366	18	0.27	0	1043	75	44	5	360	25	0.27	0	1017	51	44	4	388	22	0.23	0	1010	66	45	5	367
4	529	26	0.28	0	1120	18	52	3	503	30	0.33	0	1183	41	50	3	515	27	0.33	0	1247	76	49	3	522
3	558	22	0.33	0	1022	27	49	2	563	22	0.32	0	1093	63	50	3	514	21	0.42	0	1077	74	51	3	532
1				1	969	97	52	4				1	816	90	43	2				1	1029	72	48	3	
2	580	55	0.26	0	998	80	44	2	470	42	0.39	0	1036	90	39	3	455	33	0.43	0	1074	90	43	3	549
2	529	30	0.25	0	1024	78	53	5	522	20	0.27	0	1026	50	52	1	521	27	0.27	0	1058.6	77	46	3	530
3	475	24	0.33	1	1038	38	52	2	470	14	0.32	1	1085	66	55	5	453	24	0.36	1	1141	48	54	6	459
5	248	27		1	974	77	44	4	269	30		1	1047	62	46	5	280	21		0	1127	72	45	5	249
3	383	115	0.17	1	1001	36	45	4	404	15	0.15	1	1032	53	45	4	390	20	0.16	1	1033	60	44	5	390
4	346	20	0.23	0	1021	78	51	3	350	30	0.22	0	1075	88	52	4	344	25	0.23	0	1127	47	52	3	325
3	344	20	0.27	0	1056	71	49	4	354	20	0.26	0	1077	65	52	4	298	24	0.34	0	1077	63	52	3	313
2	516	31	0.27	0	1088	53	49	3	519	25	0.27	0	1058	46	49	3	514	26	0.27	0	1068	43	51	5	524
2	488	25	0.24	0	979	5	47	3	464	31	0.25	0	1019	79	47	4	469	32	0.26	0	1038	99	49	5	452
5	423	42	0.36	0	1114	74	49	4	440	18	0.32	0	1099	49	54	4	424	26	0.34	0	1155	41	56	6	410
1	575	22	0.29	0	1077	16	52	5	632	26	0.23	0	1094	16	47	4	607	25	0.26	0	1195	77	56	3	600
4	330	22	0.17	0	1000	32	45	3	316	20	0.19	0	987	41	45	2	304	26	0.2	0	1028	45	47	3	310
3	484.8	18		0	1079.6	84	46.7	2	437.4	12		0	1078.2	87	45.6	5	428.2	17		0	1086.6	93	42.1	3	432.4
3				1	1120	66	49.6	5				1	1115	64	51.9	5				1	1124.9	42	50.6	3	
3	545	24	0.28	1	1041	35	54	3	542	22	0.28	0	1071	51	52	4	553	23	0.28	0	1099	47	53	4	563
4	352	34		0	1024	48	49	4	367	30		0	1044	64	48	5	374	34		0	1095	58	52	3	353
4	270	29		0	1012	47	47	4	284	24		0	1020	87	50	3	286	28		0	1050	95	47	3	275
4	564	25		1	1109	64	54	5	558	33		1	1110	74	51	5	577	27		1	1083	55	52	5	607
4	513	26		1	1073	52	54	4	539	26		0	1121	48	51	5	526	35		0	1076	61	52	6	495
4	599	26	0.23	0	1082	88	50	5	543	39	0.31	1	1087	70	49	5	552	22	0.3	1	1072	48	52	3	555

t1gbisd	biecv	bilge	t1bis	t1bissd	t2bis	t2bissd	t1gbis	t1gbissd	bisecv	bislge	tnslge	lgea	lgeb	lgec	lged	alvedv	ilvedv	alvesv	ilvesv	lvef	diagnosis
41		0	1188	101	51.7	9	376	37		0	0	0	0	0	0	240	137	195	112	19	1
56		0	1010.1	144	46.8	8	551.6	54		0	2	0	0	0	1	132.2	71	50.1	27	62.1	3
		0	1250.7	84	56.6	11				0	0	0	0	0	0	261.3	160	177.8	109	32	1
38		0	1036.9	73	53.6	8	474	33		0	0	0	0	0	0	76.9	41.2	25.5	13.7	66.8	2
19		1	1241.3	90	57.2	10	470.7	13		1	17	0	0	0	1	107	66	45	28	58	4
32		0	1186.6	66	66.9	15	532.2	24		0	0	0	0	0	0	246	125	193	98	21.5	1
33		1	1221.7	86	59.4	6	411.6	28		1	7	1	0	0	1	92.3	51.9	42.8	24	53.7	3
21		0	1045.1	54	45.5	4	409.9	20		0	0	0	0	0	0	183	99	126	68	31	1
25		0	1058.3	67	47.2	8	377.5	42		0	0	0	0	0	0	193.9	114.8	151.5	89.7	21.9	1
		0	1011.8	73	45.5	7				0	0	0	0	0	0	95	54	52.6	30	45	1
32		0	1134.7	51	51.6	4	492.8	24		0	0	1	0	0	0	132.1	84	84	53	38.3	1
		0	1131.3	78	45.5	7				0	0	0	0	0	0	151	105	97	68	36	1
		0	1092.4	77	49.3	6				0	0	0	0	0	0	189	126	113	76	40	1
28		0	1120	70	48	6	466	35		0	3	0	1	0	0	148	94	92	59	38	1
14		1	1022	67	47	4	435	16		0	8	0	1	0	1	266	170	223	142	16	1
21		1	1138	113	52	4	410	18		1	0	1	0	0	1	137	83	85	52	38	4
23		1	1118	26	48	1	439	9		1	17	0	0	0	1	87	46	50	27	43	4
36		0	1014	12	42	1	424	11		0	4	0	0	0	1	120	88	62	45	48	2
28		0	1028.9	83	45.9	5	518.3	39		0	0	0	0	0	0	208	115.6	112.4	62.3	46.1	1
		0	984.2	29	51.5	4				0	0	0	0	0	0	148.3	92.1	42.7	26.5	71.2	2
34		0	1109	37	55	2	510	32		1	9	1	0	0	0	132	74	49	27	63	2
25		0	1097	37	50	2	351	12		0	12	0	1	0	1	193	110	140	80	28	2
27		0	1087	15	44	4	291	13		1	5	1	0	0	0	197	139	150	106	24	1
		0	1020	24	47	2				0	0	0	0	0	0	253	139	193	106	23	1
		0	874	51	45	2				0	1	1	0	0	0	118	83	47	33	60	4
38		0	952	84	45	2	469	6		1	2	1	0	0	0	178	102	103	59	42	1
23		0	1138	71	57	5	229	23		0	0	0	0	0	0	298	197	229	152	23	1
44		0	1096	62	50	2	426	42		0	0	0	0	0	0	164	92	114	63	31	1
20		0	995	39	49	5	441	26		0	1	0	0	0	1	126	77	47	29	62	2
27	0.34	1	1092.7	71	45.8	4	373.4	34	0.33	1	17	1	0	0	0	187.8	88.7	35.2	18.2	79	2
29	0.28	0	977.9	50	42.9	4	560.9	40	0.25	0	1	0	0	0	1	94	52	30	17	68	4
24	0.35	0	1154.1	69	54.4	6	410.5	26	0.4	0	1	1	0	0	0	349	125	276	94	21	1
20	0.4	0	1067.8	55	52.3	5	382.1	25	0.29	1	10	1	0	0	0	157	97	68	43	56	1
30	0.32	0	1112.2	55	41	4	252.9	20	0.29	0	0	0	0	0	0	329	186.9	228.2	129.6	30.7	1
36	0.37	1	1020.7	56	53.9	5	460.3	27	0.28	1	16	1	0	0	0	249.8	112.8	115.9	52.3	54	2
25	0.28	0	1126	76	51.2	5	351.4	28	0.25	0	0	0	0	0	0	95	69.4	56.2	41.1	40.8	4
23	0.34	0	1102.6	76	50.3	6	556.3	22	0.3	0	0	0	0	0	0	163	87	75	40	67	1
27	0.27	0	1064.5	36	41.9	3	373.4	19	0.3	0	0	0	0	0	0	145	107	86	64	40	1
26	0.26	0	1034.7	42	41	1	545	29	0.25	1	5	1	0	0	0	270.8	147	166.4	90.3	38.8	1
41	0.31	0	1018	57	43	3	617	30	0.25	0	0	0	0	0	0	212	114	119	64	44	1
32	0.34	0	1190	55	50	3	544	19	0.39	0	0	0	0	0	0	201	102	140	71	30	1
27	0.25	0	1074	60	43	4	384	21	0.25	1	4	1	0	0	0	78	46	30	18	61	3
25	0.34	0	1273	37	48	4	480	30	0.39	0	0	0	0	0	0	160	108	94	63	42	4
26	0.39	0	1011	61	49	5	535	17	0.36	0	0	0	0	0	0	69	41	31	19	55	4
		1	1046	57	48	4				1	17	0	0	0	0	325	208	199	127	39	1
31	0.31	0	1049	92	35	4	556	29	0.3	0	0	0	0	0	0	170	83	102	50	40	1
22	0.27	0	1031	91	45	2	523	25	0.27	0	0	0	0	0	0	227	142	155	103	27	1
32	0.36	1	1045	30	50	2	457	24	0.34	1	17	1	0	0	0	103	63	38	23	63	2
26		0	1080	56	47	4	224	23		1	12	0	0	0	0	283	168	226	134	20	1
27	0.16	1	1079	40	45	3	391	20	0.16	1	12	1	0	0	0	134	75	46	26	66	2
29	0.26	0	1094	50	54	5	321	49	0.26	1	5	1	0	0	0	306	183	248	149	19	1
24	0.31	0	1068	58	46	5	330	28	0.29	0	2	1	0	0	0	124	74	42	25	66	2
29	0.26	0	1030	35	49	3	538	29	0.24	0	1	1	0	0	0	108	59	35	19	68	2
26	0.28	0	1133	40	50	3	454	31	0.3	0	0	0	0	0	0	244	145	180	107	26	1
19	0.37	0	1186	44	54	5	415	28	0.37	0	0	0	0	0	0	246	205	189	158	23	1
20	0.29	0	1039	17	46	2	634	44	0.21	0	0	0	0	0	0	204	132	126	81	38	1
17	0.19	0	1031	70	46	4	296	26	0.21	0	0	0	0	0	0	106	73	57	39	47	3
30		0	1062.1	65	43	3	474.2	11		0	0	0	0	0	0	171	100	134	78	21	1
		1	1081.6	33	49	4				1	17	1	0	1	0	105	70	44	30	58	4
24	0.27	0	1090	42	53	4	557	26	0.28	0	2	1	0	0	0	153	111	64	47	58	2
38		0	1060	94	51	5	320	32		0	0	0	0	0	0	144	96	66	58	40	1
29		0	1045	60	47	4	267	23		0	0	0	0	0	0	250	159	190	122	24	1
35		1	1081	34	50	3	615	22		0	11	1	0	0	0	199	107	91	49	54	2
34		0	1100	38	57	2	525	12		0	11	1	0	0	0	152	87	68	39	55	2
34	0.29	0	1025	70	45	3	586	42	0.25	0	3	0	1		0	119	69	55	32	54	3

66	157353H	Gulam Kadir Khan	50	1	1135	32	54	54	598	15	0	1046.8	80	53.6	3	612.9	39		0	1057	69	49	4	638
67	802374G	Hema Devi	63	2	1155	63	52	3	431	28	0	1061.2	52.6	51	4	399	21	0.32	0	1029	72	55	4	416
68	301399H	Munindra Baro	35	1	1110	50	51	2	440	21	0	974.7	83	54.6	4	426.2	16	0.34	0	1196	39	64	7	430
69	248460H	Subodh Kumar	40	1	1145	57	54	5	310	16	0	1142	79	50	3	301	33	0.33	0	1124	51	50	2	288
70	159165H	Debasish Mondal	45	1	1104	44	48	4	398	26	0	1027	39	50	2	455	17	0.29	1	1056	35	52	2	431
71	092341H	Tapan Kumar Maji	40	1	1010	79	49	5	443	14	0	1024	41	47	5	439	11	0.3	0	1085	73	48	4	459
72	131823G	Methilia Das	49	2	1106	73	48	4	485	30	0	962	76	53	5	454	25	0.32	0	1027	46	50	4	463
73	127131H	Pallabi Das	30	2	998	93	58	6	403	16	0	1072	58	59	4	417	27	0.33	0	1057	52	60	5	444
74	785829g	MD Neksar Ali	59	1	1029.5	193	63.8	7			0	982.8	100	57.8	5				0	1019.4	109	55.5	8	
75	950936g	Jayita Chakraborty	42	2	1143.3	110	68.9	9	441.6	54	0	1121.1	130	54.5	9	440.4	37		0	1233.3	100	53	7	420.6
76	882699g	Mowlana Aman Ullah	55	1	1157.7	108	63.6	6			0	953.8	73	54.4	7				0	1030.5	80	53.3	9	
77	868518g	MD Jalil Ahmed	36	1	971.4	86	58.4	7			0	946.9	47	48.3	5				0	973.9	64	51.1	9	
78	906083c	Rathna Kumari	45	2	1130.1	194	55.7	11			0	1167.6	192	60.6	6				0	1099	119	60	7	
79	905060D	Bhuvaneswari	39	2	1036.6	116	74.3	9			0	1121.4	96	54.9	4				0	1141	75	55.3	8	
80	791822c	Ravi S.	46	1	1144.1	110	51.4	9	536.9	31	0	931.3	89	54.5	7	548	28		0	1029.9	70	54.6	7	565
81	948090g	Amal Laha	50	1	1082.6	39	43	2	607.2	28	0	1004.1	49	45.3	5	583.5	32		0	1018.1	40	46.4	6	593.8
82	051627b	Gopal. A	42	1	1074.5	124	55.9	6	400.8	38	0	932.7	111	53.7	5	393.1	37		0	994.1	65	54.1	7	407.6
83	402551g	Saroj Maji	35	1	1023.5	62	51.7	9	474	20	0	921.1	49	49.4	5	525.1	25		0	976.1	52	48.3	8	528.8
84	418500D	Sounderarajan M	52	1	1084.8	101	54.3	10	592	58	0	937.5	52	55.7	9	621.2	30		0	981.7	83	54.7	12	644.1
85	511013C	Pachaiappan	42	1	1047.3	127	63.9	8	405.6	29	0	1021.6	97	52.7	7	462.4	42		0	1000.4	76	49.4	7	461.1
86	459915c	Yellamma	37	2	1030	28	52	5	521	30	0	1006.9	52	51.8	5	539.1	26		0	1027.7	78	51.9	8	565.9
87	783927c	Kavitha	37	2	1081.2	154	53	3	418.4	24	0	903.5	92	51.4	5	415.4	37		0	1062	75	55.1	9	445.1
99	763275g	Sankar Giri	28	1	1029.2	42	54.8	6			0	976.9	68	50.3	7				0	998.8	55	47.8	8	
89	570873c	Selvi	40	2	1135.4	85	57.1	10	385.8	34	0	1018.3	122	53.4	5	432.3	28		0	1107.8	54	53.8	8	454.8
90	979437g	Vallikannu R.M.	39	2	1063.8	162	69.1	10	433	32	0	1003.3	92	54.7	5	487.9	26		0	1071.7	87	53.6	9	508.1
91	035128C	Malarkodi	44	2	983.8	210	83.9	10			0	852.9	170	51.5	7				0	1086	84	56	13	
92	515469C	Bharathi	45	2	1050	50	59	14	465.1	69	0	1068.4	87	53.8	5	465.1	69		0	1099.8	73	58.8	12	486.3
93	914394D	Girija	41	2	1117.5	171	53.1	9	567.3	38	0	1028	72	49.6	6	554.9	42		0	1059.5	101	50.4	9	551.1
94	914385D	Premalatha	39	2	1070	80	49.9	18	470.9	27	0	985.2	116	59.3	12	484.7	39		0	1117.5	85	53.9	12	515.3
95	973249G	Kasthuri A	48	2	1020	18	59.5	16	490.2	65	0	1018.1	124	48.7	8	461.6	29		0	1054.8	85	47.8	11	446.2
96	866999A	Antonyswamy. J	60	1	980.9	155	63.7	11	455.8	32	0	1057.5	62	57.3	6	500.8	29		0	1065.5	89	56	6	505
97	707153G	Kousik Sahu	49	1	1060	80	67.9	28	359	30	0	1018.1	102	54.9	5	387.9	38		0	1072.6	100	59.3	13	427.3
98	953904G	Bibi Anjum	51	2	1107	110	47.4	7	474.6	76	0	1081.2	103	45.9	4	500.1	33		0	1117.4	89	49.6	11	457.2
99	014681H	Francis Xavier A	29	1	1185.7	148	56.4	5	534.1	38	0	1020.8	112	55.9	10	569.1	29		0	1067.2	89	55.3	11	576.8
100	329517B	Arulselvan D.	44	1	1104.6	182	51.1	8	536.6	36	0	973.9	98	48.3	8	564.1	34		0	1065.5	54	50.7	7	584.5
101	002510H	Preetam Lal Batra	53	1	1118.6	49	55.1	6			0	1153.1	103	55.9	6				0	1022.5	77	54.1	8	
102	022040G	Geetha M	33	2	1195	37	55	4	438	41	0	1170	35	60	6	438	17		0	1178	44	62	4	432
103	108300H	Muniyandi	42	1	1042	100	49	3	447	19	0	1049	89	50	4	498	32		0	1023	36	52	5	481
104	278652G	Anik Bhattacharjee	50	1	1057	32	50	5	585	35	0	1013	57	50	6	605	32		0	958	96	50	5	624
105	150197H	Momena Kabir Bithi	18	2	994	25	40	4	439	22	0	1055	45	53	5	476	17		0	1027	45	54	5	498
196	664495C	Boopathy V.	42	2	1061.3	105	59.7	5	422	33	0	1038.4	92	55.9	5	430.9	26	0.33	0	1033.6	72	49.5	4	457.6
107	881945D	Balu T.	60	1	1189.5	56	66.2	5.2	454	41	0	1021.2	78	56	6	514.4	38	0.35	0	1108.8	58	57	7	536.2
108	534706G	Sarabhu Moidu	51	1	1088.1	47	53.8	4	297.3	13	0	1240.7	99	49.1	3	307.1	24	0.36	0	1147.6	35	43.4	5	325.7
109	856580G	Joanna S	42	2	1018	21	52	5	489	40	0	1056	51	49	3	480	29	0.29	0	1045	62	43	4	468
110	274919C	Arjunan.P	57	1	1091	37	51	4	465	27	0	1014	31	41	4	401	18	0.36	0	945	20	42	4	436
111	052642C	Mohan I	62	1	973	69	48	5	441	29	0	920	37	50	4	428	31	0.24	0	969	41	47	3	436
112	541931B	Lakshmi	43	2	1132	26	51	3	238	14	0	1086	20	52	3	292	14	0.27	0	1098	33	49	3	265
113	126112F	Chinna Thai	41	2	1011	90	48	4	198	15	0	1049	48	53	1	230	7	0.23	0	1098	38	60	4	209
114	106896H	Shankari Das	62	2	1075	25	56	4	446	34	0	977	39	52	4	474	22	0.26	0	1015	50	49	2	481
115	143367H	Shanthi	56	2	1002	54	50	3	295	5	0	910	78	54	4	304	19		0	979	41	55	5	311
116	576720B	Rajathi M.	34	2	1093	42	55	2	440	20	0	1072	27	42	4	415	19	0.35	0	1048	62	48	3	432
117	168702H	Anil Kumar Sinha	53	1	979	36	49	4	483	32	0	1057	74	51	5	492	21	0.29	0	1018	25	56	4	533
118	216347H	Jukzang Dema	39	2	1058	78	52	3	505	17	0	1055	16	47	2	412.2	7	0.5	0	1085	36	53	5	490
119	218472H	Sonjoy Shil	20	1	1147	101	52	4	574	38	0	1011	25	50	1	506	24	0.28	0	997	38	51	5	527
120	492114D	Venkatesh.K	43	1	1023	67	49	3	510	15	0	1034	49	54	2	535	12	0.29	0	1005	21	52	3	523
121	599118G	Ravi	62	1	1082	64	50	4	413	15	0	1127	36	49	3	456	27	0.35	0	1130	52	53	3	458
122	951322B	Kasthuri.M	70	2	1018	48	53	4	433	27	0	1062	11	52	3	429	31	0.35	0	1050	55	51	4	455
123	020011H	Chittaranjan Mahato	70	1	1136	73	70	4	433	18	0	1021	47	61	3	445	20	0.37	0	1083	62	56	2	439
124	156032H	Raj Kumar Das	37	1	1030	57	50	3	448	16	0	1017	73	50	2	507	24	0.28	0	950	52	43	5	494
125	706283G	Revathi M	27	2	1016	89	51	17	413	13	0	1183	40	50	4	493	29	0.32	0	1180	56	58	4	498
126	220197H	Lavanya A.	38	2	1195	64	51	5	425	39	0	1043	63	54	2	450	16	0.31	0	1098	45	56	4	474
127	724462C	Mohanavel	37	1	1053	58	50	4	496	26	0	981	63	45.9	4	549	22	0.26	0	978	39	46	3	574
128	432402D	Muniyammal. B	48	2	955	99	55	6	425	15	0	1048.4	37	58.4	3	433.3	26	0.35	0	1049	59	59	6	452
129	680910A	Selvaraj.I	68	1	1052	72	38	3			0	1048	62	40	4				0	926	27	48	3	
130	750578B	John Thomas Prabhakaran D	46	1	1005	66	55	3	425	33	0	942	84	51.6	5	445.5	29	0.25	0	973	95	51	6	444
131	003717H	Rajiya Sultana	48	2	1113	39	50	1	468	29	0	992	70	54	2	461	22		0	1092	18	54	3	454

40		0	1117.6	53	55.1	4	653	35		0	1064	54	54	2	629	29		0	1058	45	61	3	631	21	
20	0.29	0	1136.7	63	59	4	418	28	0.3	0	1138	75	59	3	395	21	0.33	0	1147	74	55	5	399	22	0.33
23	0.38	0	1059.9	55	46.1	2	447.8	21	0.33	0	1140	31	60	6	449	15	0.35	0	1116	75	53	5	460	22	0.32
26	0.35	0	1036	49	62	5	270	16	0.37	0	1146	50	54	7	308	29	0.32	0	1028	52	48	5	359	23	0.23
25	0.27	0	1056	56	51	3	444	26	0.27	0	1045	54	55	6	430	20	0.27	0	1044	59	54	3	406	22	0.29
18	0.31	0	1079	81	47	4	432	24	0.33	0	1006	48	45	3	418	23	0.33	0	1024	61	47	5	524	21	0.21
33	0.32	0	1029	42	54	5	434	26	0.34	0	1034	34	53	4	450	30	0.32	0	1105	63	50	5	454	19	0.33
27	0.28	0	1098	46	55	4	445	29	0.35	0	1016	31	59	4	417	30	0.3	0	1097	46	54	4	404	24	0.36
		0	1032	71	52	6				0	1070.6	95	63.1	10				0	1065.7	87	56.7	11			
39		0	1107	108	56	11	411	32		0	1056.7	112	59.2	10	433.1	38		0	1111.5	97	62.5	11	382.8	18	
		0	1008.7	47	54.2	12				0	1032.6	77	56	11				0	1066.1	68	50.9	9			
		0	974.8	50	47.3	4				0	980.4	60	47.4	5				0	1021.3	59	49.7	7			
		0	1066	88	56.9	8				0	1059.2	108	62.1	13				0	1110.1	98	62.4	8			
		0	1114.9	55	50.2	5				0	1165.5	95	54.3	5				0	1162.8	70	55.8	7			
26		0	1024.2	81	50.4	5	563	30		0	969.2	93	46.9	5	561.1	30		0	1025.3	38	46.3	9	572.4	20	
30		0	1007.4	41	44	4	609	15		0	1022.3	76	41.2	6	606.4	23		0	1028.2	59	50.5	5	579.2	22	
17		0	950.2	85	53.1	9	453.7	30		0	1033.4	73	53.6	10	445.5	29		0	968.2	70	54.2	11	435.9	43	
29		0	1154.4	141	49.5	6	417	46		0	1016.7	100	50.5	7	517.7	45		0	999	77	50.9	10	512.1	45	
23		0	963.2	49	51.6	7	638.7	23		0	976.4	63	53.9	6	618.7	26		0	981.8	79	52.7	5	649.4	32	
43		0	997.9	78	50.8	7	474	33		0	1000.2	70	51.8	8	487.2	32		0	1033.4	60	49.1	8	471.8	40	
33		0	983	80	51.6	9	580.6	31		0	1015.9	44	49.9	6	552.9	38		0	1042.1	77	52.6	8	554	30	
31		0	1055.7	84	49	7	451.5	26		0	1052.8	76	48.2	6	439.3	38		0	1063.2	95	55.7	8	458	35	
		0	993.3	75	46.2	4				0	1012.8	51	48.7	6				0	990	53	47.7	7			
30		0	1082	76	49.9	9	454.8	34		0	1030.9	60	51.7	7	444.2	42		0	1005.3	62	57.8	9	444.7	25	
27		0	1100.8	86	56.1	9	480	28		0	1176.1	112	51.7	7	489.9	29		0	1077	92	55.6	10	492.1	29	
		0	1048.4	68	50	7				0	1048.5	119	48.9	8				0	962.9	58	59.3	12			
32		0	1106.1	80	57.4	13	491.7	30		0	1111.8	119	59	17	507.1	29		0	1170.7	88	57.6	6	518.9	30	
30		0	1032.3	60	46	5	579.2	70		0	1077.9	79	45.1	5	573.1	45		0	1012.8	63	46	8	552.3	33	
24		0	1085.9	74	44.7	11	526.4	31		0	1041	137	55.5	8	501.1	22		0	1097.7	94	58.1	7	519.6	25	
30		0	981.1	36	46.5	6	493.1	28		0	958.8	124	45.9	5	466.1	33		0	1025.6	100	42.8	9	459.5	45	
32		0	983.6	94	52.4	4	532.5	37		0	1058.9	54	55.5	10	519.1	36		0	1050	51	60.5	8	524	29	
34		0	985.3	107	62.3	10	426.8	22		0	1026.5	112	58.6	5	401	31		0	1021.9	107	59	10	417.9	40	
32		0	1099.2	71	45.9	4	517	33		0	1054.4	64	45.3	6	520.3	48		0	1073.4	79	49.2	7	451.4	29	
35		0	996.7	86	47.3	5	589.7	30		0	1049.5	69	53.5	10	569.6	18		0	1023.7	75	56.2	12	561.1	38	
27		0	1089	84	47.7	4	600.5	23		0	939.9	82	46.2	7	575.2	27		0	1025.1	28	49.8	8	603.4	21	
		0	968.8	96	51.7	6				0	989.4	109	52.2	9				0	1091.7	70	53.5	10			
20		0	1157	56	52	3	456	29		0	1193	80	60	6	427	23		0	1081	55	52	5	478	26	
17		0	1007	66	53	4	473	17		0	1096	75	53	5	487	32		0	1041	67	51	4	511	27	
28		0	1073	31	53	5	577	24		0	942	43	55	4	618	18		0	1005	69	47	5	536	18	
11		0	1112	88	51	4	441	23		0	1017	26	51	1	424	16		0	967	48	52	2	470	30	
37	0.29	0	1158	58	55.5	7	444.6	30	0.33	0	1044.7	103	51.1	4	425.3	37	0.33	0	1056.9	61	49.9	3	450.3	31	0.32
30	0.35	0	1080.7	41	52.4	5	556.1	44	0.32	0	991.1	97	56.1	5	510	24	0.35	0	1188.1	48	60.4	7	511.1	41	0.4
27	0.32	0	1185.4	38	42	4	324.1	29	0.32	0	1277.7	37	45.8	5	310.8	16	0.35	0	1201.4	31	40.4	5	306.9	24	0.27
23	0.31	0	1035	66	45	4	487	25	0.28	0	1068	62	47	4	479	17	0.3	0	995	64	41	4	498	29	0.27
2	0.29	0	947	16	42	3	376.2	9	0.38	0	1003	11	44	4	459	8	0.28	0	1030	62	46	4	462	4	0.26
11	0.24	0	983	41	49	4	431	22	0.25	0	1016	67	53	4	430	21	0.26	0	1059	62	48	2	407	12	0.29
14	0.31	0	1070	11	49	3	312	8	0.25	0	1124	41	52	2	286	16	0.28	0	1080	36	49	3	278	8	0.3
17	0.27	0	1091	54	51	4	190	15	0.3	0	942	67	59	4	205	14	0.26	0	1098	9	56	5	182	15	0.31
31	0.26	0	1032	56	50	4	495	26	0.25	0	1021	59	52	2	465	23	0.28	0	1065	30	52	4	480	28	0.27
8		0	1011	36	51	4	307	11		0	964	67	54	3	305	11		0	959	40	53	5	283	9	
31	0.32	0	1017	58	41	1	439	13	0.31	0	1040	47	52	5	414	19	0.34	0	1091	77	60	4	432	15	0.32
18	0.24		1020	65	52	5	506	26	0.27		994	47	52	6	516	10	0.25		1044	55	52	4	519	26	0.26
17	0.38	0	1154	35	48	4	505	26	0.38	0	1096	28	52	5	489	10	0.38	0	1034	69	52	2	508	23	0.33
27	0.25	0	985	34	45	1	522	35	0.25	0	1040	68	46	2	540	22	0.25	0	1028	38	49	4	520	19	0.26
15	0.29	0	974	90	49	4	554	10	0.25	0	1013	102	54	2	499	25	0.32	0	1032	27	52	5	525	23	0.3
16	0.34	0	1093	34	46	2	447	11	0.35	0	1137	42	52	1	455	15	0.35	0	1123	59	56	5	474	15	0.32
25	0.31	0	1110	30	49	3	460	28	0.32	0	964	62	53	4	441	21	0.31	0	1048	71	50	3	463	32	0.28
18	0.4	0	1088	41	58	4	447	17	0.39	0	1134	66	59	2	454	17	0.39	0	1086	50	56	2	466	16	0.36
30	0.27	0	975	52	44	2	536	24	0.23	0	953	74	52	4	514	22	0.25	0	979	47	45	5	520	24	0.25
26	0.31	0	1151.4	86	51	6	455	17	0.36	0	1179.8	49	47	2	451	22	0.37	0	1090	57	43	6	500	22	0.29
17	0.29	0	1049	39	54	2	454	19	0.3	0	1091	25	56	3	448	17	0.32	0	1119	667	51	4	462	22	0.31
16	0.25	0	948.5	35	45.6	3	581.2	25	0.26	0	1006	44	49	5	565	21	0.25	0	1046	50	43	3	572	23	0.26
23	0.32	0	1066.2	85	54.6	5	440.5	18	0.34	0	1083	43	55	5	415	21	0.38	0	1017	39	49	4	469	30	0.28
		0	958	93	48	5				0	1061	65	47	1				0	1031	25	45	1			
40	0.26	0	1023.1	72	48.8	4	456.8	13	0.26	0	961	54	54	4	430	28	0.27	0	974	66	51	6	461	26	0.23
23		0	1080	66	64	4	452	14		0	1091	25	59	1	443	20		0	1084	67	52	5	430	21	

0	1054	58	51	3	595	20		0	1054	49	52	3	593	19		0	1042	49	49	4	614	35		0	1051
1	1031	72	54	4	396	29	0.32	0	1064	33	55	4	390	20	0.33	0	1093	77	52	3	407	33	0.31	0	1105
0	1062	81	52	5	464	36	0.3	0	1083	42	56	4	451	16	0.32	0	1072	51	55	5	461	36	0.31	0	1156
0	1013	67	50	5	359	26	0.23	0	1075	34	51	2	325	28	0.28	0	1032	70	48	4	346	32	0.25	0	1037
0	1060	51	59	4	414	29	0.29	1	1064	53	58	5	379	23	0.33	1	1024	44	56	6	402	26	0.29	0	1054
0	987	50	47	4	379	28	0.38	0	959	39	46	3	404	38	0.35	0	989	83	43	4	423	46	0.33	0	995
0	1082	64	52	3	448	22	0.33	0	1119	69	52	3	449	20	0.33	0	1190	60	50	4	451	21	0.35	0	1115
0	1114	92	53	5	426	37	0.34	0	986	69	55	5	391	14	0.36	0	1033	73	53	4	403	22	0.34	0	1080
0	915.6	102	55.1	7				0	990.1	91	51.7	6				0	1080.7	104	55.9	10				0	1135
0	1077.3	133	56.4	7	385.1	58		0	1152.2	126	55.8	7	373.4	29		0	1029.4	105	52.3	4	377	30		0	1062.5
0	1026.1	90	51.6	7				0	1029.8	77	49.1	5				0	1022.3	49	51.1	6				0	1065.3
0	1014	53	51.7	7				0	1046.9	90	46.5	5				0	1020.9	64	50.5	7				0	1044.3
0	1074.8	95	61.1	10				0	1090	103	59.4	14				0	1020.3	104	60.8	21				0	1061.9
0	978.6	50	50.3	4				0	985.6	64	51.3	4				0	940.5	52	51.5	8				0	1023.8
0	1005.4	60	49.8	6	568.8	33		0	1008.1	56	49.2	6	574.1	32		0	1032.9	73	48.1	3	568.3	37		0	1010.3
0	1024.4	52	51.5	5	591	36		0	1036.9	45	53.2	11	582.3	29		0	1072.4	57	52.5	5	564.9	32		0	1087.9
0	1027.3	50	55.7	7	440.8	46		0	1035.1	94	51.8	6	466.2	38		0	1067	94	49	8	459.3	38		0	941.1
0	981.6	56	51.1	10	530	35		0	935.5	119	49.7	7	505.7	43		0	995.5	72	46.6	4	520.4	43		0	1020.9
0	939.9	62	52.3	6	630.1	50		0	966.1	55	54.6	5	658.9	68		0	996.7	78	55.1	7	660	40		0	969.8
0	933.6	122	50.7	8	493.4	45		0	984.7	91	47.5	8	500.6	36		0	986.6	47	47.7	6	495.3	31		0	1028
0	1027.1	140	49.3	8	556.5	44		0	997.4	58	45.2	7	563.7	46		0	983.2	41	50.8	6	591.8	72		0	993.1
0	994.4	94	52.2	6	443.9	55		0	1014.2	92	50.6	5	472.2	33		0	1021.7	81	51.8	8	462.6	39		0	1015.8
0	965.2	55	47.2	4				0	933.2	62	47.7	7				0	951.6	48	47.4	4				0	1014
0	1006	70	54.9	7	445.6	55		0	999.8	63	53.5	4	456.8	41		0	1028.3	72	50.8	6	457.1	24		0	1030.9
0	1071.4	109	55.9	10	515.6	36		0	999.9	98	51.9	6	511	35		0	1062.3	84	54.1	13	504.6	24		0	1106.3
0	961.6	110	53.1	6				0	961.7	138	51.6	6				0	1122.2	50	50.1	6				0	1030.1
0	1087	84	60.9	14	518.6	41		0	1124.9	136	52.5	9	521.8	42		0	1078.8	130	62.8	16	534	36		0	1168.4
0	10001	74	49.3	8	556.4	42		0	954.4	46	45.9	8	574.5	45		0	1049.4	59	43.9	8	565.2	28		0	928.8
0	976	109	56.4	10	527.3	32		0	949.9	106	51.7	8	502.7	30		0	935.2	69	51.2	6	506.9	25		0	1061
0	1003.7	97	47.6	8	496.4	47		0	971.6	111	48.1	8	535.9	56		0	1020.5	68	52.4	10	488.1	59		0	1023.1
0	837	100	58.5	6	540.1	45		0	896.5	127	56	5	533.4	22		0	1034.4	74	57.9	9	534.6	44		0	1113.3
0	985	87	53.8	7	434.5	40		0	1019.4	101	55.6	6	416.5	41		0	1099.3	141	55.3	8	426	54		0	1077.1
0	1061.4	78	46.7	5	474.1	41		0	1058.1	153	50	5	477.1	37		0	1098.5	80	50.8	9	444.4	37		0	1150.1
0	1007.2	97	54.5	12	575.4	33		0	1012.8	106	53.9	10	565.5	23		0	1009.8	96	45.6	8	572.4	27		0	1079.6
0	1029.7	77	50.1	7	598.4	30		0	1026.3	56	50.5	7	594.8	32		0	1024.3	66	52.8	7	612.4	28		0	1044.6
0	1068.8	75	55.1	6				0	1051.9	95	55.3	5				0	1032.2	83	54.8	6				0	1045.4
0	1108	95	50	6	466	28		0	1081	53	51	5	470	26		0	1110	90	55	4	487	28		0	1121
0	1023	69	49	5	476	45		0	1010	54	49	2	453	34		0	1038	46	50	5	522	27		0	1057
0	950	46	53	2	507	14		0	1021	97	47	5	505	30		0	1063	86	49.4	2	595	39		0	987
0	915	72	49	2	514	21		0	1005	20	52	1	501	25		0	952	81	56	5	492	38		0	1012
0	1027.7	80	51.9	5	467.1	43	0.29	0	1013.5	76	51.8	4	469.9	36	0.28	0	1045.7	75	50	6	484.9	38	0.28	0	1078.1
0	1132.5	65	56.2	3	530.1	30	0.36	0	1190.1	95	52	6	543	32	0.36	0	1266.8	70	46.7	5	526.3	28	0.4	0	1246
0	1164.5	106	45.2	5	280.3	25	0.3	0	1178.9	79	44.8	5	287.7	21	0.29	0	1165.1	89	44.5	5	301.1	22	0.27	0	1264
0	985	69	45	3	482	25	0.28	0	1048	64	46	4	464	32	0.32	0	1016	75	39	3	485	27	0.29	0	1018
0	1007	31	46	4	442	20	0.28	0	992	46	46	3	490	10	0.23	0	975	51	43	3	460	25	0.25	0	1034
0	1014	59	47	2	440	37	0.24	0	995	64	49	1	462	9	0.22	0	1022	33	50	4	443	23	0.24	0	1042
0	1043	45	46	1	318	9	0.25	0	1067	46	45	2	320	14	0.25	0	1086	40	46	3	321	14	0.25	0	1047
0	931	72	56	4	176	10	0.31	0	994	38	50	1	186	12	0.29	0	1077	27	56	3	170	7	0.33	0	1088
0	1059	53	52.3	2	504	35	0.25	0	1024	47	52	1	463	32	0.28	0	1070	54	51	3	495	19	0.26	0	1080
0	1140	58	53	5	294	7		0	1043	39	51	2	337	12		0	951	45	55	2	262.4	29		0	1087
0	1077	52	59	3	444	33	0.31	0	1064	43	51	1	437	14	0.31	0	1072	70	48	3	446	22	0.3	0	1035
	991	30	54	4	525	29	0.24		995	32	54	2	489	20	0.28		969	50	50	5	478	37	0.28		1173
0	993	52	50	3	524	40	0.3	0	1060	67	51	4	519	28	0.33	0	1072	71	51	4	524	39	0.33	0	1103
0	1018	57	47	3	506	24	0.27	0	1029	55	49	3	512	32	0.27	0	1004	63	47	4	513	28	0.26	0	991
0	1005	58	53	3	524	25	0.29	0	959	59	49	2	545	35	0.26	0	972	64	46	3	534	33	0.27	0	1023
0	1088	70	52	2	485	21	0.3	0	1066	54	53	3	486	24	0.29	0	1028	58	51	4	502	36	0.27	0	1055
0	1033	92	48	3	469	32	0.27	0	1026	78	51	4	477	32	0.26	0	1053	62	54	5	459	29	0.29	0	1085
0	1028	42	53	5	474	21	0.34	0	1062	55	53	4	484	18	0.33	0	1084	68	51	2	484	25	0.34	0	1116
0	945	35	48	4	525	38	0.23	0	938	41	48	4	534.3	21	0.22	0	952	40	49	5	519	30	0.24	0	949
0	1140	50	56	4	482	45	0.33	0	1087	43	47	3	481	15	0.31	0	1185	86	55	4	450	15	0.37	0	1070
0	1064	61	46	4	468	30	0.29	0	1089	36	50	4	452	27	0.32	0	1094	61	49	4	455	20	0.31	0	1114
0	963	58	45	3	582	29	0.22	0	970	31	45	2	577	24	0.23	0	1013	40	45	2	578	24	0.24	0	1013
0	1002	52	53	3	463	32	0.28	0	997	42	50	3	472	25	0.27	0	1037	62	53	6	454	37	0.3	0	1023
0	1060	41	48	5				0	1081	56	49	5				0	1096	41	45	4				0	1090
0	954	62	51	5	460	25	0.23	0	956	48	55	4	450	22	0.24	0	971	93	52	4	463	24	0.23	0	975
0	1087	50	48	5	461	32		0	1029	28	53	1	442	28		0	1031	26	51	3	472	14		0	1011

49	50	4	650	29		0	1035	48	52	5	648	24		0	1092	57	48	5	657	21		0	1063	51	49
45	49	6	418	29	0.3	0	1167	74	56	5	409	23	0.32	1	1121	53	49	4	394	33	0.33	0	1086	59	49
54	52	3	413	31	0.38	0	1120	72	48	4	451	26	0.33	0	1125	42	57	7	424	17	0.37	0	1042	60	58
92	47	4	317	35	0.28	0	1028	37	50	3	335	19	0.26	0	1016	68	45	5	314	37	0.27	0	1029	47	45
44	56	3	422	31	0.27	0	1049	34	55	2	433	19	0.25	0	1040	64	49	4	420	39	0.25	0	995	47	50
87	45	2	434	29	0.31	0	1032	68	46	3	491	40	0.23	0	1071	54	47	4	463	17	0.31	1	1004	48	47
36	49	5	451	31	0.33	0	1108	54	50	3	470	28	0.3	0	1171	109	44	3	464	20	0.33	0	1093	55	48
41	52	5	435	32	0.31	0	1123	52	50	5	403	22	0.36	0	1075	66	52	4	385	29	0.37	0	1061	20	54
76	52	8				0	1102.8	95	53.5	7				0	1115.2	98	53.7	6				0	1067.7	99	58.7
100	56.8	6	385.2	33		0	1124.5	105	57.8	9	375.3	23		0	1105.4	78	53	6	405.6	38		0	1089.3	90	57.3
69	50.5	7				0	1034.6	49	48.8	6				0	1065	82	52.5	7				0	1065.2	102	54.4
53	47.7	4				0	1042.4	60	49.2	4				0	1037.6	81	54.5	9				0	1013.5	100	45.1
103	53.6	7				0	1107.2	109	57.5	10				0	1107.7	114	56.7	12				0	1019.3	96	58.8
96	53.1	6				0	1095.3	52	49.9	7				0	1097.8	80	53.1	8				0	1074.3	109	50.3
42	50.8	9	577.5	21		0	1036.8	61	50.3	6	581.6	17		0	962.5	36	50.1	8	563.5	23		0	941.7	39	46.7
50	52.5	6	582.8	20		0	1043.4	45	51.6	10	582	26		0	1038.4	55	47	8	572.8	18		0	1014.8	65	46.8
97	45.7	7	449.4	27		0	980.7	63	53.3	12	453.4	36		0	989.2	47	48.8	7	430.2	56		0	1026.4	81	51.5
50	48.2	5	521.8	27		0	982.3	60	45.9	6	540.3	31		0	1030	90	50.5	9	475.4	49		0	1012.3	93	46.4
46	53.2	5	659.7	48		0	1013.6	59	54.5	10	657.8	31		0	1027.2	88	50.4	7	645	37		0	999.7	82	52.2
65	49.6	10	491	40		0	1029.4	70	47.1	6	478.2	36		0	1049.1	100	54.9	12	450	43		0	952.2	70	45.5
81	49.1	8	544.3	39		0	996.1	63	47.9	5	569	31		0	1051.9	83	55.1	13	567	36		0	1001.2	93	46.3
63	52.3	8	462.2	32		0	1033.2	60	54.6	8	464.2	34		0	1050.9	88	53.3	8	412.2	25		0	1045	168	52.7
55	47.1	4				0	1018.5	55	51.1	10				0	1012.2	75	49	12				0	1008.9	47	44.9
60	53.8	6	463.8	26		0	1012.8	61	52.7	8	452.9	26		0	1192	42	52.3	7	451.7	32		0	1051.2	104	55.3
128	50.1	6	518.5	35		0	1110.1	105	52.3	6	511.3	332		0	1078.2	98	55.6	11	523.6	34		0	1080.5	91	52.7
80	54.3	8				0	1026.5	80	55.3	12				0	980.8	55	50.9	8				0	611.5	194	51.5
99	60	16	529.7	41		0	1140.9	121	59.9	13	512.5	34		0	1095.2	93	55.8	10	532.5	28		0	1049.3	99	52.8
126	47.7	10	562.6	95		0	1076.8	51	48.3	8	564.7	21		0	1180.9	119	49.6	10	539.7	39		0	1039.3	131	53.9
87	50.5	7	514.9	24		0	1089.8	87	52.9	9	534.1	24		0	1256.3	46	55.4	10	461.7	17		0	1179.3	105	49.5
54	45.3	6	471.2	30		0	1022.3	95	45.7	6	464.8	27		0	1185.5	80	49.8	4	353.1	32		0	1058.4	103	43.8
103	58.8	7	540.2	38		0	1107.6	87	54.8	4	533.6	17		0	976.8	75	57	6	538.7	30		0	965.1	50	61.2
102	51.6	8	412.5	35		0	1041.6	89	54.9	6	445.1	33		0	969.4	76	52.1	11	437.4	44		0	972.9	86	49.5
85	47.4	8	479.1	32		0	1096.1	88	49.2	7	459.6	29		0	1129.8	81	47.5	8	491.4	44		0	1035.2	64	45.2
191	51.5	9	545.2	31		0	1019.9	68	51.7	9	567.3	35		0	1054.9	99	53.6	9	565.8	51		0	1008	79	52.3
48	51.3	9	613.8	27		0	1048.7	44	50.2	7	608.7	33		0	1044.4	77	54.3	9	517.8	50		0	1002.4	102	49.7
77	51	5				0	1048.3	75	51.4	7				0	1092.2	51	53.5	8				0	1031.8	96	52
112	53	4	450	21		0	1092	51	51	4	467	14		0	1052	49	54	5	479	27		0	1084	102	52
71	50	2	534	25		0	1050	55	52.3	3	521	36		0	1018	68	49	3	508	27		0	914	90	49
63	50	5	593	17		0	1000	51	49	5	556	14		0	1066.2	65	50	2	530	5		0	1161	28	53
26	51	1	482	39		0	999	10	48	3	497	20		0	1038	53	48	4	457	31		0	990	80	52
70	47.5	6	469.6	35	0.3	0	1044.2	50	51	4	471.3	24	0.29	0	1060.8	103	51.9	7	360.9	23	0.45	0	999.8	81	45.9
92	55.3	4	527.7	26	0.39	0	1211.7	48	51	5	519.8	30	0.39	0	1222	100	52	5	503.1	32	0.41	0	1126.1	61	49.6
54	40.4	3	294.1	28	0.29	0	1261.6	24	44.1	4	250	18	0.36	0	981	46	46.3	5	330.4	21	0.23	0	977	91	45.5
51	46	3	474	32	0.3	0	1028	65	45	4	480.3	25	0.3	0	1153	13	44	4	346	16	0.52	0	1118	43	46
60	47	3	430	13	0.3	0	1025	37	45	3	459	26	0.27	0	1009	62	49	5	496	16	0.23	0	984	36	47
51	52	1	443	6	0.25	0	1007	46	49	4	389	13	0.3	0	1033	64	48	2	412	12	0.27	0	1021	39	47
24	42	4	293	13	0.28	0	1008	30	44	2	296	8	0.27	0	1028	37	43	1	292	21	0.24	0	1046	57	48
28	53	5	187	14	0.3	0	1071	60	48	5	170	8	0.33	0	1030	35	52	3	181	10	0.2	0	923	52	51
52	50.7	4	476	23	0.28	0	1081	54	50	4	472	24	0.29	0	1043	22	47	3	505	22	0.23	0	1014	14	50
85	46	5	250	22		0	1124	56	50	4	261	15		0	1081	78						0	1046	56	
81	51	1	439	23	0.3	0	1035	54	51	5	456	31	0.29	0	1081	41	56	3	379	12	0.38	0	1032	58	55
47	51	3	476	34	0.33		982	44	50	3	530	29	0.23		1137	52	49	3	542	40	0.26		1072	105	48
53	50	3	531	29	0.33	0	1065	57	52	3	499	29	0.36	0	1027	30	53	2	566	30	0.27	0	1120	101	51
42	48	3	539	27	0.23	0	1021	43	50	4	529	19	0.25	0	1002	30	48	4	511	36	0.26	0	999	50	49
38	47	1	516	27	0.31	0	1024	37	47	2	545	22	0.28	0	1020	56	45	4	555	27	0.26	0	983	57	46
37	50	3	455	23	0.33	0	1082	39	52	2	474	26	0.31	0	1115	34	53	4	491	23	0.3	0	1134	43	52
69	48	4	479	19	0.27	0	1053	59	50	4	459	28	0.29	0	1065	77	44	4	517	16	0.24	0	1016	53	50
48	53	4	476	22	0.35	0	1119	49	53	2	476	15	0.35	0	1058	69	55	3	456	16	0.36	0	995	48	55
34	51	4	537	23	0.22	0	973	35	49	3	529.5	21	0.23	0	1048	81	48	5	484	34	0.3	0	1003	77	44
34	54	3	476	18	0.32	0	1087	41	45	5	484	26	0.31	0	1043	66	44	4	497	34	0.28	0	1034	52	51
38	46	5	475	22	0.3	0	1111	40	48	4	465	25	0.31	0	1157	63	53	5	462	34	0.31	0	1104	67	53
41	46	3	556	38	0.26	0	1011	38	44	2	578	19	0.24	0	984	48	47	5	499	28	0.31	0	1009	41	41
53	52	6	448	25	0.31	0	1037	49	49	2	473	28	0.28	0	1086	83	53	5	463	32	0.3	0	1055	44	52
90	49	4				0	1020	29	48	3				0	1031	25	44	3				0	1060	41	45
77	48	4	467	25	0.23	0	1017	72	48	3	479	34	0.22	0	991	70	49	6	452	38	0.23	0	964	67	47
99	53	4	447	16		0	1082	45	54	2	454	14		0	953	60	57	4	391	13		0	1062	21	44

3	654	25		0	1053	56	51	4	630	28		0	1056	59	51	4	631	33		0	1073	71	42	4	628
3	433	29	0.28	0	1083	65	49	4	387	29	0.34	0	1071	62	52	4	392	34	0.33	0	1132	79	49	6	412
5	440	24	0.33	0	1011	53	53	4	476	24	0.28	0	1119	40	49	5	475	33	0.3	0	1171	96	54	5	453
3	326	23	0.26	0	1021	43	44	3	339	22	0.24	0	1046	42	50	4	324	27	0.26	0	1074	67	46	3	327
2	452	13	0.23	0	983	72	50	2	460	28	0.23	0	1021	59	51	4	451	26	0.23	0	1031	63	48	6	436
2	498	23	0.27	0	1007	66	47	5	416	21	0.33	0	971	54	47	2	440	22	0.31	0	1017	72	47	3	463
3	471	21	0.3	0	1049	37	50	2	441	30	0.33	0	1107	65	50	4	449	24	0.33	0	1122	54	49	4	457
3	399	41	0.35	0	989	79	63	4	375	42	0.37	0	1172	113	59	4	410	33	0.33	0	1122	69	49	4	415
10				0	1070.2	82	52.1	5				0	1108.9	138	53.8	10				0	1045.3	91	51.4	5	
5	430	32	NA	0	1099.9	109	71.7	13	415.3	39		0	1197.1	94	69.1	7	385.8	60		0	1150.3	116	63.2	10	391.5
7				0	1011.6	84	49.7	7				0	1044.2	57	51.8	10				0	1056.8	61	53.1	10	
10				0	1110.1	52	43.5	8				0	1176.7	111	37.9	11				0	1082.3	88	44.3	13	
11				0	1056	117	53.1	9				0	1027.9	104	54.9	10				0	1070.2	103	55.5	9	
8				0	1027.7	63	53.2	9				0	1063	72	49.3	7				0	1083.9	101	49.2	7	
6	542.1	66		0	926.9	65	49.9	5	566.1	21		0	977.9	89	49.7	4	562.6	33		0	1003.7	66	51.2	8	570.3
5	588.6	21		0	1033.6	59	50	6	557	34		0	1048.9	48	49.6	5	539.3	45		0	1070.9	88	53.9	9	585.8
8	479	33		0	974.1	54	51.2	6	452.8	29		0	983.2	68	52.4	10	460.6	32		0	1008	88	49	6	445
5	512.1	35		0	977.3	84	46.4	6	525.5	43		0	980.2	79	45.7	6	532.3	27		0	974.2	60	46.6	6	501.1
4	651.9	70		0	985.2	56	51.8	5	663.1	77		0	1012.8	65	53.8	5	625.2	42		0	1025	62	54.8	7	641.6
5	484.5	39		0	964.5	62	49.6	8	489.1	50		0	1016.7	36	50.7	6	460.2	40		0	995.2	63	48	4	459.4
12	554.8	70		0	1013.8	52	51.3	9	555.6	42		0	1012.7	59	49.9	9	605.7	105		0	1068.8	105	40.5	10	562.8
7	428.2	44		0	1009.5	89	49.1	4	342.1	20		0	1016.4	70	51	6	381	24		0	1017.3	98	51.1	6	402.1
5				0	994.8	75	44.7	5				0	957.2	52	44.3	4				0	1009.3	42	46.2	7	
13	460.4	25		0	1043.7	102	49.6	6	442.4	25		0	868.9	121	53.4	7	436.7	28		0	1299.5	64	53.5	10	446.3
6	494	23		0	1104.2	102	57.1	10	488.6	43		0	1008.3	90	57.6	6	474	32		0	1134.8	106	55.3	10	460.6
12				0	746.1	128	46.1	4				0	730.2	49	48	5				0	805.8	92	50.7	7	
9	571.6	171		0	1101.2	191	55.4	13	531.2	38		0	1082.6	115	54.8	9	510.4	43		0	1082.6	115	64.5	14	495.9
16	545.6	25		0	1030.6	71	48.1	5	576.4	33		0	1035.5	72	46	4	564	45		0	1062.5	80	49.1	7	543.3
15	581.8	139		0	1174.9	219	52.1	17	499.2	50		0	889.8	199	51.1	18	542.9	65		0	971.6	236	43	14	542.9
7	327.5	30		0	1146.9	79	45.9	10	382.7	41		0	1172.5	61	50.4	9	388	28		0	1091.2	111	45.8	8	418.9
9	531.8	26		0	986.9	91	60.7	7	537.7	22		0	994	73	69.1	19	521	24		0	1030.7	91	53.8	5	540.9
6	426	43		0	942.5	73	52.4	6	420.9	35		0	996.4	61	48.7	8	445.6	37		0	1068.1	107	52	9	395.6
5	508	47		0	1068.3	105	46.5	4	493.3	41		0	1083.4	152	48.1	5	483.5	59		0	1092.5	79	46.9	6	502.8
8	572.1	47		0	983.3	52	55.9	16	603.9	67		0	1006.3	69	51.9	7	583.8	52		0	1033.4	75	53.1	10	592.8
8	493.9	31		0	1037.6	86	50.9	8	558.4	41		0	1057.5	51	53.8	11	589.9	27		0	1070.1	82	50.6	7	602.5
7				0	1023.7	94	49.7	5				0	1062.5	69	48.1	6				0	1084.2	74	50.3	8	
5	482	35		0	1025	59	54	5	486	27		0	1052	79	49	4	473	20		0	1044	82	51	5	464
5	524	38		0	928	66	48	5	532	34		0	932	67	51	4	526	44		0	1073	58	47	3	525
4	588	20		0	1182.3	38	44	2	577	14		0	1187	46	45	3	475	13		0	1193.6	39	45	2	462
5	465	30		0	969	49	43	3	420	40		0	1000	71	47	3	468	39		0	1036	54	45	4	473
5	476.5	29	0.27	0	1008.4	64	46.3	6	479.6	32	0.27	0	1013	84	56.3	8	448.3	33	0.31	0	1069.6	67	51.3	9	487.6
3	530.6	34	0.35	0	998.6	36	49.6	5	522.6	50	0.32	0	1235.6	58	53.5	5	484.3	29	0.44	0	1224.4	92	54.2	6	516.8
5	339.4	29	0.22	0	1021.3	51	47.9	3	339.5	27	0.23	0	1000.6	57	47	5	334.9	24	0.23	0	1018.1	51	45.5	5	335.1
3	436	32	0.4	0	1065	68	40	4	408	17	0.39	0	1043	88	41	4	417	39	0.37	0	1061	41	47	4	416
2	492	18	0.23	0	1007	21	48	3	471	8	0.26	0	1021	32	55	4	453	8	0.28	0	997	26	52	4	468
5	438	12	0.24	0	1011	38	45	2	405	23	0.27	0	1014	53	48	2	417	35	0.26	0	1009	52	49	3	416
3	285	22	0.25	0	1008	66	45	3	288	10	0.25	0	965	71	43	2	320	23	0.21	0	1041	68	43	3	307
4	191	18	0.18	0	920	84	50	1	193	14	0.18	0	1007	58	54	3	178	18	0.21	0	1066	98	55	4	206
4	504	29	0.23	0	1045	50	50	4	473	27	0.27	0	1067	58	51	4	467	19	0.28	0	1093	53	52	2	490
				0	1000	65						0	1019	99						0	1070	54			
4	449	34	0.28	0	1011	47	50	4	378	31	0.37	0	1044	53	50	3	426	28	0.31	0	1078	38	51	4	423
2	557	33	0.23		1041	78	49	2	597	53	0.19		1088	68	46	3	593	60	0.21		1240	55	48	3	556
3	544	40	0.32	0	1198	105	48	1	567	42	0.32	0	1092	83	52	3	565	43	0.29	0	922	18	48	3	538
3	521	27	0.25	0	976	31	46	3	542	25	0.22	0	998	29	48	3	530	18	0.24	0	1027	31	46	2	531
1	527	31	0.28	0	950	44	49	2	503	19	0.29	0	990	48	44	3	527	24	0.28	0	1011	47	49	3	559
2	490	29	0.3	0	1071	36	49	2	505	30	0.27	0	1078	48	53	3	408	30	0.4	0	1125	52	55	5	430
4	474	13	0.27	0	1021	50	49	3	494	41	0.25	0	1015	71	49	4	482	34	0.26	0	1046	84	48	2	474
3	480	18	0.31	0	1032	40	54	5	481	23	0.32	0	1070	54	55	4	477	20	0.34	0	1109	82	55	3	461
3	560	30	0.21	0	976	58	44	3	538	34	0.22	0	994	94	47	4	498	27	0.27	0	1007	42	48	4	503
4	471	47	0.3	0	1061	52	49	4	466	30	0.32	0	1006	59	46	5	441	29	0.33	0	1037	54	49	5	449
4	467	41	0.3	0	1081	50	52	5	465	34	0.29	0	1100	52	55	3	441	28	0.33	0	1121	49	51	4	452
6	551	31	0.26	0	1045	65	45	4	507	41	0.32	0	1028	37	49	5	477	36	0.35	0	1007	51	42	2	515
3	481	24	0.28	0	1023	64	54	5	475	28	0.28	0	1074	86	55	3	453	25	0.31	0	1082	84	54	6	406
2				0	1081	56	45	4				0	1096	41	47.3	4				0	1090	90	51	3	
4	487	26	0.2	0	953	70	47	3	463	31	0.21	0	984	60	50	6	479	26	0.21	0	972	40	47	4	459
2	382	11		0	972	37	53	4	372	13		0	1052	59	55	5	378	16		0	1009	16	48	5	352

31		0	1095	40	51	5	618	21		0	0	0	0	0	0	224	114	111	55	51	2
34	0.31	0	1218	127	50	5	395	37	0.36	0	2	1	0	0	0	92	58	23	15	75	2
36	0.34	0	1108	63	50	6	443	25	0.34	0	0	0	0	0	0	331	246	259	192	22	1
21	0.26	0	1022	41	46	5	320	27	0.26	0	0	0	0	0	0	150	94	93	59	38	1
40	0.25	0	1017	53	49	4	432	24	0.25	0	0	0	0	0	0	94	59	30	19	68	2
42	0.28	0	1013	80	44	5	476	8	0.26	0	1	0	1	0	0	171	78	60	27	65	2
25	0.33	0	1085	59	48	4	417	27	0.38	0	0	0	0	0	0	111	79	78	55	30	1
38	0.33	0	1050	75	53	5	408	22	0.33	0	0	0	0	0	0	156	123	101	80	35	1
		0	1088.6	91	51.8	7				0	0	0	0	0	0						
52		0	1098.9	44	59.2	8	408.9	38		0	0	0	0	0	0	47.7	36.4	22.9	17.5	51.9	
		0	1085.6	85	53.6	8				0	0	0	0	0	0						
		0	1049.9	99	48.7	6				0	0	0	0	0	0	85.7	49	38.1	22	55.6	
		0	1076.6	101	58.2	10				0	0	0	0	0	0	146.2	79	55.1	29.8	62.3	
		0	1051.6	81	57.3	7				0	0	0	0	0	0	104.4	71.8	37.9	26.1	63.7	
22		0	998.4	39	49.5	7	567.9	25		0	0	0	0	0	0	98.5	55.6	29.6	16.7	69.9	
40		0	1040.9	66	47.7	7	565.6	29		0	0	0	0	0	0						
34		0	987.1	47	51.1	11	456.4	37		0	0	0	0	0	0						
33		0	957.4	60	44	7	525.5	25		0	0	0	0	0	0						
37		0	1017.1	83	51.4	9	646.1	42		0	0	0	0	0	0	150.8	103.2	61.4	42	59.3	
40		0	986.4	65	52.6	11	459.1	50		0	0	0	0	0	0	124.5	72	50.4	29	59	
30		0	1020.7	101	42.1	10	562.9	41		0	0	0	0	0	0	82	60	32	24	60	
31		0	1023.2	58	53.1	9	422.2	37		0	0	0	0	0	0	59.9	35.9	17.4	10.4	71	
		0	1003	57	46.3	8				0	0	0	0	0	0	139.1	72.4	54.7	28.5	60.6	
29		0	1226.3	73	52.9	11	4723	31		0	0	0	0	0	0	92.7	64	27.7	19.3	70.2	
34		0	1107.1	87	56	11	495.2	39		0	0	0	0	0	0	125.8	72.5	43.3	25	65.5	
		0	1015.7	60	53.4	8				0	0	0	0	0	0	69.3	53	28	22	59	
34		0	1091.8	68	52	9	507.1	33		0	0	0	0	0	0						
65		0	1092.8	85	49.6	9	539	29		0	0	0	0	0	0	89	60.8	25	17.1	72	
65		0	1362.2	104	48.5	7	485.8	56		0	0	0	0	0	0	82	64	32	24	61	
40		0	1117.1	54	47.3	6	413.3	55		0	0	0	0	0	0	102.6	60.7	39.3	23	61.7	
25		0	987.7	78	52.4	5	538.8	25		0	0	0	0	0	0	115.1	63.5	50	27.6	56.6	
25		0	1020.7	106	51.2	9	424	22		0	0	0	0	0	0	84.6	51.7	39.4	24.1	53.4	
54		0	1113.6	87	49.2	7	478	36		0	0	0	0	0	0		31		16.5	47	
68		0	1027	85	50.7	9	578.3	39		0	0	0	0	0	0	107	60	43	24	60	
28		0	1068.9	109	51	7	597.6	31		0	0	0	0	0	0	108.6	61.1	34.2	19.3	68.5	
		0	1047.6	86	50.6	9				0	0	0	0	0	0	154	77	56	28	63	
25		0	1085	74	53	6	459	27		0	0	0	0	0	0	80	62	33	26	59	
23		0	1016	56	48	3	509	27		0	0	0	0	0	0	108	65	43	26	60	
13		0	1194.6	34	46	2	542	9		0	0	0	0	0	0	115	64	50	28	57	
22		0	1001	49	45	3	498	9		0	0	0	0	0	0	166	90	83	45	50	
43	0.28	0	1002.3	58	44.9	7	426.1	33	0.33	0	0	0	0	0	0						
36	0.39	0	1256	118	51.3	5	508.5	23	0.41	0	0	0	0	0	0	105.8	69	44.1	29	58	
32	0.23	0	993	34	45.5	4	327.4	23	0.24	0	0	0	0	0	0						
36	0.38	0	1121	13	47	5	378	16	0.45	0	0	0	0	0	0	91	49	34	18	62	
19	0.26	0	1008	80	47	3	452	11	0.28	0	0	0	0	0	0	122	73	50	30	59	
30	0.26	0	1014	82	45	2	416	4	0.26	0	0	0	0	0	0	78	47	30	18	61	
13	0.23	0	1029	37	42	2	311	12	0.22	0	0	0	0	0	0	81	67	30	25	63	
20	0.17	0	1022	41	54	5	195	5	0.19	0	0	0	0	0	0	87	63	28	20	68	
25	0.26	0	1032	70	48	3	493	33	0.24	0	0	0	0	0	0	80	50	27	17	66	
		0	1047	40						0	0	0	0	0	0	86	60	41	29	52	
24	0.32	0	1087	48	51	5	450	30	0.29	0	0	0	0	0	0	67	44	23	15	65	
33	0.27		1124	46	47	4	570	27	0.23		0	0	0	0	0	145	83	52	30	64	
35	0.27	0	1170	45	52	2	554	28	0.33	0	0	0	0	0	0	109	70	34	22	70	
27	0.24	0	1003	39	47	4	533	22	0.24	0	0	0	0	0	0	136	75	58	32	58	
54	0.25	0	1005	41	46	2	562	33	0.25	0	0	0	0	0	0	77	55	24	17	70	
28	0.37	0	1131	57	47	4	480	26	0.31	0	0	0	0	0	0	100	70	44	31	56	
29	0.28	0	1055	55	45	4	498	28	0.26	0	0	0	0	0	0	90	62	35	24	61	
22	0.37	0	1040	39	51	4	482	16	0.32	0	0	0	0	0	0	126	71	49	28	61	
34	0.27	0	1034	62	46	5	469	23	0.31	0	0	0	0	0	0						
27	0.33	0	1050	58	47	5	499	18	0.28	0	0	0	0	0	0						
30	0.32	0	1117	34	51	2	452	30	0.32	0	0	0	0	0	0						
26	0.3	0	1010	66	45	5	527	39	0.28	0	0	0	0	0	0						
25	0.38	0	1080	79	52	4	467	29	0.3	0	0	0	0	0	0						
		0	1020	29	34	3				0	0	0	0	0	0						
28	0.22	0	999	90	44	5	455	43	0.23	0	0	0	0	0	0	128	73	60	34	54	
22		0	1010	46	57	5	383	17		0	0	0	0	0	0	174	102	97	57	44	