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Normal Reference Range of T1 and T2 Myocardial Mapping in Healthy Indian Population Relative to Age and Gender

Research Article

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Abstract

Context: Data on T1 and T2 mapping reference range on 3T MRI scanners in healthy Indian population is scarce.

To find the reference range of T1 and T2 myocardial mapping in healthy Indian population relative to age and gender and to find specific reference range for cardiac base, mid and apex.

Settings and Designs: Prospective observational study.

Methods and Materials: 50 subjects were chosen after exclusion of cardiovascular morbidities and history of COVID-19 infection and underwent myocardial T1 and T2 mapping at 3T Philips Ingenia scanner.

Statistical Analysis Used: SPSS v23 (IBM Corp.) was used for data analysis

Results and Conclusions: Mean myocardial T1 and T2 mapping values at 3T scanner were 1269.96 ± 37.90 and 47.21 ± 1.47 ms respectively. There was no correlation or association found between T1 and T2 mapping values with age. Mean T1 mapping values were higher in females (1287.62 ± 46.55ms). No statistically significant difference was found in T2 mapping values between the genders. The meanT1 values in base, mid and apical segments were 1255.08 ± 39.90, 1260.91 ± 47.97 and 1293.88 ± 49.95 ms respectively. The mean T2 values in base, mid and apical segments were 46.05 ± 2.81, 46.04 ± 2.24 and 49.98 ± 2.53 ms respectively. The mean T1 and T2 values in apical segment were higher as compared to mid and base.

Keywords: T1 Mapping; T2 Mapping; Age; Gender; Segments

Introduction

Myocardial mapping is a parametric method allowing visualization and quantification of focal or diffuse diseases of the myocardium. The water molecules and other molecules present in the tissues determine the T1 and T2 values of these tissues. Alteration in the tissue composition due to pathological processes can lead to changes in T1 and T2 values as compared to normal myocardium [1]. T1 values can help in the identification of fibrosis, amyloid deposition, lipid accumulation and iron overload etc [2]. T2 mapping values help in detection of edema in infarction, myocarditis and other inflammatory pathologies and intramyocardial hemorrhage [3,4]

T1 value is a tissue specific time constant and can be used to distinguish different tissues. T1 values are known to increase with increase in the magnetic field strength [5]. T1 values are also dependent on physiological parameters and myocardial T1 mapping values varied according to age and gender of patients according to

some studies [6].T2 relaxation time or spin –spin relaxation is also tissue specific time constant. Increase in myocardial water content due to edema is considered to be the main cause of increase in T2 relaxation time [7]

To the best of our knowledge, there is limited literature on normal reference range of T1 and T2 mapping values in Indian population using 3T scanner. This makes the determination of pathological process a challenging task without contrast administration. The aim of this study is to evaluate and categorize the reference range of myocardial mapping in healthy Indian populations well as to find the reference range for each cardiac segment dividing it into base, mid and apex .

Methods

The study protocol conforms to the Declaration of Helsinki and written informed consent was taken from all patients and was approved by the Institutional Ethics Committee.

50 healthy asymptomatic volunteers from age 20 to 81 were included in the study.

Exclusion criteria were:

1) Evidence of cardiovascular disease found during physical examination and history taking

2) Claustrophobia

3) Patients having non-MRI compatible aneurysm clips, cochlear implants and other MR non compatible metallic prosthesis

4) Pregnancy

5) Past history of COVID-19 infection.

Cardiac MRI was performed using 3T Philips Ingenia scanner. For T1 value determination basal,mid and apical short axis Modified Look Locker (MOLLI) images were acquired with breath-hold in expiration and auto segmentation was done according to cardiac segmentation model proposed by American Heart Association(AHA). T2 mapping was performed using mGRASE sequence in basal, mid and apical short axis slices just like T1 mapping. Imaging parameters are described in [Table 1]. Data was analyzed using IntelliSpace Portal (ISP) software available on the Philips workstation and values were generated with T1 and T2 R2 maps. Representative images of Native T1 mapping in base (Figuere 1),mid (Figure 2), apex(Figure 3) and T2 mapping in base(Figure 4), mid (Figure 5) and apex (Figure6) sections are shown in (Figure 1-6) respectively.

Statistical Method

Data were coded and recorded in MS Excel spread sheet program. SPSS v23 (IBM Corp.) was used for data analysis. Descriptive statistics were elaborated in the form of means/standard deviations and medians/IQRs for continuous variables, and frequencies and percentages for categorical variables. Group comparisons for continuously distributed data were made using independent sample 't' test when comparing two groups. Linear correlation between two continuous variables was explored using Pearson's correlation (if the data were normally distributed) and Spearman's correlation (for non-normally distributed data). Statistical significance was kept at p < 0.05.

Table 1: Summary of Imaging Parameters

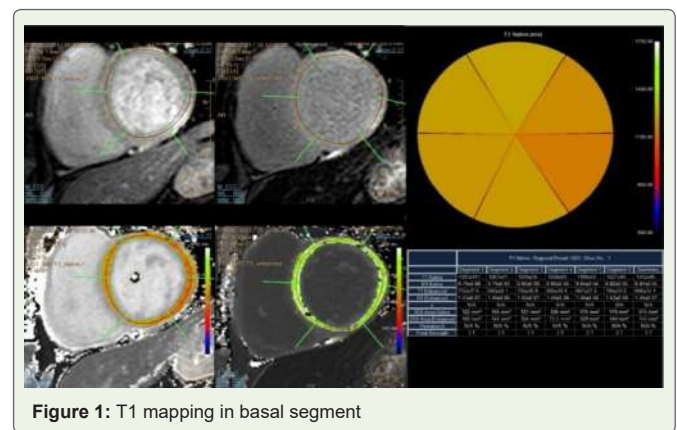|	T1 MAPPING	T2 MAPPING
Sequence	Molli	Mgrase
Magnetic Field	3t	3t
Flip Angle	20	90
Image Matrix	228x191	152x148
Acquisition	Single Shot Ssfp	Single Shot Ssfp
Band Width	1082	135
Parallel Acquisition	Sense/2	Sense/2
Slice Thickness	10mm	10mm
T1 Increment	20ms	Not Applicable
Acquisition Window	194ms	92ms
Inversion/Saturation	5	Na
Acquisition Heart Beats	5,3,3	1
Recovery Beat	1	1
Acquisition Time	10-20rr	10-20rr
Ti/Saturation Time	128	Not Applicable
Numberof Echos	Not Applicable	9
Te Incrementation	Not Applicable	8ms

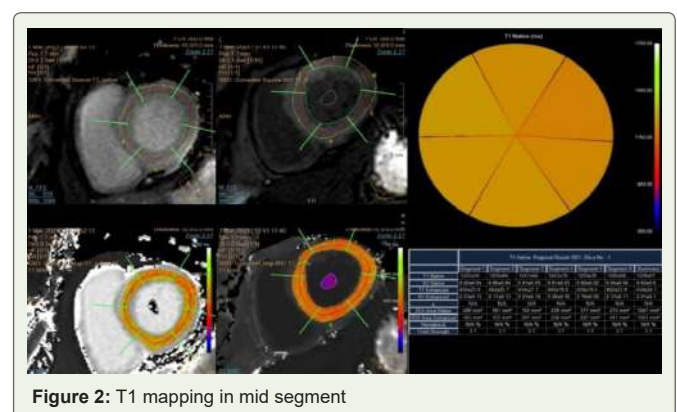**Figure 1:** T1 mapping in basal segment

Figure 2: T1 mapping in mid segment

Results

Study Population

The mean Age (Years) of participants was 40.26 ± 13.34. 12 (24.0%) of the participants had age between 20-29 Years,13 (26.0%) participants between 30-39 Years, 14 (28.0%) participants between
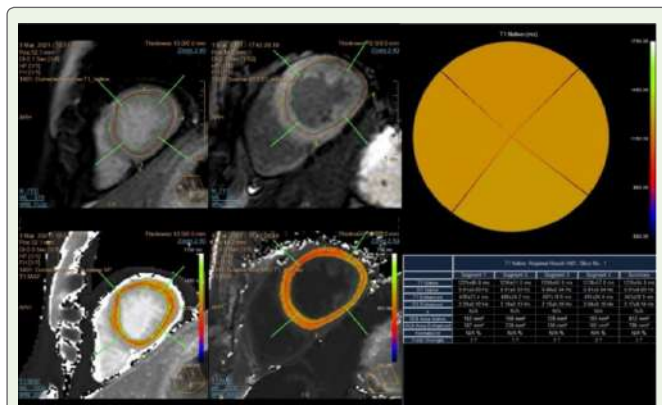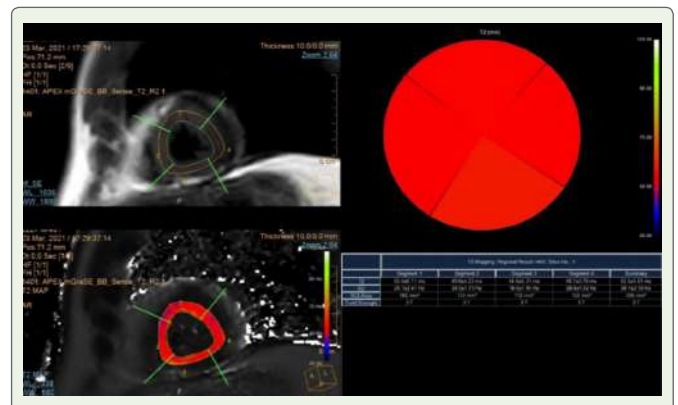
Figure 3: T1 mapping in apical segment

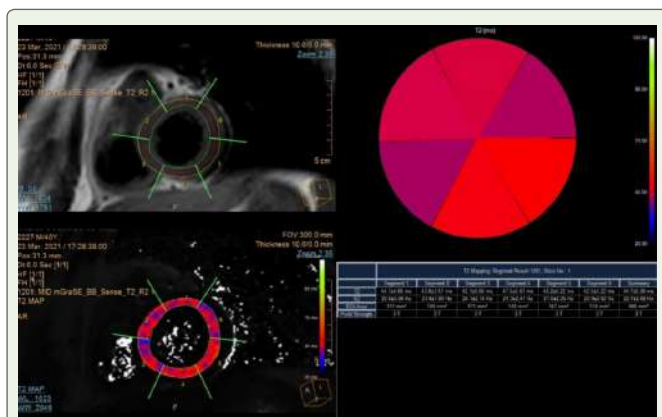**Figure 4:** T2 mapping in basal segment

Figure 5: T2 mapping in mid segment

Figure 6: T2 mapping in apical segment

Table 2: Summary of study population demographics

Basic Details	Mean ± SD || Median (IQR) || Min-Max || Frequency (%)
Age (Years)	40.26 ± 13.34 || 39.00 (30.50-47.75) || 20.00 - 81.00
Age	
20-29 Years	12 (24.0%)
30-39 Years	13 (26.0%)
40-49 Years	14 (28.0%)
50-59 Years	7 (14.0%)
≥60 Years	4 (8.0%)
Gender	
Male	32 (64.0%)
Female	18 (36.0%)

Normal T1 and T2 mapping values irrespective of Age and Gender

The mean (SD) of T1 Mapping (Average) was 1269.96ms (37.90). The median (IQR) of T1 Mapping (Average) was 1262.90ms (1243.53-1283.19). The T1 Mapping (Average) ranged from 1182.83 - 1379.97ms as shown in (Table 3).

The mean (SD) of T2 Mapping (Average) was 47.21 ms (1.47). The median (IQR) of T2 Mapping (Average) was 47.37 ms (46.1-48.25). The T2 Mapping (Average) ranged from 44.07 - 50.5ms as shown in (Table 4).

Normal T1 and T2 mapping values and relation to Age and Gender

(Average) in the 5 groups. The middle horizontal line represents the median T1 Mapping (Average), the upper and lower bounds of the box represent the 75th and the 25th centile of T1 Mapping (Average) respectively, and the upper and lower extent of the whiskers represent the Tukey limits for T1 Mapping (Average) in each of the groups.

The T1 Mapping values (Average) were not normally distributed in the 5 subgroups of the variable Age. Thus, non-parametric tests (Kruskal Wallis Test) were used to make group comparisons. There was no significant difference between the groups in terms of T1 Mapping (Average) and age ($\chi2 = 0.880$, $p = 0.927$)as shown in Table 5. Strength of Association (Kendall's Tau) = 0.02 (Little/No Association).
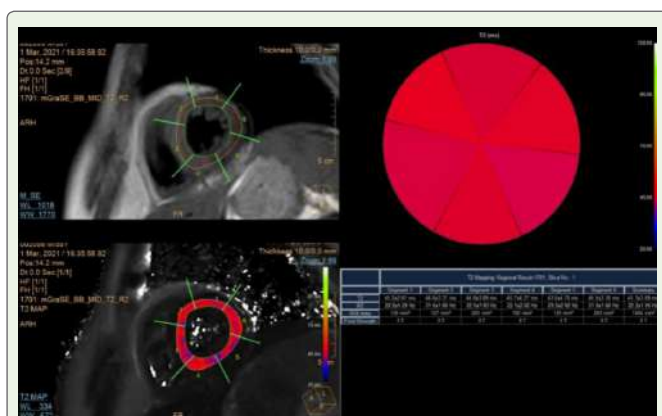
40-49 Years ,7 (14.0%) participants between 50-59 Years and 4 (8.0%) participants had Age: ≥60 Years.

32 (64.0%) of the participants were males and 18 (36.0%) of the participants had female gender.

The baseline characteristics of the volunteers are shown in (Table 2).

Table 3: T1 Mapping Values(Average) in study population(n = 50)

T1 Mapping (Average)	
Mean (SD)	1269.96 (37.90)
Median (IQR)	1262.9 (1243.53-1283.19)
Range	1182.83 - 1379.97

Table 4: T2 Mapping (Average) in study population (n = 50)

T2 Mapping (Average)	
Mean (SD)	47.21 (1.47)
Median (IQR)	47.37 (46.1-48.25)
Range	44.07 - 50.5

Non-parametric tests (Spearman Correlation) were used to explore the correlation between the two variables, as at least one of the variables was not normally distributed.

There was no statistically significant correlation between T1 Mapping (Average) and Age (Years) (rho = -0.04, p = 0.769) as shown in (Table 6).

The T2 Mapping values (Average) were not normally distributed in the 5 subgroups of the variable Age. Thus, non-parametric tests (Kruskal Wallis Test) were used to make group comparisons.

There was no significant difference between the groups in terms of T2 Mapping (Average) ($\chi 2$ = 3.803, p = 0.433) as shown in (Table 7). Strength of Association (Kendall's Tau) = 0.05 (Little/No Association).

There was no statistically significant correlation between T2 Mapping (Average) and Age (Years) (rho = 0.08, p = 0.573) as shown in (Table 8).

The T1 Mapping values (Average) were normally distributed in the 2 subgroups of Gender. Thus, parametric tests (t-test) were used to make group comparisons.

There was a significant difference between the 2 groups in terms of T1 Mapping (Average) (t = -2.289, p = 0.031), with the mean T1 Mapping (Average) being highest in female gender as shown in Table 9. Strength of Association (Point-Biserial Correlation) = 0.35 (Medium Effect Size)

The T2 Mapping values (Average) were normally distributed in the 2 subgroups of the variable Gender. Thus, parametric tests (t-test) were used to make group comparisons.

There was no significant difference between the groups in terms of T2 Mapping (Average) (t = -0.927, p = 0.360) as shown in (Table 10).

Strength of Association (Point-Biserial Correlation) = 0.13 (Small Effect Size)

Normal T1 and T2 mapping values and relation to cardiac segments

Non-parametric tests (Friedman test) were used to make statistical inference as T1 values in Base, Mid and Apex were not normally distributed. Friedman test was used to explore the difference between paired variables.

The mean (SD) of T1 Mapping-Base was 1255.08 ms (39.90). The median (IQR) of T1 Mapping-Base was 1253.20ms (23.70). The range of T1 Mapping-Base was 1162.30 - 1368.80ms.

The mean (SD) of T1 Mapping-Mid was 1260.91ms (47.97). The median (IQR) of T1 Mapping-Mid was 1252.50 ms (35.98). The range of T1 Mapping-Mid was 1141.50 - 1394.10ms.

The mean (SD) of T1 Mapping-Apex was 1293.88ms (49.95). The median (IQR) of T1 Mapping-Apex was 1287.50 ms (52.20). The range of T1 Mapping-Apex was 1189.50 - 1413.00ms.

The difference observed was statistically significant between Apex vs Base and Apex vs mid (Friedman Test: $\chi 2$ = 41.3, p = <0.001) as shown in (Table 11) and (Table 12).

The mean (SD) of T2 Mapping-Base was 46.05ms (2.81). The median (IQR) of T2 Mapping-Base was 45.80 ms (2.70). The range of T2 Mapping-Base was 38.80 - 54.10ms

The mean (SD) of T2 Mapping-Mid was 46.04 (2.24)ms. The median (IQR) of T2 Mapping-Mid was 46.30ms (3.18). The range of T2 Mapping-Mid was 40.40 - 49.40ms

The mean (SD) of T2 Mapping-Apex was 49.98 (2.53)ms. The median (IQR) of T2 Mapping-Apex was 50.20 (2.92)ms. The range of T2 Mapping-Apex was 43.30 - 55.40ms

The difference observed was statistically significant Apex vs Base and Apex vs mid (Repeated Measures ANOVA: F = 10.2, p = <0.001) as shown in (Table 13) and (Table14).

Discussion

Our study has reported the normal reference range of myocardial T1 and T2 values in healthy Indian subjects aged between 20-81 years using 3T scanner and have also tried to find age and gender dependence on T1 and T2 mapping values.

Table 6: Correlation Between T1 Mapping (Average) And Age (Years) (N = 50)

Correlation	Spearman Correlation Coefficient	P Value
T1 Mapping (Average) vs Age (Years)	-0.0	0.769

Table 5: Normal T1 And T2 Mapping Values And Relation To Age And Gender

T1 Mapping (Average)	Age					Kruskal Wallis Test	
	20-29 Years	30-39 Years	40-49 Years	50-59 Years	≥60 Years	χ2	p value
Mean (SD)	1270.92 (51.23)	1271.77 (42.55)	1266.57 (31.38)	1274.97 (29.92)	1264.29 (19.24)	0.880	0.927
Median (IQR)	1259.93 (1251.65-1271.1)	1269.67 (1259.43-1277.27)	1260.78 (1241.65-1286.2)	1275.1 (1253.9-1300.07)	1263.62 (1256.99-1270.92)		
Min - Max	1182.83 - 1374.87	1213.17 - 1379.97	1236.83 - 1344	1231.6 - 1310.17	1241.47 - 1288.47		

Table 7: Comparison of the 5 Subgroups of the Variable Age in Terms of T2 Mapping (Average) (n = 50)

T2 Mapping (Average)	Age					Kruskal Wallis Test	
	20-29 Years	30-39 Years	40-49 Years	50-59 Years	≥60 Years	χ2	p value
Mean (SD)	46.93 (1.15)	47.25 (1.42)	47.74 (1.38)	46.38 (2.02)	47.52 (1.64)		
Median (IQR)	47.07 (46.02-47.78)	47.67 (45.77-48.17)	47.6 (46.84-48.48)	46.57 (44.73-47.53)	48.1 (47.13-48.49)	3.803	0.433
Min - Max	45.07 - 48.8	44.83 - 49.17	45.7 - 50.5	44.07 - 49.5	45.13 - 48.77		

Table 8: Correlation between T2 Mapping (Average) and Age (Years) (n = 50)

Correlation	Spearman Correlation Coefficient	P Value
T2 Mapping (Average) vs Age (Years)	0.1	0.573

Table 9: Comparison of the 2 Subgroups of the Variable Gender in Terms of T1 Mapping (Average) (n = 50)

T1 Mapping (Average)	Gender		t-test	
	Male	Female	t	p value
Mean (SD)	1260.02 (28.27)	1287.62 (46.55)		
Median (IQR)	1260.57 (1243.1-1270)	1276.9 (1258.54-1307.48)	-2.289	0.031
Min - Max	1182.83 - 1344	1213.17 - 1379.97		

Table 10: Comparison of the 2 Subgroups of the Variable Gender in Terms of T2 Mapping (Average) (n = 50)

T2 Mapping (Average)	Gender		t-test	
	Male	Female	t	p value
Mean (SD)	47.07 (1.53)	47.46 (1.38)		
Median (IQR)	47.15 (45.76-48.22)	47.52 (46.87-48.15)	-0.927	0.360
Min - Max	44.07 - 49.6	44.83 - 50.5		

Table 11: Assessment of difference in paired variables for T1 Mapping (n = 50)

Variable	T1 Mapping			Friedman Test	
	Mean (SD)	Median (IQR)	Range	χ2	P Value
Base	1255.08 (39.90)	1253.20 (23.70)	1162.30 - 1368.80		
Mid	1260.91 (47.97)	1252.50 (35.98)	1141.50 - 1394.10	41.3	<0.001
Apex	1293.88 (49.95)	1287.50 (52.20)	1189.50 - 1413.00		

Table 12: Comparison of T1 mapping values in different cardiac segments

Comparison of T1 mapping values	Adjusted P-Value
Mid vs Base	0.978
Apex vs Base	<0.001
Apex vs Mid	<0.001

Table 13: Assessment of difference in paired variables for T2 Mapping (n = 50)

Variable	T2 Mapping			Repeated Measures ANOVA	
	Mean (SD)	Median (IQR)	Range	F	P Value
Base	46.05 (2.81)	45.80 (2.70)	38.80 - 54.10		
Mid	46.04 (2.24)	46.30 (3.18)	40.40 - 49.40	10.2	<0.001
Apex	49.98 (2.53)	50.20 (2.92)	43.30 - 55.40		

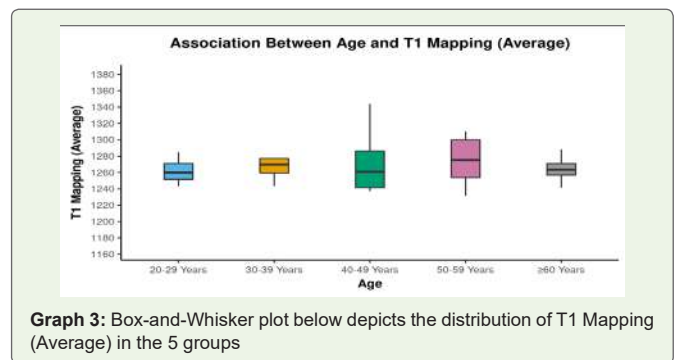Table 14: Comparison of T2 mapping values in different cardiac segments

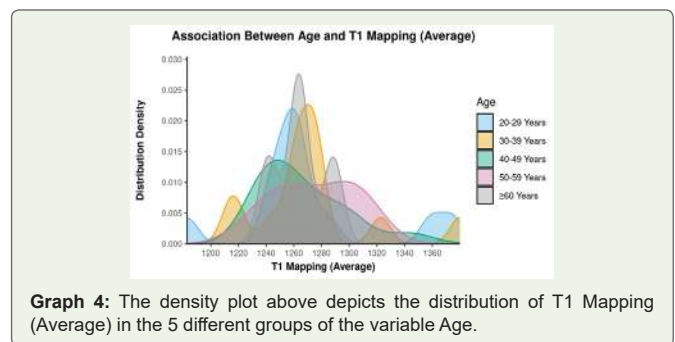| Comparison	Adjusted P-Value
Mid vs Base	0.999
Apex vs Base	<0.001
Apex vs Mid	<0.001
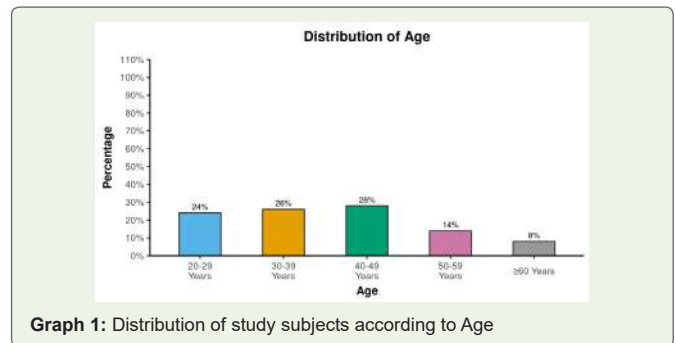
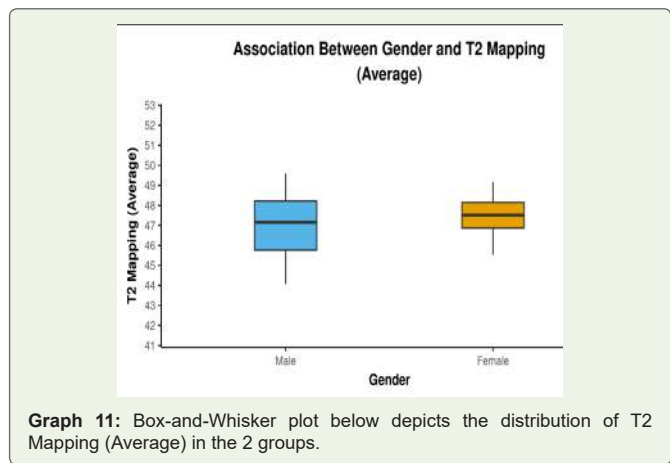**Graph 1:** Distribution of study subjects according to Age
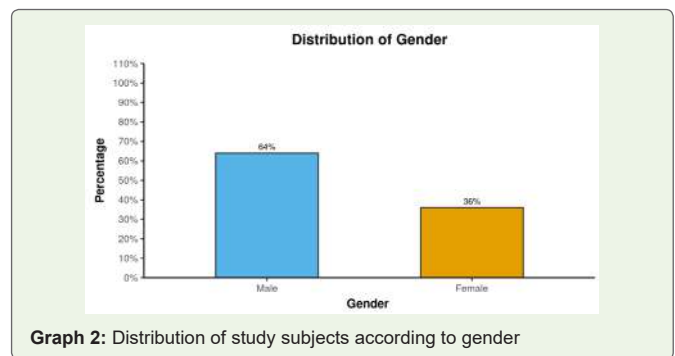
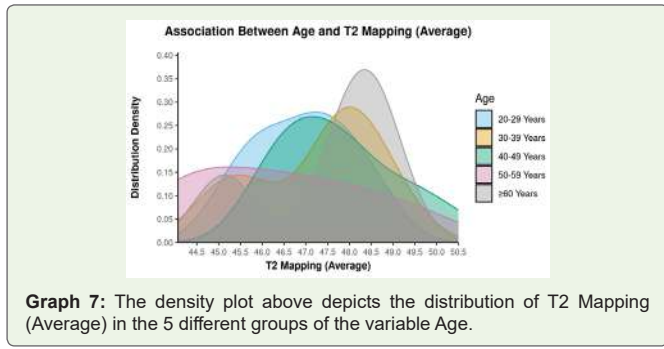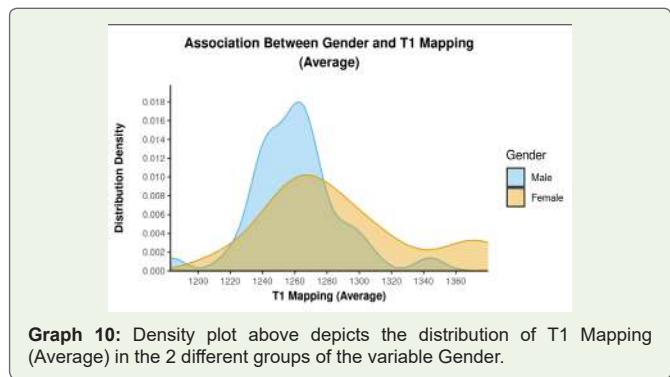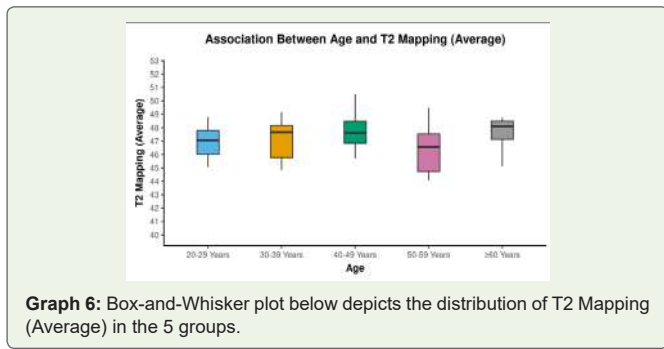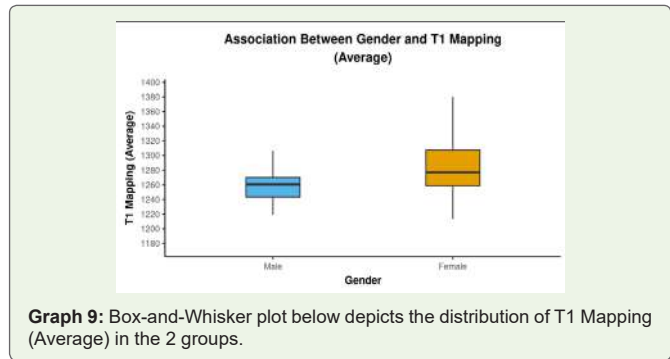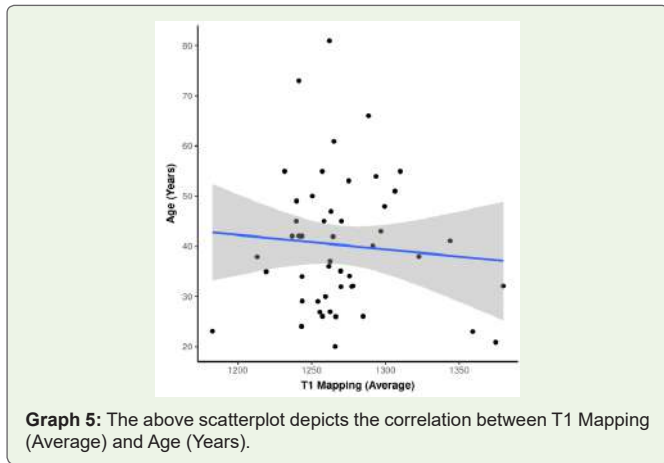**Graph 2:** Distribution of study subjects according to gender

Graph 3: Box-and-Whisker plot below depicts the distribution of T1 Mapping (Average) in the 5 groups

Graph 4: The density plot above depicts the distribution of T1 Mapping (Average) in the 5 different groups of the variable Age.

Graph 5: The above scatterplot depicts the correlation between T1 Mapping (Average) and Age (Years).

Graph 6: Box-and-Whisker plot below depicts the distribution of T2 Mapping (Average) in the 5 groups.

Graph 7: The density plot above depicts the distribution of T2 Mapping (Average) in the 5 different groups of the variable Age.

Graph 8: The above scatterplot depicts the correlation between T2 Mapping (Average) and Age (Years).
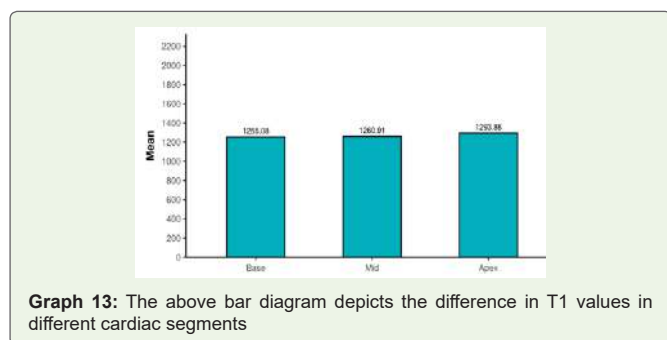

Graph 9: Box-and-Whisker plot below depicts the distribution of T1 Mapping (Average) in the 2 groups.

Graph 10: Density plot above depicts the distribution of T1 Mapping (Average) in the 2 different groups of the variable Gender.

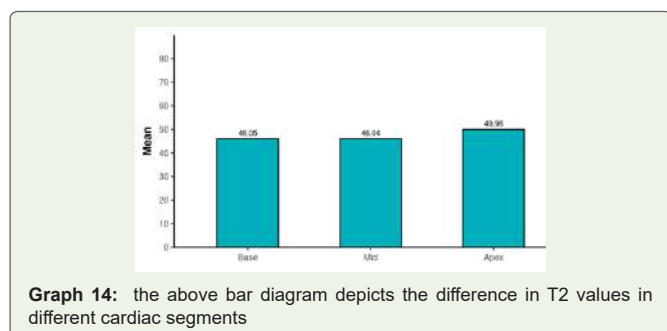**Graph 11:** Box-and-Whisker plot below depicts the distribution of T2 Mapping (Average) in the 2 groups.

Graph 12: Density plot above depicts the distribution of T2 Mapping (Average) in the 2 different groups of Gender.

Graph 13: The above bar diagram depicts the difference in T1 values in different cardiac segments

Graph 14: the above bar diagram depicts the difference in T2 values in different cardiac segments

The findings are summarized as follows:

1. Mean myocardial T1 and T2 mapping values using a 3T MRI scanner were found to be1269.96 ± 37.90 and 47.21 ± 1.47 ms respectively.

2. No correlation or association found between T1 and T2 mapping values with age.

3. Mean T1 mapping values were higher in females (1287.62 ± 46.55ms), however no statistically significant difference was found in T2 mapping values between the genders.

4. The meanT1 values in base, mid and apical segments were 1255.08 ± 39.90ms, 1260.91 ± 47.97ms and 1293.88 ± 49.95 ms respectively.

5. The mean T2 values in base, mid and apical segments were 46.05 ± 2.81, 46.04 ± 2.24 and 49.98 ± 2.53 ms respectively.

6. The mean T1 and T2 values in Apical segment were higher as compared to mid and base.

T1 values

The mean T1 mapping value of the study population was 1269.96±37.90ms with mean T1 value in males being 1260.02ms and females being 1287.62ms.

Higher mean T1 values were noted amongst females. Similar finding was noted by Clotilde Roy et al [6] where women were found to have higher T1 values as compared to men. Whereas Darius Dabir et al [5] and Stefan K Piechnik [8] did not find any statistically significant difference in T1 values between males and females in his study.

No statistically significant correlation or association was found

between the age groups and T1 values in our study. Darius Dabir et al [5] also did not find any difference in T1 values between study subjects belonging to different age groups however Clotilde Roy et al [6] found that T1 values increased with increased age. Stefan K Piechnik et al [8] contrary to this found that T1 values decreased with age.

In our study we found that T1 values were higher in the apical segments as compared to those in the base and mid. We however did not find a statistically significant difference in the T1 values in base and mid segments. Knobelsdorff-Brenkenhoff et al [9] noted that the T1 values successively increased from the base to apex and attributed it to Partial-volume effects owing to the curvature of the left ventricle with blood signal being included into the voxel.

T2 values

The mean T2 values of the study population were 47.21±1.47ms. The mean T2 value in males was 47.07±1.53ms and in females was 47.46±1.38ms.

There was no significant difference in T2 values amongst the two genders. Similar findings were also noted by Clotilde Roy et al [6] and Darius Dabir et al [5]. However, Florian Bönner et al [9] found that female volunteers displayed significantly increased median T2 values (p < 0.01 for each slice) as compared to males. She also found that, that the apico-basal T2 gradient was also significant in the aged heart for males (apical: 63.7 ± 4.7 ms; basal: 60.3 ± 4.6 ms, p < 0.01) and females (apical: 66.1 ± 5.4 ms; basal: 60.3 ± 3.7 ms, p < 0.01) whereas the differences in myocardial T2 between male and female within the slices disappeared.

In Florian Bönner et al's [10] study, older volunteers had raised T2 values compared to the respective sex and slice location in younger volunteers (all p < 0.01) whereas there was no correlation found between age and T2 values in our study. On the contrary Clotilde Roy et al [6] found that T2 values significantly decreased with increasing age. No association between age and T2 values was found in this study.

In our study just like T1 values were higher in the apical segments as compared to those in the base and mid, the same trend was observed with T2 values as well with higher t2 values recorded in apical segment. Knobelsdorff-Brenkenhoff et al [9] had reported a rising trend in T2 values from base to apex just like T1 values. We however could not demonstrate any statistically significant difference between base and mid segment T2 values.

Limitations

This was a single-centre hospital study using only 3T Philips Ingenia scanner. Comparison study has not been done to values that can be obtained using scanners of different manufacturers as cardiac mapping values may vary slightly in scanners of different manufacturers and at different magnetic field strength.

Conclusion

Our study found the normal reference range of T1 and T2 myocardial mapping in healthy Indian population relative to age and gender and cardiac segments.

We also found that no association or correlation was found between T1 and T2 mapping values and age signifying that age doesn't alter the tissue characteristics much.

Statistically significant difference was found between T1 mapping values in males and females with females having higher mean T1 mapping values and hence this should be kept in mind while interpreting T1 mapping values in females.

Statistically significant difference in T1 and T2 mapping values was found between apex and base and apex and mid segments with the apical segment showing higher T1 and T2 values. This may be attributed to the partial volume effects due to curvature of the left ventricle as explained by Knobelsdorff-Brenkenhoff et al. [9].

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