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Quantification of Liver Fat on 3T MRI: Comparison between MDIXON and MR Spectroscopy

Research Article

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Abstract

Objective: To calculate the hepatic fat fraction using mDIXON MRI sequence and to then compare it to the fat fraction calculated using MR Spectroscopy which is considered to be the gold standard for estimation of hepatic fat amongst imaging techniques. The aim was to find if mDIXON fat fraction values correlate with MR Spectroscopy fat fraction values.

Methods and Materials: 61 patients who were referred for MRI Liver to evaluate hepatic fat- fraction and who fulfilled the inclusion criteria were included in this study. All patients were subjected to MRI Liver scan on 3T MRI (Philips Ingenia) with fixed parameter specifications. Single reader assessed the images obtained using mDIXON and MR spectroscopy and post processing was done and fat fraction values were calculated using both the techniques.

Statistical Analysis: Used STATA software version 12(manufactured by Stata Corp LP, College Station, Texas).

Results & Conclusions: mDIXON fat fraction values showed a high degree of correlation with MR spectroscopy fat fraction values (correlation coefficient-0.975), signifying that mDIXON technique can be used in isolation to quantify hepatic steatosis.

Introduction

Non-alcoholic fatty liver disease is an emerging epidemic in our country with prevalence of approximately 9-32% [1]. NAFLD is closely related to metabolic syndrome, the prevalence of which is also continuously rising [2,3,4]. The spectrum of NAFLD ranges from simple steatosis, steatohepatitis to advanced fibrosis and cirrhosis [5]. Mortality rates are higher in patients with NAFLD than the general population due to cardiovascular complications, metabolic and liver related disorders. The increased cardiovascular risk correlates with the severity of steatosis [6, 7]. Accurate detection and treatment response are required owing to the systemic and hepatic complications associated with NAFLD.

Liver biopsy is considered to be the gold standard for diagnosis of NAFLD and confirming the presence of associated steatohepatitis. However, liver biopsy is an invasive procedure and other non-invasive imaging techniques can be used for diagnosis. Imaging techniques are frequently used for non-invasive assessment of hepatic steatosis- USG and CT are usually the first investigations undertaken and are routinely available but they lack sensitivity and accuracy in quantifying hepatic steatosis [8,9,10]. MR spectroscopy is considered

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to be the gold standard amongst imaging modalities in calculating hepatic fat fraction [11,12,13]. However MR spectroscopy can be done only one voxel at a time and does not scan the entire liver at once.

Hence the objective of this study is to calculate the hepatic fat fraction using mDIXON MRI sequence and to then compare it to the fat fraction calculated using MR Spectroscopy which is considered to be the gold standard for estimation of hepatic fat amongst MRI techniques. The aim is to find if mDIXON fat fraction values correlate with MR Spectroscopy fat fraction values.

Methods

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

61 healthy asymptomatic volunteers from age 28 to 72 were included in the study, 42.6 % (26) of volunteers were females and 57.4%(35) were males.

Inclusion criteria-Patients who have been diagnosed with Fatty Liver on ultrasonography or have been incidentally recognized to have Fatty Liver on CT.

Exclusion criteria

1) People with focal hepatic masses and known hepatic diseases

2) claustrophobic patients

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

4) pregnancy

All patients were subjected to an MRI Scan of the Abdomen on the 3T Philips IngeniaMRI Machine and the following sequences were acquired: mDIXON and MR Spectroscopy.

The patients were placed in the supine and headfirst position and underwent scanning with breath hold for 10 seconds for mDIXON sequence. MR spectroscopy sequence lasted for 20 seconds without any breath hold. ROIs in mDIXON sequence were made in the right lobe of liver and voxel was placed in a similar location for MR spectroscopy. No contrast was administered. All images were transmitted to the post-processing workstation. Few examples are shown as in (Figure 1 and 2).

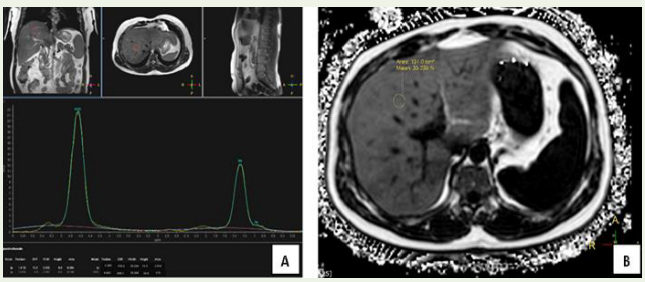


Figure 1: A) Shows MR spectroscopy fat fraction graph and B) mDIXON calculated fat fraction values in a patient with grade-III steatosis.

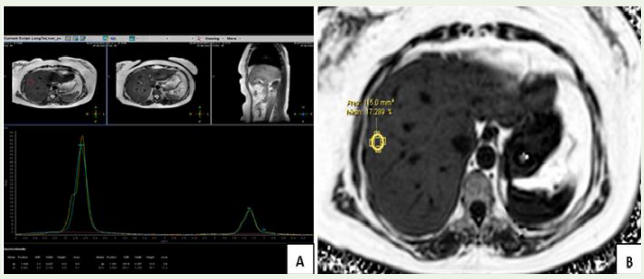


Figure 2: A) Shows MR spectroscopy fat fraction graph and B) mDIXON calculated fat fraction values in a patient with grade-II steatosis.

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 $p < 0.05$.

Results

When the current study tried to find association with MR Spectro and M-Dixon findings, it showed that the proportion of grades among both techniques as similar.

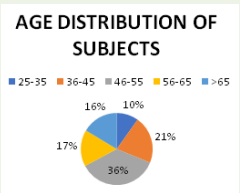
Tests of Normality

The present study checked for the normality of the fat fraction values using M-Dixon and MR Spectro techniques using Shapiro-Wilk test(as samples are less) and found that the values doesn't follow normal distribution.(as p value <0.05)

Correlation between M-Dixon and Mr Spectroscopy

As the study population fat fraction values doesn't follow normal distribution, a non-parametric test, Spearman's rho was done.

As the fat fraction values in both M-Dixon & MR spectroscopy didn't follow a normal distribution, non-parametric tests were used to find out the correlation. The current study used Spearman rho correlation test which found correlation co-efficient to be 0.975, representing that there is strong correlation between M-Dixon technique with MR-Spectroscopy in determining fat fraction values.



Graph 1: Pie chart showing age group distribution among the study population

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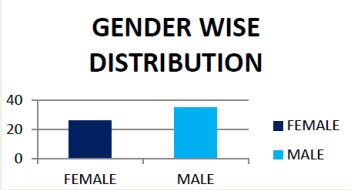
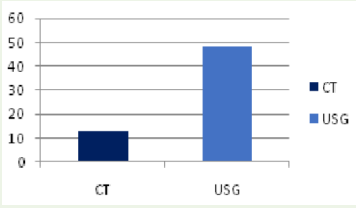
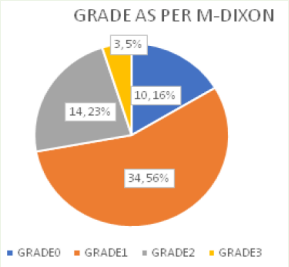


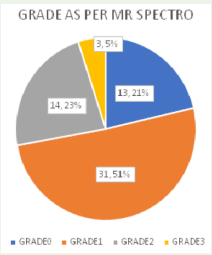
Graph 2: Bar Chart Showing Gender Distribution among the Study Population



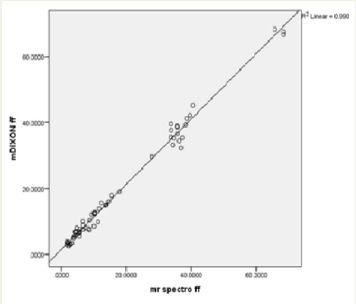
Graph 3: Bar Graph Showing Previous Investigations.



Graph 4: Pie Chart Showing Grade as Per M-Dixon.



Graph 5: Pie Chart Showing Grade as Per MR-Spectroscopy.



Graph 6: Spearman Rho Correlation Test Which Found a Correlation Co-Efficient Of 0.975.

Table 1: Summary of Imaging Parameters

PARAMETER	mDIXON
FOV	400 X 350
VOXEL SIZE	2.5 X 2.5 X 6
TR/TE/delta TE	5.6/0.97/0.7
SECTION THICKNESS	6mm
INTERSECTION GAP	-3
ECHOS	6
NUMBER OF SLICES	77
BREATH HOLD TIME	10 seconds
PARAMETER	**MR SPECTROSCOPY**
VOXEL SIZE	30 X 30
SPECTRAL RESOLUTION	1.95
SOUND PRESSURE LEVEL	-8.7
SPECTRAL BW(Hz)	2000

Table 2: Distribution of Age Groups amongst Study Population

		Frequency	Percent
AGE GROUPS	25-35	6	9.8
	36-45	13	21.3
	46-55	22	36.1
	56-65	10	16.4
	>65	10	16.4
	Total	61	100.0

Table 3: Distribution of Gender among Study Population

		Frequency	Percent
GENDER	FEMALE	26	42.6
	MALE	35	57.4
	Total	61	100.0

Table 4: Showing Prior Investigation in Patients

PRIOR INVESTIGATION	NO.OF STUDY SUBJECTS
USG	**48**
CT	**13**

Table 5: Table Showing Grade as Per M-Dixon

		Frequency	Percent
	GRADE0	10	16.4
	GRADE1	34	55.7
	GRADE2	14	23.0
	GRADE3	3	4.9
	Total	61	100.0

Table 6: Table Showing Grade as Per Mr Spectroscopy

	Frequency	Percent
GRADE0	13	21.3
GRADE1	31	50.8
GRADE2	14	23.0
GRADE3	3	4.9
Total	61	100.0

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Table 7: Grade as Per M-Dixon * Grade As Per Mr Spectro Cross Tabulation

		GRADE AS PER MR SPECTRO				Total
		GRADE0	GRADE1	GRADE2	GRADE3	
GRADE AS PER M-DIXON	GRADE0	8	2	0	0	10
	GRADE1	5	28	1	0	34
	GRADE2	0	1	13	0	14
	GRADE3	0	0	0	3	3
Total		13	31	14	3	61

When the current study tried to find association with MR Spectro and M-Dixon findings, it showed that the proportion of grades among both techniques as similar.

Table 8: Tests of Normality

Tests of Normality						
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
M-DIXON ff	.222	61	.000	.806	61	.000
MR Spectro ff	.227	61	.000	.792	61	.000

The present study checked for the normality of the fat fraction values using M-Dixon and MR Spectro techniques using Shapiro-Wilk test(as samples are less) and found that the values doesn't follow normal distribution.(as p value <0.05)

Table 9: Correlation between M-Dixon and Mr Spectroscopy

Correlations				
			mDIXON ff	mrspectro ff
Spearman's rho	M-DIXON ff	Correlation Coefficient	1.000	.975**
		Sig. (2-tailed)	.	.000
		N	61	61
	MR spectro ff	Correlation Coefficient	.975**	1.000
		Sig. (2-tailed)	.000	.
		N	61	61
**. Correlation is significant at the 0.01 level (2-tailed).				

As the study population fat fraction values doesn't follow normal distribution, a non-parametric test, Spearman's rho was done.

Discussion

In our study of 61 patients ,42.6%(26) were females and 57.4%(35) were males .The mean age of the study population was 50.99+/-11.42 years with maximum age being 72 years and minimum age being 28 years . Maximum number of participants belonged to 46-55 years age group (36.1%, 22 patients).

Out of the 61 patients included in our study, 48 patients had underwent USG Abdomen prior and

33(68.75%) patients were diagnosed as grade I, 14(29.16%) as grade II and 1(2.08%) as grade III steatosis as per ultrasonography findings. 13 patients were incidentally detected with hypodense liver on plain CT scan for CT abdomen or during HRCT Chest.

In this study using mDIXON Quant we found that out of 61 patients ,34 patients (55.7%) had grade I steatosis followed by 14 patients (23%) having grade II steatosis. Similar results were found using MR spectroscopy where 31 patients (50.8%) had grade I steatosis and 14 patients (23%) had grade II steatosis. Three patients had grade III steatosis as per both mDIXON and MR spectroscopy.

Our study population fat fraction values did not follow normal distribution (Normality was checked using Shapiro-Wilk test) and hence Spearman's rho test (Non parametric test) was done. The correlation coefficient between mDIXON and MR spectroscopy fat fraction values was 0.975 indicating a very strong correlation between the two techniques.

Guido M Kukuk [14] in their study consisting of 59 patients with liver disorders found that there was excellent correlation between 6E mDIXON and MR spectroscopy (mean difference 0.03%) with R= 0.984 which is closely resembles the correlation coefficient of 0.975 found in our study. In their study Guido et al had also compared 6E mDIXON with histology and had found a strong correlation with R=0.941 ,we however had not conducted invasive biopsies in our patients , but this suggests that 6E Dixon sequences like mDIXON Quant have excellent correlation with histopathology as well. They had also compared dual echo mDIXON with six echo mDIXON and had found that Dual echo mDIXON yielded lower PDFF values than six echo mDIXON (mean difference 1.0%,p<0.001) showing that 6 echo mDIXON is more accurate .

Mazen Noureddin et al[15] in a study consisting of 50 patients with biopsy proven NAFLD conducted the study at 0 and 24 weeks and found a robust correlation of MRI-PDFF with MRS-PDFF at 0 and 24 weeks with r=0.98 and p<0.001. Noureddin also commented that patients who had decrease (≥1%) or increase in MRI-PDFF that was confirmed with MRS-PDFF showed a parallel decrease or increase in body weight and serum SGOT and SGPT levels at 24 weeks. This small increase or decrease in liver fat could not be quantified with histology and hence concluded that MRI-PDFF was more sensitive than histology in quantifying hepatic steatosis.

Similar findings were also reported by Yu-Zhen Zhao et al[16] who studied prevalence of NAFLD in overweight and obese Chinese children and adolescents and found an excellent correlation between MRI PDFF values and MRS PDFF values with r=0.973 and p<0.01 when MRI-PDFF was measured with ROI corresponding to the MRS voxel. Bland-Altman analysis demonstrated a good agreement between these two methods.

Boris Guiu et al[17] found that the correlation between triple echo with low flip angle PDFF sequence and MR spectroscopy for hepatic fat quantification was statistically significant with Pearson correlation coefficient of 0.989 (p<0.0001) when he conducted a study in 37 patients with Type II Diabetes Mellitus.

In a similar study conducted by Kim Nhien Vu et[18],seven echo spoiled gradient echo PDFF sequence and MR spectroscopy was compared and it found that 7 echo MRI-PDFF excellently correlated with MRS with interclass correlation coefficient of 0.916.

Study of accuracy of MRI-PDFF using 2 echo, 3echo and 6echo methods was done by Takeshi Yokoo[19] in their study using MRS PDFF as the reference standard [47]. Regression slope of 2,3 and 6 echo PDFF methods were 0.8522,0.8528 and 0.7544 without multifrequency modelling and 0.9994,0.9775 and 0.9821 with multifrequency modelling. Classification accuracy was 88.3-92%, 95.1-96.3% and 94.5-96.3% respectively using multifrequency modelling. All these results pointed out that MRI-PDFF technique is an accurate method of determining hepatic fat fraction.

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Mona Zaky et al[20] in their study compared mDIXON fat fraction values with histology and found that estimation of fat fraction using mDixon method revealed sensitivity of 83.3% and specificity of 85.7% compared to liver biopsy results.

Ilkay S. Idilman et al [21] in their study comprising of 70 patients with NAFLD concluded that there was close correlation between multiecho MRI PDFF and liver biopsy (r=0.82) and PDFF was successful in differentiating moderate or severe steatosis from mild steatosis with area under the curve of 0.95. The correlation between MRI PDFF and histology was lesser when fibrosis was present (r=0.60) than when fibrosis was absent (r=0.86) suggesting that presence of fibrosis reduced the accuracy of MRI PDFF.

Limitations

There are a few limitations of this study:

1. Histological confirmation for grading of fatty liver was not done.
2. This was a single-center hospital study. Our results might not be applicable to other geographic location within the country with different sociocultural habits.
3. No follow up of patients was done with volunteers undergoing measures to reduce fatty liver.
4. Inter and intra-reader comparison of mDIXON values and MR spectroscopy fat fraction values processing was not done.

Conclusion

mDIXON fat fraction values showed a high degree of correlation with MR spectroscopy fat fraction values (correlation coefficient-0.975), signifying that mDIXON technique can be used in isolation to quantify hepatic steatosis.Statistically significant association was found between fat fraction values using both techniques.

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