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## **PROJECT COMPLETION REPORT**

1. **Project Number** : 6110
2. **Title of the Project** : TITLE OF THE PROJECT/WORK ?ROLE OF INTRAVOXEL INCOHERENT MOTION IMAGING (IVIM) IN POST TRANSARTERIAL CHEMOEMBOLISATION (TACE) RESPONSE EVALUATION OF HEPATOCELLULAR CARCINOMA(HCC)
3. **Funding Agency Name** : SCIENCE & ENGINEERING RESEARCH BOARD
4. **Project Reference Number provided by the Funding Agency:**  
Dr Jineesh , Associate professor , IS and IR, SCTIMST
5. **Principal Investigator (Name & Address) :**  
Dr Jineesh , Associate professor , IS and IR, SCTIMST
6. **Co-Investigators (Name & Address):**
  - i. **i. Dr Anoop Associate professor**  
IS and IR  
SCTIMST
  - ii. **Dr Santhosh Kannath**  
Professor , IS and IR
  - i.

ii.

7. **Implementing Institution** : SCTIMST

8. **Collaborating Institutions** :

9. **Date of Commencement** : 14/06/2019

10. **Duration** : 2 YEARS

11. **Date of Completion** : 13/06/2021

12. **Objectives as approved :**

assess the feasibility and efficacy of intravascular incoherent motion imaging (IVIM) in response evaluation of HCC after TACE

13. **Deviation made from original objectives if any, while implementing the project and reasons thereof :**

No deviation

14. **Field/Experimental work giving full details of summary of methods adopted, data collected supported by necessary tables, charts, diagrams and photographs :**

Ours was a prospectively designed study done all the consecutive cirrhotic Child Pugh A and B patients with HCC referred to the interventional radiology department for TACE from April 2018 to March 2020. The institutional ethics approval was obtained and informed consent taken from all patients. The inclusion criteria included cirrhotic HCC with Child Pugh A or B with BCLC A or B with MRI/CT showing arterial phase enhancement and venous washout. The exclusion criteria were liver lesions <1cm, INR >1.7, platelet count <50000/dL and patients not giving consent. A total of 39 patients (48 lesions) fulfilling the criteria were selected (Figure 1). PreTACE MRI with IVIM was done within one week before TACE and six weeks after the procedure in a 3T MR scanner (Discovery; General electric GE healthcare; USA) using 32 channel phased array coils. Post TACE lesions were classified into based on

LIRADS response assessment(LIRADS-LR) into LR-TR nonviable and LR-TR viable lesions<sup>11</sup>.LR-TR non-viable (group1) is defined as complete absence of arterial enhancement in the post TACE MRI. Lesions showing residual nodular arterial enhancement with venous washout was considered as LR-TR viable (group 2).

MR sequences including axial breath hold fat suppressed T1W, respiratory triggered T2FS of the upper abdomen and multiphase dynamic contrast enhanced MRI including arterial phase, venous phase and delayed phase were obtained . The IVIM sequences [TR-2500ms, TE69.6ms, FOV 420X420mm, matrix128x160, slice thickness 5mm, b values (0,50,100,200,400,600,800)] were acquired by respiratory gating using spin echo-planar sequence. Post-processing of IVIM was performed by loading the 7 b values in Osirix MD software using biexponential fit method. A 2D free hand ROI was drawn in tumour in all slices and average values were obtained obtain the mean b value as described by Murtz et al<sup>12</sup>. Image analysis was done by a single radiologist (J.V) having 10 year experience in DWI imaging and blinded to the subject disease status. Parameters including true diffusion (Dslow), pseudo diffusion (Dfast), perfusion fraction (f) and ADC were generated in pre and post TACE cases(Figure 3). Since a few patients had multiple lesions , all the lesions were evaluated

#### TACE procedure

All patients underwent femoral arterial access with 5F arterial sheath and angiogram of superior mesenteric artery, coeliac artery and inferior phrenic artery were done using 5F diagnostic catheter . Superselective cannulation of the lesions were done by 2.7F progreate microcatheter (Terumo.Japan) .The lesions were treated using 60mg epirubicin mixed with 20 ml lipiodol till maximum uptake and segmental artery temporarily embolised by thin gel foam . In cases with suspected extrahepatic supply bases on MRI ( capsular extension ) angiogram of extrahepatic feeders were obtained All the extrahepatic supply to the lesion was

embolised in the initial setting. The completion of the embolization was checked by 3D rotation angiogram to ensure complete uptake of lipiodol by the entire lesion

### ***Statistical analysis***

Descriptive analysis of the patients were done. The mean preTACE and postTACE values of IVIM parameters were compared using paired t-test. Post TACE values of non viable and viable groups were compared using the t-test of unequal variances. Mean differences between preTACE and postTACE values IVIM parameters were calculated and compared between both groups using a t-test of unequal variances. An ROC analysis was done to find the sensitivity and specificity of each of IVIM parameters. All the statistical analysis were performed using SPSS software (version 20).

### **15. Detailed analysis of results :**

Of the total 48 lesions, 34 lesions showed complete response( LR-TR non-viable/group 1) and 14 lesions showed viable lesions( LR-TR viable/ group 2) with a complete response rate of 70.8%.

The pre TACE values of Dslow, Dfast, ADC and perfusion fraction in group 1 were  $1.208 \pm 0.581 \times 10^{-3} \text{mm}^2/\text{s}$ ,  $33.7 \pm 10.406 \times 10^{-3} \text{mm}^2/\text{s}$ ,  $1.37 \pm 0.5302 \times 10^{-3} \text{mm}^2/\text{s}$  and  $19.92 \pm 10.54$  and for group 2 was  $1.241 \pm 0.237 \times 10^{-3} \text{mm}^2/\text{s}$ ,  $31.63 \pm 11.266 \times 10^{-3} \text{mm}^2/\text{s}$ ,  $1.258 \pm 0.275 \times 10^{-3} \text{mm}^2/\text{s}$  and  $18.52 \pm 6.58$  respectively. There was no statistical difference in the pretreatment values between both groups [t-Test for independent samplest  $p = .116$ (for Dslow),  $p = .625$  (Dfast),  $p = .545$ (ADC) and  $p = .542$  (perfusion fraction)].Group 1 showed a significant increase in Dslow ( $1.208 \pm 0.581$  vs  $1.560 \pm 0.494$ ,  $p$ -value-  $0.0207$ ) and ADC ( $1.37 \pm 0.53$  vs  $1.65 \pm 0.4287$ ,  $p$  value  $0.016$ ) after TACE. There was also significant

decrease in Dfast (33.7 +/- 10.4 vs 23.75 +/- 12.13, p value 0.0005) and f (19.92 +/- 10.54 vs 12.9 +/- 10.41, p value 0.012) values after TACE in group 1 .In group 2 Dslow, ADC, Dfast and perfusion fraction showed no significant change (Table 2).

The absolute and percentage change in the IVIM parameters were calculated in both groups ( Table 3/figure 3 ). Dslow showed the highest significance in p values(0.031) among the parameters of IVIM in paired t-test compared to Dfast , ADC and perfusion fraction. Group 1 had higher values for the variable percentage change in Dslow (M = 45.21, SD = 58.65) than the 2 group (M = 3.52, SD = 25.15).. A t-test for independent samples (equal variances assumed) showed this difference was statistically significant,  $t(30) = 2.14$  ,  $p = .04$  , 95% Confidence Interval .The percentage change in ADC between group 1 (M = 28.54, SD = 36.1) was higher than the 2 group (M = 10.69, SD = 15.94) but was not statistically significant,  $t(30) = 1.94$ ,  $p = .062$ , 95% Confidence Interval [-0.94, 36.63]. The 1 group had lower values for percentage change in perfusion (M = -38.64, SD = 43.08) than the 2 group (M = 14.85, SD = 83.66) but was not statistically significant,  $t(11.23) = -1.91$ ,  $p = .082$ .

The change in Dslow had the highest AUC(0.741) among IVIM parameters with greater than 0.075 increase between preTACE and postTACE values having a sensitivity and specificity of 81.8% and 60% respectively to differentiate LRTR viable from nonviable lesions . ADC increase of  $0.23 \times 10^{-3} \text{mm}^2/\text{s}$  showed an AUC of 0.64 with a sensitivity of 54% and specificity of 90% for detecting viable from non-viable lesions (Figure 4).

Sub analysis of the group showed that Among 24 BCLC A lesions, 22 were LR-TR non viable and two were viable . Of 24 BCLC B lesions, half the lesions (12) were LRTR non-viable, while the remaining half were viable (Table 4) .The relationship between BCLC category and response was statistically significant (P-value- 0.02, indicating that complete response was higher for BCLC A lesions

**16. Summary sheet of not more than 2 pages under following heads :**

**(Title, Introduction, Rationale, Objectives, Methodology, Results, Translational Potential)'**

**Role of Intravoxel incoherent motion (IVIM) imaging in response assessment of Hepatocellular carcinoma after trans-arterial chemoembolization (TACE)- a prospective study**

Response evaluation of hepatocellular carcinoma (HCC) currently is based on arterial phase enhancement which doesn't take into microstructural changes in the tumor after trans-arterial chemoembolization (TACE)

**Aim** -This prospective study was conducted to assess the feasibility and efficacy of intravascular incoherent motion imaging (IVIM) in response evaluation of HCC after TACE. 39 cirrhotic patients with 48 HCC underwent MR imaging 1 week within and 6 weeks after TACE. IVIM parameters like  $D_{slow}$  (true diffusion),  $D_{fast}$  (pseudodiffusion), perfusion fraction and ADC were measured prior to and postTACE. The pre and post TACE values in LR-TR(LIRADS – treatment response) nonviable and viable lesions were compared using paired t-tests. ROC curve analysis was done to calculate sensitivity and specificity and propose cut-off values.

**Result** -Non-viable lesions showed a significant increase in  $D_{slow}$  (1.208 +/- 0.581 vs 1.560 +/- 0.494, p-value- 0.0207) and ADC ( 1.37 +/- 0.53 vs 1.65 +/- 0.4287, p value 0.016) after TACE. There was also significant decrease in  $D_{fast}$  (33.7 +/- 10.4 vs 23.75 +/- 12.13, p value 0.0005) and  $f$  (19.92 +/- 10.54 vs 12.9 +/- 10.41, p value 0.012) values after TACE in non-viable lesions compared to viable lesions. The change in true diffusion had the highest AUC(0.741) among IVIM parameters with greater than 0.075 increase between preTACE and postTACE values having a sensitivity and specificity of 81.8% and 60% respectively for complete response

**Conclusion** -IVIM imaging is feasible to assess the response in HCC after TACE. True diffusion is more sensitive and specific than apparent diffusion in evaluating the response

**17. Contributions made towards increasing the state of knowledge in the subject :**

Increased the awareness of IVIM in HCC

**18. Conclusions summarising the achievements and indication of scope for future work :**

IVIM imaging is feasible to assess the response in HCC after TACE. True diffusion is more sensitive and specific than apparent diffusion in evaluating the response

**19. Science and Technology benefits accrued :**

**a. List of research publications with complete details :**

Reddy Bursapalle M, Valakkadaa J, Ayappan A. Role of intravoxel incoherent motion (IVIM) imaging in response assessment of hepatocellular carcinoma after transarterial chemoembolization (TACE) – A prospective study. Radiología (English Edition) [Internet]. 2023 Mar 3

**b. Manpower trained on the project :**

<b>i. Research Scientists or Research Fellows</b>	:	
<b>ii. No. of PhD's produced</b>	:	
<b>iii. Other Technical Personnel trained</b>	:	<b>1</b>
<b>c. Patents taken, if any</b>	:	<b>NIL</b>
<b>d. Products developed, if any</b>	:	<b>NIL</b>

**20. Abstract: (In 300 words for possible publication in ..... Bulletin)**

**a.** Response evaluation of hepatocellular carcinoma (HCC) currently is based on arterial phase enhancement which doesn't take into microstructural changes in the tumor after trans-arterial chemoembolization (TACE)

Aim -This prospective study was conducted to assess the feasibility and efficacy of intravascular incoherent motion imaging (IVIM) in response evaluation of HCC after TACE.

39 cirrhotic patients with 48 HCC underwent MR imaging 1 week within and 6weeks after TACE. IVIM parameters like Dslow (true diffusion ), Dfast (pseudodiffusion ), perfusion fraction and ADC were measured prior to and postTACE . The pre and post TACE values in LR-TR(LIRADS – treatment response) nonviable and viable lesions were compared using paired t-tests. ROC curve analysis was done to calculate sensitivity and specificity and propose cut-off values.

Result -Non-viable lesions showed a significant increase in Dslow (1.208 +/- 0.581 vs 1.560 +/- 0.494, p-value- 0.0207) and ADC ( 1.37 +/- 0.53 vs 1.65 +/- 0.4287, p value 0.016) after TACE . There was also significant decrease in Dfast (33.7 +/- 10.4 vs 23.75 +/- 12.13, p value 0.0005) and f (19.92+/- 10.54 vs 12.9 +/- 10.41, p value 0.012) values after TACE in non-viable lesions compared to viable lesions . The change in true diffusion had the highest AUC(0.741) among IVIM parameters with greater than 0.075 increase between preTACE and postTACE values having a sensitivity and specificity of 81.8% and 60% respectively for complete response

Conclusion -IVIM imaging is feasible to assess the response in HCC after TACE. True diffusion is more sensitive and specific than apparent diffusion in evaluating the response

**d. Details of Equipment:nil**

No.	Sl.
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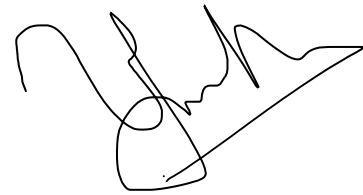
**21. Procurement/Usage of Equipment:**

**a.**

	Name of Equipment	Make/ Model	Cost (Rs.)	Date of Installation	Utilisation	Remarks regarding maintenance breakdown

S u g g e s t i o n s f o r d i s p o s a l o f e q u i p m e n t ( s):						

b.



21/11/23

(Name and Signature of PIs with date)

**Routing:** Signed copy of "Project completion Report" by PI → [root@sctimst.ac.in](mailto:root@sctimst.ac.in), [rpc@sctimst.ac.in](mailto:rpc@sctimst.ac.in)