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A Novel Method for Non-Invasive Diagnosis of Hepatitis C Virus Using Electromagnetic Signal Detection: A Multicenter International Study

Gamal Shiha, Waleed Samir, Zahid Azam, Premashis Kar, Saeed Hamid, Shiv Sarin

***Abstract*—**A simple, rapid and non-invasive electromagnetic sensor (C-FAST device) was- patented; for diagnosis of HCV RNA. Aim: To test the validity of the device compared to standard HCV PCR. Subjects and Methods: The first phase was done as pilot in Egypt on 79 participants; the second phase was done in five centers: one center from Egypt, two centers from Pakistan and two centers from India (800, 92 and 113 subjects respectively). The third phase was done nationally as multicenter study on (1600) participants for ensuring its representativeness. Results: When compared to PCR technique, C-FAST device revealed sensitivity 95% to 100%, specificity 95.5% to 100%, PPV 89.5% to 100%, NPV 95% to 100% and positive likelihood ratios 21.8% to 38.5%. Conclusion: It is practical evidence that HCV nucleotides emit electromagnetic signals that can be used for its identification. As compared to PCR, C-FAST is an accurate, valid and non-invasive device.

***Keywords*—**C-FAST- a valid and reliable device, Distant cellular interaction, Electromagnetic signal detection, Non-invasive diagnosis of HCV.

I. Introduction

HEPATITIS C virus (HCV) is considered a major cause of chronic liver disease and cirrhosis, resulting in hepatocellular carcinoma and liver failure [1]. HCV is a single-strand, positive sense RNA virus with a genome of approximately 10.000 nucleotides coding for 3000 amino acids [2]. The global prevalence of HCV infection, as determined by immunoserology, ranges from 1.0% in Europe to 5.3% in Africa. At least 6 major HCV genotypes are identified [3].

Many assays are available for detecting (qualitative assays) or measuring (quantitative assays) HCV RNA [4]. Detection and quantitation of HCV RNA by PCR nucleic acid amplification offers a measure of active viremia. Using PCR, it is possible to detect HCV viremia prior to immunological sero-conversion [5] and to detect changes in the viral load in anti-body-positive chronic HCV infected patients undergoing therapy with interferon [6].

It is well accepted that all objects, whether living or nonliving, are continuously generating electromagnetic fields (EMFs) due to the thermal agitation of their particles that possess charges [7]. Interest in EMFs as alternative forms of cell-to-cell communication can be traced back to at least the second decade of the 20th century [7]. Interactions between EMFs and bio-systems have been intensively studied for over a century and a quantitative understanding of many interaction mechanisms exists [8], [9]. There is much evidence that biological processes can be induced or modulated by induction of light of characteristic frequencies [10].

Recently, distant interactions between mammalian cells through EMF coupling have been shown [11]. Distant (non-chemical) interaction in biosystems is not limited to interactions at the cellular level. Biosystem interaction has been reported at the level of plants, insects and other biosystems [7], [12].

In 1997 Cosic proposed that there is a resonant interaction between macromolecules that plays an essential role in their bioactivity. The key point of Cosic's finding is the assignment of specific spectral electromagnetic (EM) characteristics of proteins to their specific biological function [13]. Proteins with common biological functionality are known to share one significant peak, called the Consensus Frequency, which is acknowledged to represent the region responsible for the biological functionality [14]. Bio-molecules with the same biological characteristics recognize and bio-attach to themselves when their valence electrons oscillate and then reverberate in an electromagnetic field [15]. Protein interactions can be considered as resonant energy transfer between the interacting molecules [10], [15]. In simple words each protein and biomolecule has its fingerprint electromagnetic characteristics that can be used for its identification [13]. In living systems long-range electromagnetic fields exchange messages across a distance because of matching emissions and absorption spectra. Non-resonating, unwanted random signals are excluded simply because they do not resonate [7], [16].

There has been considerable interest in bacterial communities wherein a bacterium is connected to neighboring bacteria by means of narrow nanowires [17], [18]. It is believed that the purpose of the nanowires is to allow for intercellular electronic communications. More advanced on

Gamal Shiha is with the Internal Medicine Department, Mansoura University, Egypt and head of the Egyptian Liver Research Institute And Hospital (ELRIAH) (phone: +201223280501; Fax: +20502217900; e-mail: g_shiha@hotmail.com).

Waleed Samir is with the Egyptian Liver Research Institute And Hospital (ELRIAH) (e-mail: elharamin_ws@yahoo.com).

Zahid Azam is with the National institute of liver & GI diseases, Pakistan (e-mail: zahid.azam@aku.edu).

Premashis Kar is with the Department of medicine, Maulana Azad medical college, India (e-mail: premashishkar@gmail.com).

Saeed Hamid is with the Department of medicine, The Aga Khan University & hospital, Pakistan (e-mail: saeed.hamid@aku.edu).

Shiv Sarin is with the Institute of Liver and Biliary Sciences, India (e-mail: shivsarin@gmail.com).

the evolutionary scale are the more modern bacterial communities which are wireless. The electromagnetic signal sent from a bacterium to neighboring bacteria can be due to relatively low frequency electron level transitions within the DNA [19].

Accordingly, since cells and biological systems can communicate directly with each other using a form of an electromagnetic signal, would it be possible to record and replay these signals using a device? The precise direct measurement of biological EMFs has not been accomplished yet and modern sensors can provide only some threshold conditions for measurement of biological EMF [20].

The C-FAST device (patent PCT/EG2010/000044) is a biological sensor or detector in which the resonant electromagnetic energy of HCV RNA is recorded as a consensus frequency that is a molecule signature or HCV nucleic acid electromagnetic fingerprint [21]. This recorded signal is used for the detection of its identical EM match.

This particular study is designed to demonstrate the development and mode of action of the C-FAST device and extends to explore the proposed hypothesis of its relevance, accuracy and reliability in clinical practice.

II. Subjects and Methods

The present study was conducted to answer a very important question "Is the evidence about the accuracy of C-FAST as a diagnostic test is VALID so that we can apply it to specific subjects?

A. To Answer This Research Question, The Methodology Used for Measurements Guarantee the Following

1. Representative

The C-FAST device was assessed in an appropriate spectrum of patients as was revealed in the study during its three phases taking into consideration sufficient sample size of cases and their free contacts, different ages and sexes, disease severity: Mild, severe, early or late cases, both treated and untreated and even for patients with different disorder that might be associated with HCV (as HBV).

Throughout the study phases, there was an independent, blind comparison with the reference Gold Standard "PCR".

2. Reproducibility

The device was validated by two independent investigators for the same patients during the second phase of the study.

B. Study Setting

The study is composed of three phases:

1. The First Phase

A national pilot study on a total of 79 male individuals aged 18 – 23 years. Subjects were recruited from the military camp, Ministry of Defense, Abbasia - Cairo, Egypt. This phase was completed in September 2010.

2. The Second Phase

It was conducted in five local and international centers: Hepatology clinics of ELRIAH -Egypt, two centers in Pakistan and two in India.

This phase started in October 2010 and completed in February 2011. For Egypt, a total of 800 Egyptian individuals were included in the present validation study (789 male and 11 female) with age ranged from 26 – 61 years. In India, a total of 112 subjects genotype 1& 3 were recruited; 24 subjects genotype 3 from Maulana Azad Medical College and 88 subjects genotype 1&3 from institute of liver and biliary science. The age ranged from 22-53 years, of which 97 males and 15 females. In Pakistan a total of 92 subjects genotype 3 were recruited, 30 subjects from the Aga Khan University and Hospital and 62 subjects from Dow University Hospital. The age range was 30-55 years, of which 80 males and 12 females.

As a biological question, does the sensitivity and predictive values of C-FAST device as valid and reliable test allow it to be used as screening and diagnostic tool for HCV infection?

The pilot studies found that C-FAST sensitivity in diagnosis = 100 %, specificity=97.3 %, PPV = 89.3

Best guess for sensitivity of C-FAST device is 100 % as evident from the previous results of the two Egyptian pilot studies.

Best guess for false negative predictive value is 0% as evident from the previous results of the two Egyptian pilot studies.

Best guess for false positive predictive value is less than 0% as evident from the previous results of the two Egyptian pilot studies.

Actual false positive predictive value from the previous pilot study was 2.2 % as the specificity was 97.8 %.

Type I error is statistical test with 5% type I error (Alpha) is desired.

Type II error is statistical test with 5 % type I error (Beta) is desired as no difference from the pilot studies is a real possibility, then we need a high power (e.g. beta= 0.05), Power= 95%.

The difference from the pilot studies is the same or less than the expected (2.2%) a real possibility; assume equal number of positive and negative cases for evaluation and 10 % losses.

Required sample size is a total of 1600 which is necessary to have 95% chance of declaring and finding the least difference less than 2.5%. Cost will be higher, but better to spend a little more in observing more subjects than have a set of estimates that are valueless because of their large confidence intervals [22].

3. The Third Phase

It was done nationally as multicenter study on relatively larger number of participants for ensuring its representativeness. 1600 participants were randomly selected to represent both Upper and Lower Egypt from the following referral points as follows; 306 participants obtained from the national treatment reference centers of National Hepatology and Tropical Medicine Research Institute - Egyptian Ministry of Health (MOH); Cairo and Ain Shams Universities

hospitals, 494 participants obtained from Egyptian Liver Research Institute and Hospital – Elmansoura and 800 participants obtained from the central area of recruitment for the armed forces in Egypt as referral point for Upper Egypt's participants. This phase was conducted during a period of six months starting from February 2012 to August 2012. The age range was 18-57 years, of which 1370 males and 230 females.

C. Ethical Consideration

The study is approved by National committee for viral hepatitis, ministry of health, Cairo. An informed consent was obtained from each individual in the study and all were fully informed concerning the diagnostic procedures involved. All subjects had a negative test for HBsAg and a negative test for anti-HIV.

D. Study Procedure

The study throughout its three phases was done blindly. Each time; the desired subjects were prepared as negative and positive for HCV proved by RT-PCR. Meanwhile, each subject was tested by C-FAST device and results were recorded as positive or negative by the operator who was unaware of the results of the PCR .Thereafter, the results of HCV-RNA by RT-PCR and the results of C-FAST device were sent for the statistical analyses to compare the two methods regarding sensitivity, specificity, and predictive values. Again, the statistician was external and unaware of the study purpose.

E. HCV RNA Quantification

HCV-RNA was determined using a real-time polymerase chain reaction (PCR) assay (COBAS TaqMan; Roche Diagnostic systems), with a lower limit of detection of 15 IU/ml.

F. C-FAST Device

C-FAST device is a simple, non-invasive tool weighting 300 gm used to instantly diagnose HCV infected subject. The electromagnetic signals from a specific 5-untranslated region within the HCV genome of different HCV genotypes including HCV genotypes 1, 2,3,4,5 and 6 were measured and fully characterized by their key emission characteristics in the form of frequency, shape, and rate of the emission pulse in the research laboratory of the engineering authority, Ministry of Defense, Cairo, Egypt using signal processing *techniques* as previously described [23]- [27].These characteristics are called the ideal pulse or molecule signature. The ideal pulse and its key characteristics are digitized and stored on a memory card in the C-FAST device (patent). When the electromagnetic signal emitted from the subject (containing HCV genome) is captured by the ideal signal stored in the device, a perfect match occurs and the interaction forces generate a kinetic energy that can move a pointer towards the source of the ideal pulse (molecule signature) of the subject. The lower limit of detection of C-FAST is 15 IU/ml, which is similar to the gold standard PCR COBAS TaqMan.

G. Diagnosis of HCV Using EMSD by C-FAST Device

C-FAST device was used to diagnose HCV viraemia by several operators among whom inter-observer variations were tested and found to be negligible. Using C-FAST device; each case was tested by at least two different operators; blinded of the PCR results. The operator holds the C-FAST device with one hand and keeps the pointer in a neutral position, and then the subject enters an examination room at a 2 - 3 meters distance from the operator and slowly moves in front of operator. If the subject is positive, the pointer will be directed toward him and will follow him in any direction; if the subject is negative, the pointer will remain in its neutral position. For confirmation of the results, the subject may be advised to stay in place and the operator can move around the subject slowly to see if the pointer is directed toward the subject or not. This examination usually takes about one minute. A signed report containing the results of all subjects was handled to the study coordinator.

H. Cross-over Test of C-FAST Device with other Viruses

At outpatient clinics of ELRIAH hospital, 10 known cases of chronic hepatitis B and 10 known cases of coinfection hepatitis C and hepatitis B in addition to 10 known cases of Anti HCV positive, PCR negative subjects were tested by C-FAST device, which was able to detect HCV viremia in coinfected cases and tested negative in all chronic hepatitis B and also in those with no HCV viremia. At fever hospital Abbasia – Cairo, 6 cases with H1N1 (RNA virus) was tested negative using C-FAST device.

I. C-FAST Repeatability

Reliability is the consistency of the measurement; it is the degree to which an instrument measures the same way each time it is used under the same condition. Assessment of different observers at the same time for using the C-FAST device (Inter-observer reliability-Inter-rater reliability) was used. Measurements that are accurate (repeatable) provide more reliable information.

The following procedure was used during measuring repeatability; the clinic setting in which repeatability was established was the same for both the first and the second measurement of the two observers. The method of administration was identical on each occasion. At the second administration, both the participant and the rater (observer) have no knowledge of the results of the first measurement. The time to the second administration was short enough so that the condition had not changed since the first administration.

J. Statistical Analyses

All statistical analyses were done by a statistical soft-ware package "SPSS 16.0 for windows, SPSS Inc".

K. Measuring C-FAST Validity

To know how well the C fast device as diagnostic test can predict that a patient has HCV, the statistics positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity were all used to estimate the utility

of the C-FAST device in predicting the presence of HCV. A statistic that combines the utility of sensitivity and specificity is the likelihood ratio (LR) was also used. LR+ > 20 means very high; virtually certain that a person with this score has the disorder. The diagnostic sensitivity (i.e., the percentage of HCV-positive patients being correctly identified as HCV-positive) was calculated. Specificity (i.e., the percentage of HCV-negative patients being correctly identified as HCV negative) was calculated. Positive predictive (PPV) and negative predictive (NPV) values were also calculated [28], [29], [30]. Efficiency is an overall estimate of a test's ability to classify patients correctly. It is estimated by adding the numbers of the two correct classifications (true positive and true negative) and dividing by the total number of patients assessed. The positive predictive value is the probability of disease in a patient with an abnormal test result, while the negative predictive value is the probability of a patient not having a disease when the test result is negative. Likelihood ratio is a statistic used to combine sensitivity and specificity into a single estimate that indicates how a positive test result will change the odds that a patient has the disease.

L. Measuring C-FAST Reliability

Kappa was used to measure the inconsistency between observers. Kappa is an estimate of the proportion in agreement between two observers in excess of the agreement that would occur by chance. A value above 80 % indicates very good agreement [31], [32].

III. Results

A. Detection of HCV by RT-PCR Versus C-FAST Device

For measuring how accurate is the C-FAST device in predicting HCV, the comparison between PCR and C-FAST for detection of HCV viremia was conducted throughout the whole study phases. HCV RNA was detected for all subjects using a real-time polymerase chain reaction (PCR) assay (COBAS TaqMan; Roche Diagnostic Systems). The C-FAST device was utilized in all subjects to detect the HCV infected patients. Calculations and interpretation of Sensitivity, Specificity, PPV, NPV, pre and post test probabilities and odds, LR (+) were determined for comparison between PCR and C-FAST. Table I shows the demographic and laboratory data of all subjects in the study phases.

Table II shows diagnosis of HCV by using C-FAST out of those diagnosed by RT-PCR. The Sensitivity findings in the different study phases indicates that from 97.4% to 100 % of patients with HCV will have a positive C-FAST and the specificity of the test indicates that from 95.6% to 97.6 % of patients with HCV will have a negative C-FAST, Table III. For sensitivity with 95% confidence interval, between 84.9 % and 100% of patients with HCV infection had a positive C-FAST. Similarly, for specificity with 95% confidence interval, between 95.6% and 97.6 % of patients without HCV had a negative C-FAST. In this sense, these two statistics describe the proportion of patients in each disease category who are test positive and those who are test negative. The efficacy of the C-FAST device was in the range from 96.3 % to 98.2 % along the study phases.

Findings of PPV indicates that from 89.5% to 95.6% of patients who were tested positive by C-FAST had HCV, meanwhile NPV from 98.5% to 100% of patients who were tested negative by C-FAST device did not have HCV, Table III. The findings of the 95% confidence interval for PPV indicate that with 95% confidence, 89.5% to 95.6% of patients with a positive C-FAST test had HCV infection. Meanwhile, the finding of the 95% confidence interval for NPV indicates that with 95% confidence, 98.2% to 100% of patients with a negative C-FAST test do not have HCV infection.

The LR indicates how much a positive test will alter the pre-test probability that a patient will have the illness. The post-test probability is the probability that the disease is present when the test is positive. Findings of + ve LR that ranges from 21.9 to 41.7 for the study phases indicates that the probability of having HCV in the clinic setting where the test is being used is very high with a range of 89.5% to 95.6 % of patients who were tested positive by C-FAST (posttest probability). Table IV shows that almost all observers have the same % agreement. The finding of the kappa measures of C-FAST reliability during the second phase of the study that is almost equal to one indicates that the two observers are perfectly reliable for all the studied settings. They classify everyone exactly the same way. For the usefulness of the C-FAST device, the test passed muster on a series of increasingly difficult questions that address its reproducibility, accuracy, feasibility, and effects on clinical decisions and outcomes, Table V.

IV. Discussion

Chemical reactions can be induced at a distance due to the propagation of electromagnetic signals during intermediate chemical stages. Although it is well known at optical frequencies, e.g. photosynthetic reactions, electromagnetic signals hold true for much lower frequencies as well. In E. coli bacteria such electromagnetic signals can be generated by electric transitions between energy levels describing electrons moving around DNA loops. The electromagnetic signals between different bacteria within a community are a "wireless" version of intercellular communication found in bacterial communities connected by "nanowires". The wireless broadcasts can in principle be of both the AM and FM variety due to the magnetic flux periodicity in electron energy spectra in bacterial DNA orbital motions [33].

The results of this study are the first report that Electro-Magnetic Signal Detection (EMSD) can be utilized to diagnose a specific disease using a simple device. The efficacy of C-FAST device in recording and replaying the molecule signature of HCV, it is practical evidence that nucleotides in human body emit electromagnetic signals which are fully characterized and then these characteristics are used for its identification. When compared to the gold standard PCR technique, the C-FAST device has a remarkably high sensitivity and specificity. This high accuracy may solve one of the major problems in electromagnetic cellular interaction

research which is the lack of reproducibility [7]; raising a major question; How can we explain this very high accuracy of C-FAST device while experimental investigations of the interactions of EMF and biosystems still intensely controversial? The idea of resonant absorption and resonant interactions has been proposed as an explanation for the marked sensitivity of living systems to EMFs as each biological process involves a number of interactions between proteins and their targets. These interactions are based on the energy transfer between the interacting molecules [34]. So, protein interactions are highly selective, and this selectivity is defined within the protein structure. Moreover it was shown that proteins and their targets have the same characteristic frequency in common [15]. Accordingly, the concept of recognition and interaction between a particular protein and its target at distance typically explains the very high accuracy of C-FAST device; and on the other hand the reproducibility of C-FAST in diagnosis of a very specific RNA (HCV) is a real life evidence of the concept of recognition and interaction between a particular nucleic acid and its targets. The concept of bioelectromagnetic communications is receiving increasing attention in the scientific community [12], [35]. This concept is challenging the old beliefs which are the consequence of ancient thinking, dating to Democritus, Epicurus, and Lucretius, is that all matter is composed of "imperishable" atoms, tiny indivisible particles that can neither be created nor destroyed [36]. In accordance with the iron laws of "necessity" that were eventually replaced with Newton's Laws of Motion.

Interactions cannot take place between atoms or molecules unless they touch one another [37]. These ideas were pivotal for the development of Western science. A legacy of this natural philosophy is the modern molecular view of regulatory interactions in which signal molecules such as hormones or neurotransmitters or pheromones diffuse, wiggle, and bump about randomly until they chance to approach an appropriate receptor site, at which point electrostatic and other short range forces draw the signal molecule into the receptor, much like a key fits into a lock. The "key" obviously has to have a structure or shape that matches the "lock." For this model, shape is crucial [38]. We now know that atoms are not solid and indivisible, and we also know that the "lock and key" model is an incomplete picture of regulations. The random meeting between hormone and receptor, or enzyme and substrate, taking place in a sea of other randomly moving molecules, has a statistical probability approaching zero [35]. Under these conditions, the simplest biological event or regulatory process should require several thousands of years to take place. Albert Szent-Gyorgyi recognized years ago that life is simply too fast and too subtle to wait for molecules to wander around aimlessly until they happen to bump into the right targets. Electromagnetic signaling is not only physically possible; it is the ideal mechanism for communication in living systems. For this model, electromagnetic resonance and not shape, is crucial [39].

The advantage of using sensitivity and specificity to describe the application of the C-FAST device as diagnostic test for HCV infection is that these statistics: do not alter if the prevalence of disease is different between clinical populations; can be applied in different clinical populations and settings and can be compared between studies with different inclusion criteria. The finding of this multi-phases study indicates that C-FAST device can be used for diagnosis (to rule the disease in) as well as to screen a population in which many people will not have the disease (to rule the disease out). This is because of the high specificity (TN) and low false positives rate of the device as well as its high sensitivity and low false negative rate indicating that the device can identify most of the people who do not have the disease and all of the people with the disease. Moreover, the high PPV indicate a very high probability of having HCV for subjects who are C fast positive and the high NPV indicate a very high probability of not having HCV for subjects who are C fast negative with a very high probability for correct diagnosis [28], [29], [30].

The very high +ve LR more than 20% for all the study phases indicate that we are virtually certain that a person with this score has HCV. It means a conclusive change from pre-test to post-test probability. The choice of likelihood ratio is that this predictive statistic allows valid comparisons of diagnostic statistics between studies and that the diagnostic value can be applied in different clinical settings and also provides the certainty of the positive diagnosis that is above 20 % [30], [40].

This study clearly demonstrates that C-FAST is a non-invasive device, no blood sample, chemicals, kits or sophisticated laboratory equipments are needed and consequently no cost per case. Moreover, diagnosis of HCV using C-FAST is very rapid. These advantages are expected to have a huge impact on the diagnosis and screening programs of HCV worldwide where only few millions of 180 million HCV patients are already diagnosed [41]. Taking into account the prospects of emerging new HCV therapies which are expected to be very potent, orally administered avoiding interferon therapy [42], the need for rapid and mass screening of HCV worldwide will be growing over the next few years. The availability of a simple, rapid, accurate, and non-invasive method for HCV diagnosis in the era of an oral effective regimen of HCV therapy could be a turning point in HCV history. Easy diagnosis and effective treatment will prolong life and prevent death from liver disease in millions of HCV patients [33]. C-FAST is a non-invasive device capable of identifying HCV infected patients instantly, making it ideal for diagnosis of HCV and mass screening program.

TABLE I
DEMOGRAPHIC AND LABORATORY DATA OF ALL SUBJECTS IN THE STUDY PHASE

Characteristics	1stPhase	2ndPhase No. of patients = 1004	3rdPhase No. of patients =1600
Gender M/F	79/0	966 / 38	1370 / 230
Age (years range) BMI	23.3+1.9	27.3+2.7	27.6+2.4
ALT(U/ml)(mean+SD)	39.5+22.9	83.1+49.4	91.2+46.5
AST(U/ml)(mean+SD)	36.2+18.8	67.7+43.02	80.6+41.0
Albumin (g/dl) (mean+SD)	4.6+0.31	4.3+0.38	4.1+0.41
Bilirubin (mg/dl) (mean+SD)	0.83+0	0.95+0.28	1.04+0.33
Platelet count (x103/ml)	227.1+62.2	21.3+	186.4+58.5
+ve HCV – RNA by PCR (No.)	20 / 79	217 / 1004	657/1600
HCV – RNA Viremia (IU/mL)	204338+33191	366914+45100	471860+53200
Genotype 1 (%)	0 (0%)	21 (9.7%)	0 (0%)
Genotype 3 (%)	0 (0%)	51 (23.5%)	0 (0%)
Genotype 4 (%)	20 (100%)	145 (66.8%)	657 (100%)

TABLE II
DIAGNOSIS OF HCV USING C-FAST DEVICE

Study	no	Sex M/F	Genotype	True positive	False positive	True negative	False Negative
Phase I (pilot Egypt	79	79/0	4	20	2	57	0
Phase II Egypt	800	789/11	4	143	2	653	2
Phase II India	113	98/ 15	1&3	28	2	82	0
Phase II Pakistan	92	80/12	3	44	2	46	0
Phase III (multi center Egypt)	1600	1370/230	4	640	42	901	17

TABLE III
PERFORMANCE CHARACTERISTICS OF C-FAST DEVICE FOR HCV DIAGNOSIS

Study	No	Sensitivity % (95% CI)	Specificity % (95% CI)	Efficacy %	PPV% (95% CI)	NPV% (95% CI)	LR + (95% CI)	Post test probability (95% CI)
Phase I (Mansora Egypt	79	100 (98.9-100)	96.6 (94.6-98.9)	97.5	90.9 (83.4-93.7)	100 (90 – 100)	29.4% (25.4 - 42.2)	90.9% (86. 7-95.5)
Phase II Egypt	800	100 (98.9-100)	97.4 (96.6-99.9)	97.9	89.5 (83.4-93.7)	100 (90 – 100)	23.68% (20.3 - 27.4)	89.5 (82.4-93.7)
Phase II India	113	100 (84.9-100)	97.6 (90.9-99.5)	98.2	93.3 (76.4-98.8)	100 (94.4 – 100)	41.7 (10.8 –67.2)	92.6% (78.5-97.5)
Phase II Pakistan	92	100 (90-100)	95.8 (84.5-99.2)	97.8	95.6 (83.9-99.2)	100 (90 – 100)	23.8 (6.1 – 93.2)	95.4% (84.7-99.5)
Phase III (multi center Egypt)	1600	97.4 (95.8-98.4)	95.6 (94 - 96.7)	96.3	93.84% (92 -95.5)	98.2 (97 – 99)	21.9 (16.2-29.4)	93.5 (92-95)

TABLE IV
REPEATABILITY OF C-FAST DEVICE FOR THE SECOND PHASE OF THE STUDY

study	no	% of +ve response for the first observer	% of +ve response for the first observer	Proportion in agreement	Kappa %
Phase II Egypt	800	18.12	18.12	.995	99.9
Phase II India	113	50	50	1.00	100
Phase II Pakistan	92	73.5	73.5	.98	95.5

TABLE V
USEFULNESS OF THE C-FAST DEVICE IN SCREENING AND DIAGNOSIS OF HCV PATIENTS

Question	Results
Accuracy of the device	C-FAST device is as accurate as the gold standard PCR; demonstrating a specificity of 97.8%
Consistency of C-FAST device; "device reproducibility"	C-FAST results are consistent regardless of the operator discipline.
Selectivity	Cross-over testing for other viruses revealed that the device was able to detect HCV viremia only in patients with established HCV diagnosis or in cases coinfected with HBV.
Feasibility and acceptability of the device for use	Being a non-invasive, easy to perform (no blood sample, Chemicals, kits or sophisticated laboratory equipments are needed) and consequently no cost per case; it is very practical. Moreover, diagnosis of HCV using C-FAST is very rapid and the results are obtained Instantly; thus expediting the mass screening and diagnosis of HCV infected patients.

V. CONCLUSION AND FUTURE PROSPECTS

We conclude that Electromagnetic Signal Detection (EMSD) of specific HCV RNA nucleotides using the C-FAST device is an accurate, non-invasive method for HCV diagnosis and it can be used for as case – finding or opportunistic screening. The same technology could potentially be used for

diagnosis of other diseases; this may open a new horizon in the applications of EMSD in biology and medicine.

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