Comparison of AI Techniques for Prediction of Liver Fibrosis in Hepatitis Patients

Article *in* Journal of Medical Systems · August 2014

DOI: 10.1007/s10916-014-0060-y · Source: PubMed

3 authors, including:

Yuan Lin
University of Arkansas at Little Rock
2 PUBLICATIONS **25** CITATIONS
SEE PROFILE

Coskun Bayrak
Youngstown State University
129 PUBLICATIONS **744** CITATIONS
SEE PROFILE

Comparison of AI Techniques for Prediction of Liver Fibrosis in Hepatitis Patients

Brain Keltch, Yuan Lin, Coskun Bayrak
Computer Science Department
University of Arkansas at Little Rock
Little Rock, AR

ABSTRACT

Globally one in twelve people have the Hepatitis B or Hepatitis C virus. Diagnosis and treatment of this disease is guided by liver biopsies where a small amount of tissue is removed by a surgeon and examined by a pathologist to determine the fibrosis stage from F0 (no damage) to F4 (cirrhosis). Biopsies are costly and carry some risk for the patient. Non-invasive techniques for determining fibrosis stage have been developed and evaluated since 2003. Non-invasive methods have utilized serum markers, imaging test, and genetic studies. The accuracy of these non-invasive techniques has not achieved sufficient acceptance and so the invasive biopsy is still considered the gold standard.

Clinical decision support systems (CDSS) use decision support system theory and technology to assist clinicians in the evaluation and treatment process. Using historical clinical data and the relationship processed by Artificial Intelligence (AI) techniques to aid physicians in their decision making process is the goal of CDSS. The CDSS provides a large number of medical support functions to help clinicians make the most reasonable diagnosis and choose the best treatment measures.

This paper applies four artificial intelligence predictive techniques (decision trees, neural networks, naive bayes algorithms, and logistics regression) to publicly available data on 424 Hepatitis B and Hepatitis C patients. Demographic and standard serum markers are utilized to predict fibrosis stage and compare these predictions to known biopsy results. A final decision tree evaluation is applied to make a final prediction. We have also have developed a publically available web application that can be used as a prototype for presenting AI predictive results in a CDSS environment based on these models. This technique along with others could mitigate the need for some liver biopsies in the more than 500 million Hepatitis B and C patients worldwide with additional validation and verification.

Keywords: Fibrosis Stage, Hepatitis, Clinical Decision Support, Artificial Intelligence Predictive Techniques,

1. INTRODUCTION

Hepatitis B or Hepatitis C virus is a common disease throughout the world. Diagnosis and treatment of this disease is guided by liver biopsies where a small amount of tissue is removed by a surgeon and examined by a pathologist to determine the fibrosis stage from F0 (no damage) to F4 (cirrhosis) [1][2]. This disease goes largely untreated in developing countries. Biopsies are costly and carry some risk for the patient. Non-invasive techniques for determining fibrosis stage have been developed and evaluated since 2003. Non-invasive methods have utilized serum markers, imaging test, and genetic studies. The accuracy of these non-invasive techniques has not achieved sufficient acceptance and so the invasive biopsy is still considered the gold standard [3].

Knowledge of the level of liver damage in a patient with liver disease (particularly Hepatitis B and Hepatitis C) is a critical factor in determining the optimal course of treatment and to measure the effectiveness of alternative treatments in patients. The effort here expands on earlier work [4] by adding three additional artificial intelligence techniques to predict the degree of liver damage from blood serum results rather than determination from an invasive biopsy [5].

Clinical Decision Support System (CDSS) provide cost/effective solutions by correlating historical data to assist clinicians in treatment of disease. In this case we are developing a CDSS focused on predicting Fibrosis Stage from blood serum information. It is an information system which uses expert systems and artificial intelligence (AI) technology to support clinical decision. It makes integrated diagnostic and medical advice bases on the collected patients' information, providing reference for the clinical medical physician [6]. Clinical Decision Support Systems are "active knowledge systems which use two or more items of patient data to generate case-specific advice"[7].

Clinical decision support systems vary greatly in their complexity, function, and application. This effort builds on earlier work [4] and will focus on function and in

particular utilization of historical data laboratory and outcome data processed through artificial intelligence tools. The combination of historical data and predictive tools provides valuable information in the hands of physicians as they develop a course of treatment for a patient.

2. BACKGROUND: AI and CDSS

Artificial Intelligence and Data Mining techniques have proven themselves useful in a wide variety of medical and health information systems [1]. The most direct application has been in medical and clinical diagnostic systems but has included productive work in signal processing for example in ECG diagnosis [8]. Commonly applied techniques include Neural Networks, Fuzzy Logic, Decision Trees, Bayesian Classifiers, Support Vector Machines, Genetic Algorithms, and Hybrid Systems. In Clinical and Medical Decision Support Systems these techniques have been successfully applied to support the process of discovering useful information in large clinical repositories [8]. Future challenges are to increase the routine use of these techniques in the clinical setting [7]. We have done the system designed with neural networks and decision tree methods because of their successful application in similar problem domains [4] [9] [10]. In this paper we use two more techniques Naïve Bayes Classifier and Logistics Regression to strengthen the system and use Cross Validation to pick up the optimum technique to get the best prediction result.

2.1 Naïve Bayes Classifier

In machine learning and pattern recognition, classification refers to an algorithmic procedure for assigning a given piece of input data into one of a given number of categories. The term "classifier" sometimes also refers to the mathematical function, implemented by a classification algorithm, that maps input data to a category [11]. Support we have the data consist of fruits described by their color and shape. If we see a fruit is red and round then based on the data sample, which type of fruit is it most likely to be? The classifier would classify the red and round fruit as that type of fruits.

Naïve Bayes classifier has 2 assumptions. NBC assumes that the attributes are independent of each other in each class and the importance of the attributes is equal. It is made to simplify the computation and in this sense considered to be Naïve. Studies comparing classification algorithms have found the Naïve Bayesian classifier to be comparable in performance with classification trees and with neural network classifiers. They have exhibited high accuracy and speed when applied to large databases [12]. And also it has the decision-making process continued according to the specific cases which is really significant for our project. It is effective and simple algorithm but the two central assumptions may not represent the facts.

2.2 Logistics Regression

Binary (or binomial) logistic regression is a form of regression which is used when the dependent is a dichotomy and the independents are of any type. Multinomial logistic regression exists to handle the case of dependents with more classes than two, though it is sometimes used for binary dependents also since it generates somewhat different output [13]. Logistic regression is used for prediction of the probability of occurrence of an event by fitting data to a logistic curve. A logistic regression model does not involve decision trees and is more akin to nonlinear regression such as fitting a polynomial to a set of data values. Logistic regression can be used only with two types of target variables:

1. A categorical target variable that has exactly two categories (i.e., a binary or dichotomous variable).
2. A continuous target variable that has values in the range 0.0 to 1.0 representing probability values or proportions [1].

It is a stable algorithm and doesn't require the variables to be a normal distribution. But the precision of the algorithm is limited.

2.3 Hepatitis and Fibrosis Stage

One in 12 people worldwide are living with wither chronic hepatitis B or hepatitis C. This equates to an estimated 350 million people with hepatitis B and 170 million people with Heapatitis C [3] [14][15]. A liver biopsy is a procedure whereby small pieces of liver tissue are removed in order to be sent to a laboratory for examination. It is very helpful in

the diagnosis of diseases that affect the liver [16]. But it is also cost and carries risk for the patients. Biopsy is an expensive procedure ranging from $1,500 to $3,000. Complications are rare (<3%) but include internal bleeding, infection, air in chest cavity, internal organ puncture and so on. Fibrosis Stage [17] guides treatment of Hepatitis patients. Stages F0 and F1 are typically categorized as insignificant fibrosis and stages greater than F1 are categorized as significant fibrosis. Fibrosis stages are shown in Table 1. Although hepatitis is a chronic disease, fibrosis is reversible if identified in the early stages.

Table 1 Fibrosis Stage Descriptions [18][19]

Fibrosis Stage	Description
0	No fibrosis-Normal connective tissue
1	Portal fibrosis- Fibrous portal expansion
2	Periportal fibrosis- Periportal or rare portal-portal septa
3	Septal fibrosis- Fibrous septa with architectural distortion; no obvious cirrhosis
4	Cirrhosis

The database utilized for this study was collected at Chiba University hospital in Japan, and is a Practice of Knowledge Discovery in Databases 2005 Discovery Challenge dataset [20]. The data set contains patient data, laboratory, and liver fibrosis biopsy data on 771 hepatitis B and C patients. Data was processed to limit serum data within one week of biopsy data, reducing the evaluation dataset to 424 patients. The objective is to evaluate whether laboratory examinations can be used to estimate the stage of liver fibrosis.

3. AI ASSISTEDCLINICAL DECISION SUPPORT SYSTEM

Another objective of this research is to define an interface that might be useful to clinicians and identify what type of web-based tools would be most useful to represent the results of AI predictions in a CDSS environment. A beta version of the software (CDSS-AI) was developed utilizing the models in this study. We have utilized Visual

Studio 2008 for our beta version which is available at http://h202276.dreamsparkhosting.com/Default.aspx . Additionally we are utilizing two open source analytic tools for the AI component of our project. Namely, we are using "Neuro 3" a Visual Basic application for the neural network application and "Weka" for the decision tree portion of our project.

The methodology and approach of processing data, applying AI techniques, and development of the resulting knowledge base can be utilized as a pattern for other medical treatment needs represented in a CDSS. The current architectural of the beta system is shown in Figure 1.

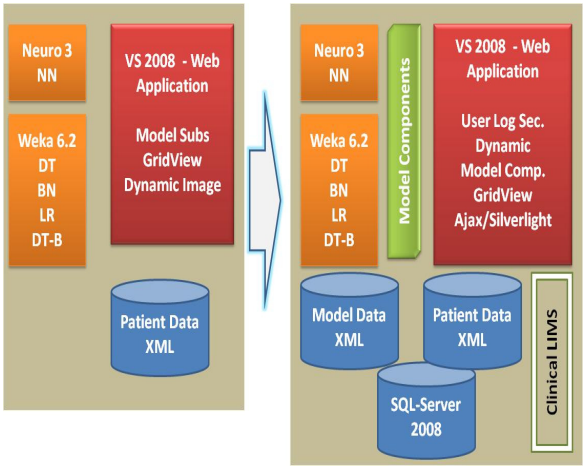

Figure 1. AI Assisted CDSS

3.1 Previous Work

The objective is to use the four algorithms to predict fibrosis stage from patient data and laboratory data. The paper "Advanced Decision Support for Complex Clinical Decisions" [4] presents two of the techniques which are Decision Tree and Neural Network. This paper adds two other methods which are Naïve Bayes Classifier and Logistics Regression. We have a data set of 424 historical that will be use to train and validate four kinds of models. Table 2 is a map of the data elements utilized in this study.

Table 2: Data Utilized for Model Building

Abbreviation	Description
ALB	Albumin
ALP	alkaline phosphatase
CHE	Cholinesterase
D-BIL	bilirubin, direct
G-GTP	gamma-glutamyltranspeptidase
G.GL	gamma-globulin

INPUT PATIENCE DATA	
Abbreviation	Description
AGE	Patient Age at Time of Test
HEP_B_C	Hepatitis B = 1 or Hepatitis C = 2

3.2 Naïve Bayes Classifier

The Naïve Bayes classifier assigns an instance s_k with attribute values ($A_1=v_1$, $A_2=v_2$, …, $A_m=v_m$) to class C_i with maximum Prob(C_i|(v_1, v_2, …, v_m)) for all i. The naive Bayes classifier exploits the Bayes's rule and assumes independence of attributes.

Likelihood of s_k belonging to C_i

$$= \text{Prob}\left(C_i \mid (v_1, v_2, \ldots, v_m)\right) = \frac{P\left((v_1, v_2, \ldots, v_m) \mid C_i\right) P(C_i)}{P\left((v_1, v_2, \ldots, v_m)\right)}$$

Likelihood of s_k belonging to C_j

$$= \text{Prob}\left(C_j \mid (v_1, v_2, \ldots, v_m)\right) = \frac{P\left((v_1, v_2, \ldots, v_m) \mid C_j\right) P(C_j)}{P\left((v_1, v_2, \ldots, v_m)\right)}$$

Therefore, when comparing Prob(C_i| (v_1, v_2, …, v_m)) and P(C_j |(v_1, v_2, …, v_m)), we only need to compute P((v_1, v_2, …, v_m)|C_i)P(C_i) and P((v_1, v_2, …, v_m)|C_j)P(C_j)

Under the assumption of independent attributes

$$P\left((v_1, v_2, \ldots, v_m) \mid C_j\right)$$
$$= P(A_1 = v_1 \mid C_j) \cdot P(A_2 = v_2 \mid C_j) \cdot \ldots \cdot P(A_m = v_m \mid C_j)$$
$$= \prod_{h=1}^{m} P(A_h = v_h \mid C_j)$$

Furthermore, P(C_j) can be computed by [14]

$$\frac{\text{number of training samples belonging to } C_j}{\text{total number of training samples}}$$

By using WEKA [21], the model classifies the Fibrosis Stage into 5 classes which represent the 5 stages. There are 8 attributes in each class. The model calculates the mean value and Stand Deviation value for each attribute. According to the definition of Naïve Bayes Classifier [22], we can get the probability of Fibrosis Stage in each class base formula:

$P(FS_1 \mid Yes) = P(ALB = FS_1 \mid Yes) * P(ALP = FS_1 \mid Yes) * \ldots * P(Heap\ B = FS_1 \mid Yes)$

(FS_1 means Fibrosis stage 1). We assume the 7 Continuous Variables are all Gaussian Distribution. For example, for the ALB: $P(ALB \mid FS_1) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{\frac{-(ALB-\mu)^2}{2\sigma^2}}$ And for the categorical variable (Hepatitis Type), use the actual number of occurrences. For example, $P(HeapB \mid FS_1) = 59/204$. Figure 2 shows the Naïve Bayes Classifier model. Classes 0 to 4 means the Fibrosis stage 0 to 4.

```
Naive Bayes Classifier

Class 0: Prior probability = 0.03

ALB:  Normal Distribution. Mean = 4.6627 StandardDev = 0.2653 WeightSum = 10 Precision = 0.10454545454545454
ALP:  Normal Distribution. Mean = 116.0848 StandardDev = 35.9898 WeightSum = 10 Precision = 2.5126582278481013
CHE:  Normal Distribution. Mean = 295.1438 StandardDev = 104.4466 WeightSum = 10 Precision = 2.0625
D_BIL:  Normal Distribution. Mean = 0.2084 StandardDev = 0.1211 WeightSum = 10 Precision = 0.09923076923076923
G_GTP:  Normal Distribution. Mean = 29.6065 StandardDev = 30.6965 WeightSum = 10 Precision = 3.7476635514018692
G_GL:  Normal Distribution. Mean = 13.867 StandardDev = 2.9603 WeightSum = 10 Precision = 0.1633333333333333
AGE:  Normal Distribution. Mean = 33.0815 StandardDev = 7.4072 WeightSum = 10 Precision = 1.0740740740740742
TYPE_B1_C2:  Discrete Estimator. Counts =  1 11  (Total = 12)


Class 1: Prior probability = 0.46

ALB:  Normal Distribution. Mean = 4.3577 StandardDev = 0.3832 WeightSum = 148 Precision = 0.10454545454545454
ALP:  Normal Distribution. Mean = 131.6939 StandardDev = 57.9128 WeightSum = 148 Precision = 2.5126582278481013
CHE:  Normal Distribution. Mean = 229.4113 StandardDev = 136.3855 WeightSum = 148 Precision = 2.0625
D_BIL:  Normal Distribution. Mean = 0.2213 StandardDev = 0.1394 WeightSum = 148 Precision = 0.09923076923076923
G_GTP:  Normal Distribution. Mean = 49.8338 StandardDev = 57.3886 WeightSum = 148 Precision = 3.7476635514018692
G_GL:  Normal Distribution. Mean = 16.7682 StandardDev = 4.2262 WeightSum = 148 Precision = 0.1633333333333333
AGE:  Normal Distribution. Mean = 44.1749 StandardDev = 14.092 WeightSum = 148 Precision = 1.0740740740740742
TYPE_B1_C2:  Discrete Estimator. Counts =  40 110  (Total = 150)


Class 2: Prior probability = 0.21
```

```
ALB:  Normal Distribution. Mean = 4.2833 StandardDev = 0.3522 WeightSum = 68 Precision = 0.10454545454545454
ALP:  Normal Distribution. Mean = 125.7438 StandardDev = 63.2619 WeightSum = 68 Precision = 2.5126582278481013
CHE:  Normal Distribution. Mean = 186.3833 StandardDev = 144.3321 WeightSum = 68 Precision = 2.0625
D_BIL:  Normal Distribution. Mean = 0.2262 StandardDev = 0.1225 WeightSum = 68 Precision = 0.09923076923076923
G_GTP:  Normal Distribution. Mean = 53.5695 StandardDev = 52.4596 WeightSum = 68 Precision = 3.7476635514018692
G_GL:  Normal Distribution. Mean = 18.3726 StandardDev = 4.6063 WeightSum = 68 Precision = 0.1633333333333333
AGE:  Normal Distribution. Mean = 46.659 StandardDev = 12.05 WeightSum = 68 Precision = 1.0740740740740742
TYPE_B1_C2:  Discrete Estimator. Counts =  29 41  (Total = 70)

Class 3: Prior probability = 0.16

ALB:  Normal Distribution. Mean = 4.1899 StandardDev = 0.4064 WeightSum = 52 Precision = 0.10454545454545454
ALP:  Normal Distribution. Mean = 138.1479 StandardDev = 63.1047 WeightSum = 52 Precision = 2.5126582278481013
CHE:  Normal Distribution. Mean = 190.0276 StandardDev = 133.1631 WeightSum = 52 Precision = 2.0625
D_BIL:  Normal Distribution. Mean = 0.2691 StandardDev = 0.1474 WeightSum = 52 Precision = 0.09923076923076923
G_GTP:  Normal Distribution. Mean = 64.5751 StandardDev = 47.8222 WeightSum = 52 Precision = 3.7476635514018692
G_GL:  Normal Distribution. Mean = 19.9298 StandardDev = 4.5383 WeightSum = 52 Precision = 0.1633333333333333
AGE:  Normal Distribution. Mean = 50.1097 StandardDev = 11.0058 WeightSum = 52 Precision = 1.0740740740740742
TYPE_B1_C2:  Discrete Estimator. Counts =  14 40  (Total = 54)

Class 4: Prior probability = 0.13

ALB:  Normal Distribution. Mean = 3.9335 StandardDev = 0.4979 WeightSum = 40 Precision = 0.10454545454545454
ALP:  Normal Distribution. Mean = 161.0614 StandardDev = 59.9489 WeightSum = 40 Precision = 2.5126582278481013
CHE:  Normal Distribution. Mean = 164.0719 StandardDev = 117.8813 WeightSum = 40 Precision = 2.0625
D_BIL:  Normal Distribution. Mean = 0.3622 StandardDev = 0.282 WeightSum = 40 Precision = 0.09923076923076923
G_GTP:  Normal Distribution. Mean = 71.8614 StandardDev = 79.1897 WeightSum = 40 Precision = 3.7476635514018692
G_GL:  Normal Distribution. Mean = 20.5923 StandardDev = 5.4772 WeightSum = 40 Precision = 0.1633333333333333
AGE:  Normal Distribution. Mean = 53.0056 StandardDev = 9.1092 WeightSum = 40 Precision = 1.0740740740740742
TYPE_B1_C2:  Discrete Estimator. Counts =  14 28  (Total = 42)
```

Figure 2. Naïve Bayes Classifier model

With this model, we can calculate the probability of each fibrosis stage then pick up the highest one as our predict result.

3.3 Logistics Regression

A graph of the Logistic Regression function is shown in Figure 3 [23]. The input is z and the output is *f(z)*. Whereas the output is confined to values between 0 and 1, the function can take as an input any value from negative infinity to positive infinity. A represents the exposure to some set of independent variables while *f(z)* represents the probability of a particular outcome, given that set of explanatory variables [16]. The definition of Logistics Regression can be written as: $F(z) = \frac{1}{1+e^{-z}}$ and $z = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_n x_n$ [21]. By using WEKA, obtained the model shown in Figure 4. We know that Base on the coefficient of the model, we can calculate the probability of the Fibrosis Stage in each class then select the highest as the final prediction. Let us take class 0 as the example. The probability of fibrosis stage 1 is

$$F(z) = \frac{1}{1+e^{-z}} \text{ the } z = -1.35+1.22(ALB) -0.28(G\_GL) -0.08(AGE) +3.03(TYPE)$$

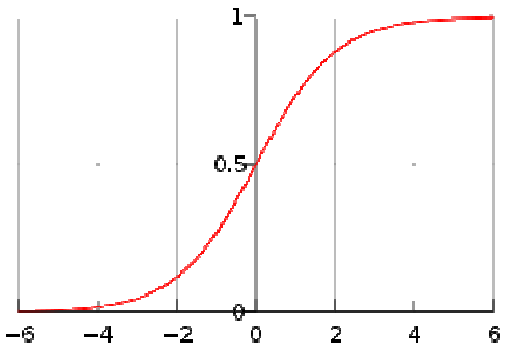

Figure 3. Logistic Regression function

```
Class 0 :
-1.35 +
[ALB] * 1.22 +
[G_GTP] * 0    +
[G_GL] * -0.28 +
[AGE] * -0.08 +
[TYPE_B1_C2] * 3.03

Class 1 :
3.17 +
[CHE] * 0    +
[D_BIL] * -1.29 +
[G_GTP] * 0    +
[G_GL] * -0.06 +
[AGE] * -0.02

Class 2 :
0.69 +
[D_BIL] * -1.91 +
[G_GL] * 0.02 +
[AGE] * 0.01 +
[TYPE_B1_C2] * -1.1

Class 3 :
-2.04 +
[CHE] * 0    +
[D_BIL] * 0.52 +
[G_GTP] * 0    +
[G_GL] * 0.06 +
[AGE] * 0.02 +
[TYPE_B1_C2] * 0.08

Class 4 :
1.2  +
[ALB] * -1.09 +
[ALP] * 0.01 +
[CHE] * 0    +
[D_BIL] * 2.15 +
[G_GTP] * 0    +
[AGE] * 0.05 +
[TYPE_B1_C2] * -0.22
```

Figure 4. Logistic Regression Model

3.4 Cross Validation

Cross Validation is a technique for assessing how the results of a statistical analysis will generalize to an independent data set [24]. We did the cross validation on each of the four techniques in the prototype which includes Decision Tree, Neural Network, Naïve Bayes Classifier and Logistics Regression. The data set is divided into two parts, the training set and test data sets. We trained multiple models on the training set then picked up the model with the smallest classification error. We divided the data set into 4 parts and cross validation will randomly pick 3 parts as the training set to predict the 4th part which looked as test set. In the end, we can accurate sum of the test sets to improve our prediction. The illustration showed in Figure 5.

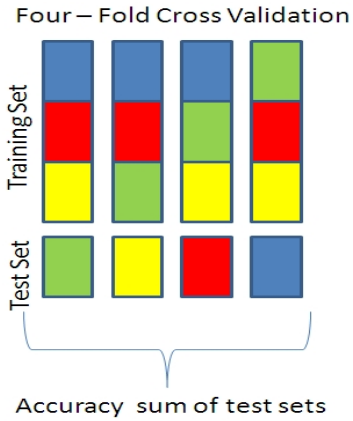

Figure 5. Cross Validation

3.5 Decision Tree Averaging

After using the four different techniques for prediction we applied a final model which was simply a decision tree which was trained on the four model fibrosis stage predictions, and the biopsy fibrosis stage in hopes of improving the accuracy of the models. As showed in Figure 6, the final decision tree increases the accuracy of the four techniques. However, it should be noted that this prediction was not cross-validated, making the increased accuracy less valuable.

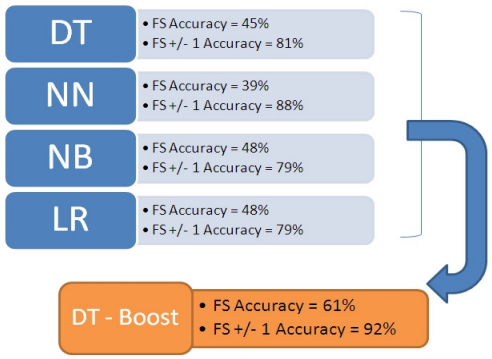

Figure 6. Decision Tree Averaging

3.6 Results and Diagnostic Accuracy

Several methods were used to predict the accuracy of the predictive models. For each model a consistency matrix was prepared, which counts the number of biopsy fibrosis stage values vs. the predicted fibrosis stage. The table for the neural network model is shown in Table 3.

Table 3. Neural Network Model Fibrosis Stage Consistency Matrix

	Biopsy Fibrosis Stage (Actual)					
Neural Network Fibrosis Stage (Predicted)		0	1	2	3	4
	0	1	2	0	0	1
	1	11	83	12	7	6
	2	1	105	63	43	24
	3	0	8	15	12	12

	4	0	4	1	5	8

From each of these tables counts of the prediction accuracy can be made for correct predictions, high predictions, low predictions, and predictions within plus or minus on fibrosis stage. Table 4 shows the counts for each model.

Table 4. Accuracy of Fibrosis Stage Predictions

Count of FS Prediction	Neural Network	Decision Tree	Naïve Bayes	Logistics Regression	DT - Average
Correct	167	191	202	205	255
Predict High	150	88	72	162	48
Predict Low	107	145	150	57	121
FS +/- 1	372	342	333	335	391

In addition the results can be grouped by Insignificant Fibrosis (F0 and F1) and Significant Fibrosis (F2, F3, and F4) to evaluate the accuracy of models to discriminate diseased cases from normal cases. These results are shown in Table 5.

Table 5. Predictive Sensitivity and Specificity

	Neural Network	Decision Tree	Naïve Bayes	Logistics Regression	DT - Average
True Positive Fraction	88%	49%	47%	34%	51%
False Negative Fraction	12%	51%	53%	66%	49%
False Postive Fraction	55%	24%	19%	11%	10%
True Negative Fraction	45%	76%	81%	89%	90%
Sensitivity	88%	49%	47%	34%	51%
Specificity	55%	24%	19%	11%	10%
Positive Predictive Value	61%	67%	71%	76%	83%
Negative Predictive Value	78%	60%	60%	57%	65%

These values show where significant disease correctly classified as positive (True Positive fraction), and the percent of cases with the disease will be classified negative (False Negative fraction). For those cases without the disease some will be correctly

classified as negative (True Negative fraction), but some cases without the disease will be classified as positive (False Positive fraction). The Sensitivity provides the probability that a test result will be positive when the disease is present. Specificity provides the probability that a test result will be negative when the disease is not present. Positive predictive value indicates the probability that the disease is present when the test is positive. Negative predictive value provides the probability that the disease is not present when the test is negative [25].

4. CONCLUSION

The four artificial intelligence methods presented showed significant variability in their accuracy, sensitivity, and specificity in predicting fibrosis stage in data on 424 hepatitis patients. Neural network methods show the highest sensitivity and specificity, but were relatively poor at predicting the exact fibrosis stage. Logistic regression and naïve bayes methods were the best a identifying the exact fibrosis stage. Logistic regression had the highest Positive Predictive Value, and neural network methods had the highest Negative Predictive Value.

We have completed the development of a web based beta system that utilizes publically available patient data to address a single clinical decision – the prediction of fibrosis stage for hepatitis patients. The CDSS-AI beta interface is shown in Figure 7. The CDSS-AI system presents the four model outputs and the final decisions tree average in a "thermometer type" output showing each prediction as a tick mark on the fibrosis scale from 0 to 4. A blue line marks the biopsy value on the output if it is available. In the patient example in Figure 7, fibrosis stage reported in the biopsy was F3. The correct fibrosis stage was reported by the neural network model, the decision tree model, and the decision tree summary model.

Study results suggest future work in expansion of the patient dataset and inclusion of more specific serum markers, and comparison with other commercial non-invasive tests including FibroScan, FIBROSpect II , FibroTest, FibroTest-ActiTest, and HCV-FibroSure [26]. Also, additional serum markers should be considered such as viral load,

platelet count as well as patient history parameters such as alcohol use and body mass index.

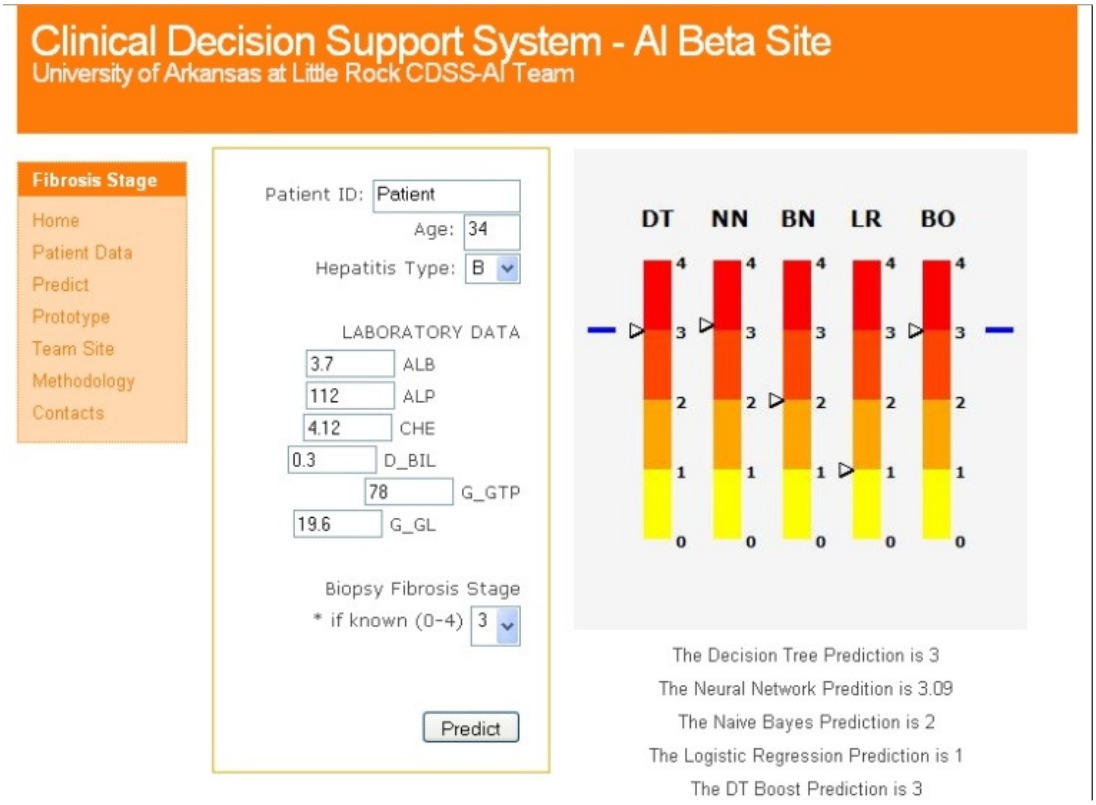

Figure 7: Beta Web Application

References

[1] http://www.dtreg.com/logistic.htm

[2] Albedawi, M., Ruiz-Rodriguez, E., and Carey, W. D., Hepatitis C virus: Prevention, screening, and interpretation of assays, Cleveland Clinic Journal of Medicine 2010; 77(9):616-626;doi:10.3949/ccjm.77a.09162

[3] http://www.hepfi.org/living/liv_abc.html retrieved from the internet on 3/15/2010

[4] Keltch, B., Lin, Y., and Bayrak, C. "Advanced Decision Support for Complex Clinical Decisions", JBiSE, 2010

[5] Carey, E., and Carey W., Noninvasive tests for liver disease, fibrosis, and cirrhosis: Is liver biopsy obsolete? Cleveland Clinic Journal of Medicine 2010; 77(8):519-527;doi:10.3949/ccjm.77a.09138

[6] Begg, R, "Artificial Intelligence Techniques in Medicine and Health Care", in Concepts, Methodologies, Tools, and Applications by Vijayan Sugumaran (ed) ISBN: 9781599049410, 2009

[7] Wyatt J. "Computer-based knowledge systems". The Lancet 1991; 338: 1431-1436

[8] Tan P.N., Steinbach M., and Kumar V., "Introduction to Data Mining", Pearson Addison Wesley, Boston, MA ISBN 0321321367, 2006
[9] Krawczyk, B., Woźniak, M., Orczyk, T., and Porwik, P., Cost Sensitive Hierarchical Classifiers for Non-invasive Recognition of Liver Fibrosis Stage, Proceedings of the 8th International Conference on Computer Recognition Systems CORES 2013, Advances in Intelligent Systems and Computing Volume 226, 2013, pp 639-647.
[10] Krawczyk, B., Woźniak, M., Orczyk, T., and Porwik, P., Adaptive Splitting and Selection Method for Noninvasive Recognition of Liver Fibrosis Stage, Intelligent Information and Database Systems, Lecture Notes in Computer Science, Volume 7803, 2013, pp 215-224.
[11] http://en.wikipedia.org/wiki/Classifier_%28mathematics%29
[12] Brighton, B. "Introduction to Artificial Intelligence" 1969
[13] Burns R. P., and Burns, R., "Business Research Methods and Statistics Using SPSS" 2008
[14] Gabr, S. A., and Alghadir, A. H., Prediction of fibrosis in hepatitis C patients: assessment using hydroxyproline and oxidative stress biomarkers, Indian Journal of Virology, Volume 25, Issue 1, pp 91-100 , January 2014
[15] Tamaki, N., Kurosaki, M., Matsuda, S., Muraoka, M., Yasui, Y., Suzuki, S., Hosokawa, T., Ueda, K., Tsuchiya, K., Nakanishi, H., Itakura, J., Takahashi, Y., Asahina, Y., and Izumi , N., Non-invasive prediction of hepatocellular carcinoma development using serum fibrosis marker in chronic hepatitis C patients, Journal of Gastroenterology, December 2013
[16] http://www.emedicinehealth.com/liver_biopsy/article_em.htm
[17] http://digestive.niddk.nih.gov/ddiseases/pubs/nash/images/liver_damage.gif
[18] http://www.sinomedresearch.org/hcv/Biopsy/stage.htm retrieved from the internet on 3/15/2010
[19] Batts, K.P. and Ludwig J., Chronic hepatitis. An update on terminology and reporting, Am J Surg Pathol. 1995 Dec;19(12):1409-17.
[20] http://lisp.vse.cz/challenge/ecmlpkdd2005/ECML/PKDD 2005 Discovery Challenge
[21] http://www.cs.waikato.ac.nz/ml/weka/. Weka Data mining Software
[22] http://en.wikipedia.org/wiki/Naive_Bayes_classifier
[23] http://en.wikipedia.org/wiki/Logistic_regression
[24] http://en.wikipedia.org/wiki/Cross-validation_%28statistics%29
[25] http://www.medcalc.org/manual/roc-curves.php
[26]http://www.cigna.com/customer_care/healthcare_professional/coverage_positions/medical/mm_0296_coveragepositioncriteria_serum_markers_for_liver_disease.pdf