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Stage – Specific predictive models for main prognosis measures of breast cancer

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Abstract

Breast cancer is a malignant tumor that starts in the cells of the breast. A malignant tumor is a group of cancer cells that can grow into near tissues or invading the distant areas of the body. The disease occurs almost entirely in women, but men can get it, too. Survival rate, recurrence detection and disease-free survival rate (DFS) are the main patient's outcome and prognosis measures. Breast cancer outcomes are vary among different stages of the disease. There are five stages of breast cancer named as 0, 1, 2, 3, and 4. Prognosis helps doctors to save patients' lives by estimating how patient will progress in the therapy plan by comparing the patient's results with another patient's has the same disease characteristics and completed his therapy plan. In Egypt breast cancer represented 21.6% of 33,000 women cancer deaths Ibrahim et al.,2014, with incidence rate (48.8/100,000) and mortality rate (19.2/100,000). We selected a sample about 1692 cases were diagnosed as breast cancer patients at the period from 2010 to 2012 taken from the cases recorded in the Tumors Hospital and Institute of First Settlement one of the National Cancer Institute “NCI” cancer hospitals in Egypt. NCI is the central cancer institute in Egypt. We select the main sufficient attributes to building a prognosis predictive model 0.1471 records have been selected form the whole sample. The data set we select is used to compute and predict the three main outcome of prognosis measure at two level, data level for the complete data set, stage level for every stage of breast cancer separately. The study uses efficient five prediction models with highest accuracy. Results shows that the 5-years survival rate and local recurrence was in continuous decreasing since 2010 to 2012. Metastatic as a type of breast cancer recurrence was 20.74% in 2010, 17.59% in 2011 and 22.35% in 2012. The DFS (Disease-Free Survival) have the worst rate ever in 2012 as 7.13% after it was 30.37% in 2010. Prognosis predictive models results shows that the SVM classifiers is the most accurate model to predict the three prognosis measures at the two data level.

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Keywords: Breast cancer; Survival rate (SR); Disease free survival (DFS); Recurrence detection; Prediction; Data mining

1. Introduction

Breast cancer is considered as the highest cancer type in women [1,2]. It is one of the most dangerous, deadly diseases at the present times, which infects women and men. The highly percentage of cases are happening to women. Early diagnosis is making the disease outcome very good, especially at the first phase.

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Breast Cancer Staging: Stage is typically communicated as a number on a size of 0 through 4 with organize 0 depicting non-invasive diseases that stay inside their unique area and stage 4 portraying intrusive tumors that have spread outside the bosom to different parts of the body [3]. Table 1 shows the TNM staging system is using for staging the breast cancer based on 3 values, these values represents Tumor size (TX, T0, T1, T2, T3, and T4), number of the involved Lymph Node (NX, N0, N1, N2 and N3) and Metastasis status (MX, M0 and M1) if the cancer has spread to other parts of the body beyond the breast.

Survival rate (SR), Disease-Free Survival (DFS) and the Detection of Recurrence: are types of the breast cancer

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prognosis outcome measures. Survival rates tell what portion of people with the same type and stage of cancer are still alive a certain amount of time usually 5 years (5-years survival rate) after they were diagnosed. They can't tell how long they will live, but they help give a better understanding about how likely it is that they treatment will be successful. Disease Free Survival (DFS) in breast cancer, the length of time after primary treatment for a cancer ends that the patient survives without any signs or symptoms of that cancer. In a clinical trial, measuring the disease-free survival is one way to see how well a new treatment works. Also called DFS, relapse-free survival, and RFS.

In Egypt breast cancer represented 21.6% of 33,000 women cancer deaths according WHO cancer country profiles 2014, with incidence rate (48.8/100,000) and mortality rate (19.2/100,000) [1]. Black African countries have the poorest prognosis and lowest incidence rates. The highest incidence rate was found in Belgium 147.5/10,000 [5]. United Kingdom has the highest 5-years survival rate with 87% in 2010 [6] and South Korea with 90% in 2012 [7].

Data mining is the process of pattern discovery and extraction where huge amount of data is involved. Data mining and healthcare field have implemented some detection systems and other various healthcare related systems from the clinical, diagnosis and prognosis data. In this paper we using classifying techniques to predict the breast cancer prognosis. We selected five classifiers: Support Vector Machine (SVM), Random Trees (RT), Linear Support Vector Machine (LSVM), Bayes Network (BN) and Logistic Regression (LR) to do this task.

2. Related work

Rohit J.Kate et al. [8] they built models to predicting breast cancer stages survivability using three classifiers: naïve bayes, logistic regression and decision trees with the SEER data set. They found that predicting the survivability for every stage separately achieving high accuracy than predicting the survivability to the dataset as one unit.

Houriye Ehtemam et al. [9] they introduced a comparison between 64 data mining models to prognoses and early diagnosis breast cancer and apply these models on 208 record with 10 attributes were between 2014 and 2015 in Iran. They found that bayes net was the highest accuracy model with 95.7%.

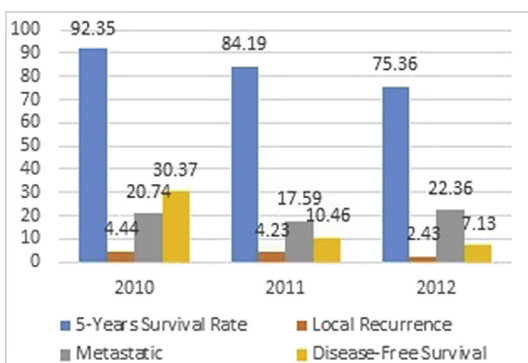


Fig. 1. Full dataset outcome by years.

Table 1
TNM staging system [4].

Stage No.	Stage Subtype	TNM Values
0	—	Tis,N0,M0
1	—	T1,N0,M0
2	2A	T0,N1,M0 Or T1,N1,M0 Or T2,N0,M0
	2B	T2,N1,M0 Or T3,N0,M0
3	3A	T0,N2,M0 Or T1,N2,M0 Or T2,N2,M0 Or T3,N1,M0 Or T3,N2,M0
	3B	T4,N0,M0 OR T4,N1,M0 Or T4,N2,M0
	3C	Any T,N3,M0
4	—	AnyT,Any N,M1

Table 2
Selected attributes.

#	Attributes
1	Year of Diagnosis
2	Date of Birth
3	Death/Last Follow Year
4	T (TNM)
5	N (TNM)
6	M (TNM)
7	Tumor Size (Category)
8	Tumor Size (Cm)
9	Stage
10	Stage Subtype
11	Histological Type
12	Histological Grade
13	LN Status
14	No. of Positive Nodes
15	ER Status
16	PR Status
17	HER-2 Status
18	HER-2 Score
19	Surgery
20	Surgery Location
21	Surgery Year
22	Therapy 1
23	Therapy 2
24	Therapy 3
25	Recurrence Type
26	Recurrence Year
27	Metastatic Location
28	Status
29	Disease Free Survival
30	Disease Free Survival – Year

Table 3
Breast cancer main outcomes by stages.

Stage	All Stages	1	2	3	4
# of Records	1471	122	741	597	11
% of Survived	82.73	89.34	87.18	76.55	45.45
% of Local Recurrence	3.54	0.82	3.24	4.52	0.00
% of Metastatic	20.46	12.30	14.98	27.97	72.73
% of DFS	14.55	24.59	17.27	9.38	0.00

M. Mehdi Owrang O [10]. using naïve bayes and association rules on SEER dataset with 16 attributes to predicting breast cancer survivability by lymph node, no. of positive lymph nodes, stage, histological grade and race.

Hadi Lotfnezhad Afsharet.al [11] using three classifiers to build a breast cancer survival prediction model on the SEER

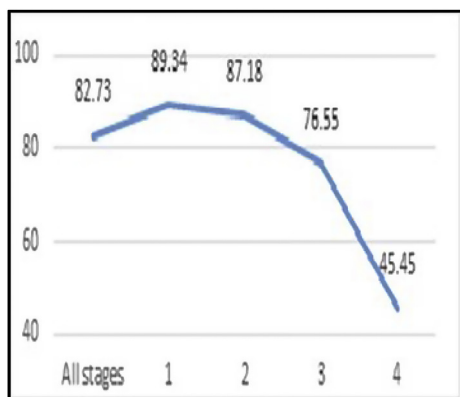


Fig. 2. 5-years survival rate by stages.

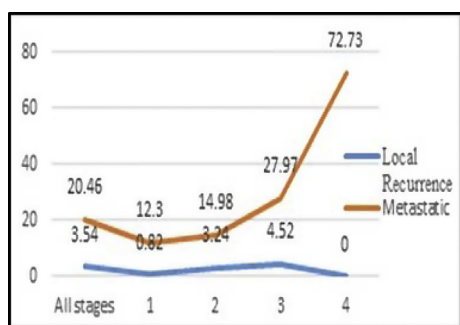


Fig. 3. Recurrence detection by stages.

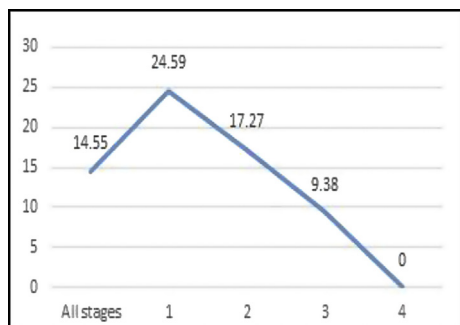


Fig. 4. Disease-free survival by stages.

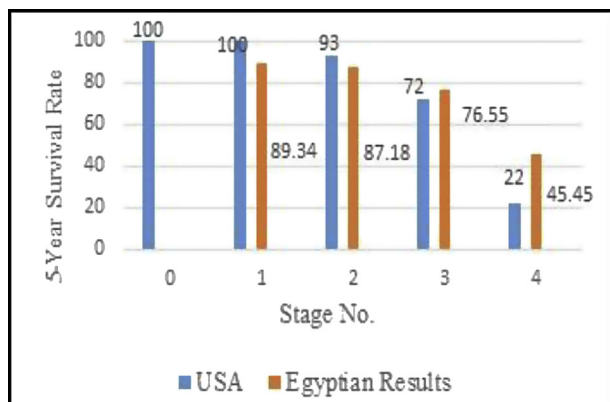


Fig. 5. Comparison between USA and Egypt by 5-years survival rate.

dataset. SVM model was achieved the highest accuracy with 97.7%, CHAID 82.2% and Bayes Net 81.8%.

Woojae Kim et al. [12] they built a model using SVM technique to predict the recurrence of the breast cancer.733 records were selected to this study. They compared between a SVM and ANN of data mining to develop a recurrence prognosis model. SVM scored 84.58% accuracy.

Hamid Karim Khani Zand [13] he made a comparison between many classifiers to predict survivability of breast cancer. He use the SEER dataset.C4.5 classifiers was more accurate than the other two classifiers with 86.7% accuracy.

Mamour Gueye et al. [14] specifying outcomes of patients with inflammatory breast cancer (IBC) treated in a hospital in Dakar. They found that the mean time to recurrence was 11.2 months. This recurrence was observed in 45.5% of cases. The median overall survival was 13.3 months (CI 95% 8.576–18.526), the survival rate was 31.8%.

Lone Winther Lietzen et al. [15] studying the OS rate based on the age ranges. The overall 1-year survival improved steadily over the period from 90.9% in 1998–2000 to 94.4% in 2007–2009.5-year survival to improve from 70.0% in 1998–2000 to 74.7% in 2007–2009.

Omar Farouk et al. [16] studying the breast cancer characteristics, biological behavior and outcome in the Egyptian women ≤ 35.Based on the results they found that the breast cancer in the young Egyptian women has more aggressive biologic behavior at advanced stages so the treatment strategies have to be tailored in a very precise manner. The median DFS was 61 months, the 3-year and 5-year disease-free survival were 58% and 50%, respectively. The 3-year and 5-year OS were 88% and 68%, respectively.

S.Kharya [17] she comparing many of classifiers: Decision Trees, Association rule, Neural Network, NAÏVE BAYES, SUPPORT VECTOR MACHINES, Logistic Regression, and Bayesian Networks to predict breast cancer prognosis. SEER data set was sued. Decision tree was achieved the highest accuracy with 93.62%.

3. Contribution

3.1. Materials and methods

3.1.1. Dataset

The National Cancer Institute “NCI” is the oldest cancer hospital and institute in Egypt. In 2014 the “NCI Tagamoo Hospital” for tumors was opened in first settlement to be first branch of the NCI specialized in breast tumors and all breast cancer cases were moved to it. Our dataset is the first

Table 4
Prognosis prediction for all the dataset.

Classifier Name	5-years S.R	Recurrence Detection	DFS
SVM	99.18	99.59	98.03
RT	93.68	96.8	87.15
BN	89.06	96.67	86.27
LR	88.72	96.26	86.13
LSVM	88.65	96.6	86.27

automation process for these cases files, also it's the first time to calculating the outcome from these records or using these data in any data mining models. We have chosen all the important attributes which use in the prognosis process. About 40 attributes were selected from the records and about 30 attributes were selected to calculate the outcome measures and build the predictive models. We selected a sample about 1692 cases were diagnosed as breast cancer patients at the period from 2010 to 2012 0.1471 records have been selected form the whole sample after preprocessing the data and excluding the missing data. Records have been transformed from paper form to be an electronic records. Table 2 shows the selected attributes.

Cases selection criteria:

1. Being a female patient.
2. The case has been diagnosed since 5 years or more.
3. A complete data record or at least has the main and necessary data.

3.2. Results

3.2.1. Outcome calculations

As shown in Fig. 1 We have notice that the 5-years survival rate was in continuous decreasing since 2010 to 2012. The 5-years survival rate was 92.35% in 2010, 84.19% in 2011 and 75.36% in 2012. Also the local recurrence of the breast cancer was in continuous decreasing as 4.44% in 2010, 4.23% 2011 and 2.43% in 2012. Metastatic as a type of breast cancer recurrence was 20.74% in 2010, 17.59% in 2011 and 22.35% in 2012. The 5-years DFS (Disease-Free Survival) have the worst rate ever in 2012 as 7.13% after it was 30.37% in 2010. Tables 1 and 2.

3.2.1.1. Breast cancer outcome by stages. Table 3. presents the three outcome measures calculated for all the stages (full dataset) and for every stage separately. We notice that Stage 1

Table 5
5-Years Survival rate by stages.

Classifier	5-Years Survival Rate				
	All Stage	1	2	3	4
SVM	99.18	98.33	99.33	99.33	100
RT	93.68	98.33	95.96	96.98	100
LSVM	88.65	97.5	91.12	95.81	100
BN	89.06	96.67	92.19	97.15	100
LR	88.72	97.5	90.71	94.97	100

Table 6
Recurrence detection by stages.

Classifier	Recurrence Detection				
	All Stage	1	2	3	4
SVM	99.59	100	99.46	99.33	100
RT	96.9	99.17	98.65	98.49	100
LSVM	96.6	100	96.9	95.81	100
BN	96.67	100	97.17	97.15	100
LR	96.26	100	96.33	94.97	100

has the finest outcome as 89.34% 5-years survival rate and 24.59% disease-free survival rate.

Figs. 2–4. represents the differences between the full dataset and stages outcomes.

Table 7
Disease-Free Survival (DFS) by stages.

Classifier	Disease-Free Survival				
	All Stage	1	2	3	4
SVM	98.03	99.17	96.77	99.5	—
RT	87.15	95	88.69	96.15	100
LSVM	86.27	95	83.98	91.12	100
BN	86.27	92.5	83.71	91.12	100
LR	86.13	90	84.25	91.46	—

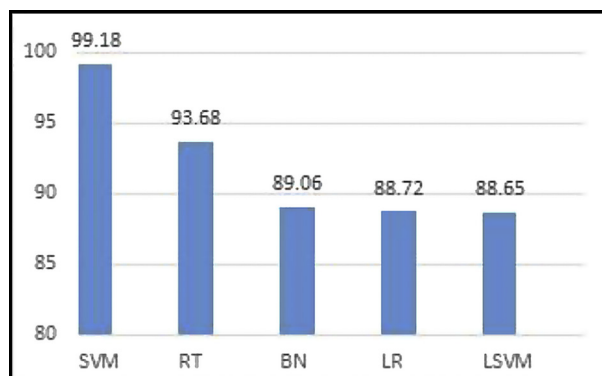


Fig. 6. 5-Years survival rate prediction accuracy.

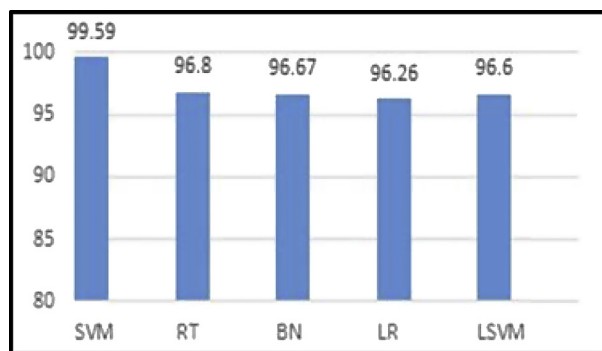


Fig. 7. Recurrence detection prediction.

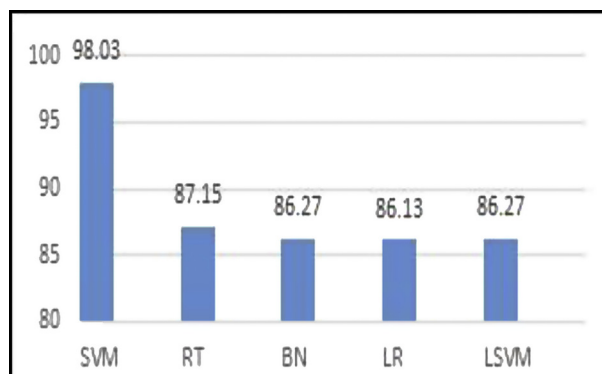


Fig. 8. Disease-free survival prediction accuracy.

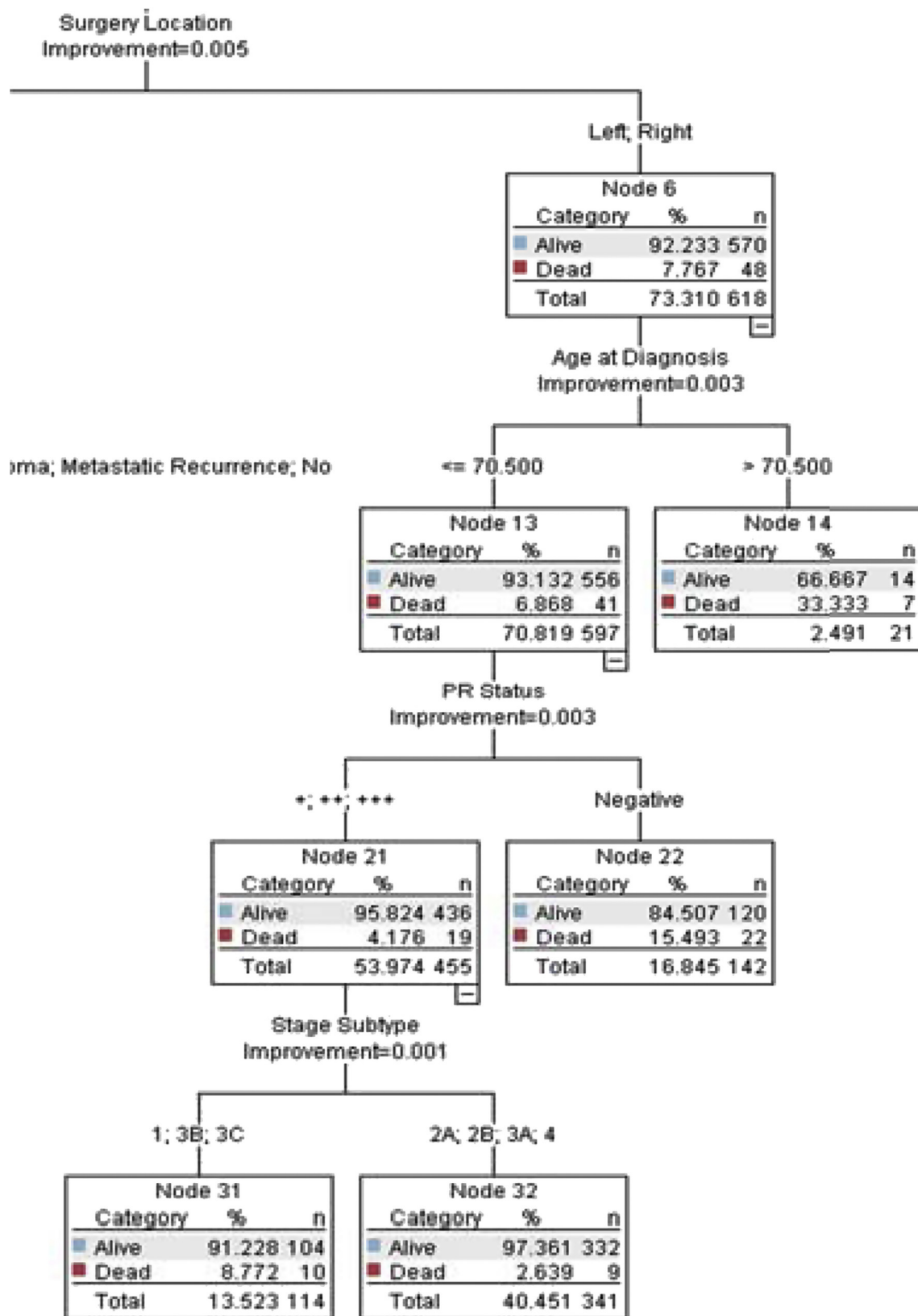


Fig. 9. Part of the 5-years survival rate predication model tree.

As Fig. 5. Shown and according to the American Cancer Society in 2012 we make this comparison between the USA 5-years survival rate and our results based on the Egyptian patient's data. We notice that the Egyptian patients does not diagnosed as in "Stage 0" ever.

Also we notice that the Egyptian patients have better prognosis at both of 3 and 4 stage than the American patients. Stage 3 have the second incidence rate in the Egyptian patients.

3.2.2. Prognosis prediction model

In this part we predict the breast cancer stage-specific prognosis by using five classifiers techniques. We selected the five classifiers: Support Vector Machine (SVM), Random Trees (RT), Bayesian Network (BN), Logistic Regression (LR), Linear Support Vector Machine (LSVM), which have achieved the highest accuracy with our dataset using "IBM SPSS Modeler" data mining software.

As Table 4, shown that the SVM and RT classifiers have the highest prediction accuracy in the 5-years survival rate. LSVM and SVM have the highest accuracy in the recurrence detection. In disease-free survival (DFS) prediction SVM and RT are the highest classifiers in the prediction accuracy.

3.2.2.1. 5-Years survival rate prediction. According to Table 5, SVM classifier has the highest prediction accuracy at the 5-years survival rate prediction. Stage 4 have the best prognosis prediction accuracy between all the stages. Table 7.

3.2.2.2. Recurrence detection prediction. As Table 6 shown the recurrence detection prediction accuracy stage 1 become the secondly after stage 4 as highest prognosis prediction for all the five classifiers.

3.2.2.3. Disease-free survival prediction. According to our dataset, stage 4 has one value for disease-free survival as breast cancer outcome in other words stage 4 has no survivors. Table 7 shows the disease-free survival by stage. SVM and logistic regression give no predictive results to DFS at stage 4 because it has one value as prediction target.

3.2.2.4. The 5-years survival rate prediction model. In this section we will introduce the random tree prediction model for the 5-years survival rate as an example for our prediction models.

1. The model configuration is: training set: 80% and 20% as testing set.
2. Model accuracy: 93.68%
3. Model rules:

Recurrence 1 Type in ["Local" "Metastatic"] [Mode: Alive].

of Positive Nodes in ["0" "1" "10" "11" "13" "14" "15" "16" "2" "21" "23" "27" "3" "4" "7"] [Mode: Alive].

Metastatic 1 Location in ["Bone, Brain, Liver, Lung" "Bone, Breast, Liver" "Liver" "Liver, Lung"] [Mode: Dead] => Dead.

Metastatic 1 Location in ["Bone" "Bone, Brain" "Bone, Brain, Lung" "Bone, Dural" "Bone, Liver" "Bone, Liver, Lung" "Bone, Lung" "Bone, Skull" "Brain" "Brain, Liver" "Breast" "Chest" "Lumbosacral" "Lung" "Metastatic Adenocarcinoma" "Metastatic Duct Carcinoma" "Metastatic Recurrence" "No"] [Mode: Alive].

Metastatic 1 Location in ["Bone, Brain" "Bone, Brain, Lung" "Bone, Dural" "Bone, Liver, Lung" "Bone, Lung" "Bone, Skull" "Brain, Liver" "Breast" "Chest" "Lumbosacral" "Metastatic Adenocarcinoma" "Metastatic Duct Carcinoma" "Metastatic Recurrence"] [Mode: Alive] => Alive.

Metastatic 1 Location in ["Bone" "Bone, Liver" "Brain" "Lung" "No"] [Mode: Alive].

HER-2 Score in ["0"] [Mode: Alive] => Alive.

HER-2 Score in ["1+" "2+" "3+"] [Mode: Alive] => Alive.

of Positive Nodes in ["12" "17" "20" "22" "28" "5" "6" "8" "9" "Unknown"] [Mode: Dead].

Metastatic 1 Location in ["Bone" "Bone, Liver" "Bone, Lung" "Brain" "Chest" "Liver, Lung" "Lung"] [Mode: Alive].

Therapy 2 in ["Chemotherapy" "Hormonotherapy"] [Mode: Alive] => Alive.

Therapy 2 in ["Non" "Radiotherapy"] [Mode: Dead] => Dead.

Metastatic 1 Location in ["Bone, Brain, Liver" "Bone, Chest" "Bone, Liver, Lung" "Liver" "Metastatic Adenocarcinoma" "Metastatic Recurrence" "No"] [Mode: Dead] => Dead.

Recurrence 1 Type in ["No"] [Mode: Alive].

Surgery Location in ["Left, Right" "No"] [Mode: Alive] => Alive.

Surgery Location in ["Left" "Right"] [Mode: Alive].

Age at Diagnosis ≤ 70.500 [Mode: Alive].

PR Status in ["+" "++" "+++"] [Mode: Alive].

Stage Subtype in ["1" "3B" "3C"] [Mode: Alive] => Alive.

Stage Subtype in ["2A" "2B" "3A" "4"] [Mode: Alive] => Alive.

PR Status in ["Negative"] [Mode: Alive] => Alive.

Age at Diagnosis >70.500 [Mode: Alive] => Alive. Figs. 6–8.

4. Tree Graph: Fig. 9 shows a part of the 5-years survival rate predication model tree.

4. Conclusions

Breast cancer is deadly disease but the prognosis of its outcome can save lives. We built a predictive model to prognosis the breast cancer outcome according to Egyptian patients. The dataset we introduced in this paper, included all the main and important attributes for prognosis the breast cancer outcome. Our prediction model achieved the highest accuracy, which will helps doctors to choose the ideal therapy plan for the new breast cancer patients. Survival rate, recurrence detection and disease-free survival (DFS) are the main patient's outcome and prognosis measures. Breast cancer outcomes are vary among different stages of the disease. Breast

cancer in Egypt represented 21.6% of 33,000 women cancer deaths with incidence rate (48.8/100,000) and mortality rate (19.2/100,000). Our dataset was about 1692 cases were diagnosed as breast cancer patients at the period from 2010 to 2012 taken from the cases recorded in the Tumors Hospital and Institute of First Settlement one of the National Cancer Institute “NCI” cancer hospitals in Egypt. NCI is the central cancer institute in Egypt. 1471 records have been selected from the whole sample. This data set is used to compute and predict the outcome and prognosis measure for the complete data set and for every stage separately by using five prediction models.

Results shows that the 5-years survival rate was in continuous decreasing since 2010 to 2012. The 5-years Survival rate was 92.35% in 2010, 84.19% in 2011 and 75.36% in 2012. The disease-free survival rate median was 2 years.

Prognosis predictive models results shows that the SVM prognosis stage level model for the 5-years survival rate archived more accurate results than the full data level at stages 2,3 and 4 as 99.33%, 99.33% and 100%. The Other models archived more accurate results at the stage level for all the four stages. Stage 4 has the more accurate in the stage level for all the models. Disease-free survival for stage 4 has one value as a prediction target, SVM and logistic regression have no results for it.

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