Implementation of Fuzzy-based Model for Prediction of Prostate Cancer

Rusliyawati¹,², Kurnia Muludi³*, Admi Syarif³, Agus Wantoro¹,²

¹ Doctoral Program of Mathematics and Science Faculty, Lampung University, Jl. Sumantri Brojonegoro No 1, Bandar Lampung, Indonesia.
² Faculty of Engineering and Computer Science, Universitas Teknokrat Indonesia, J. ZA. Pagaralam No. 9-11, Bandar Lampung, Indonesia.
³ Department of Computer Science, Faculty of Mathematics and Science, University of Lampung, Jl. Sumantri Brojonegoro No 1, Bandar Lampung, Indonesia

email: kmuludi@fmipa.unila.ac.id³,*

Abstract: Cancer is one of the leading causes of death worldwide. One type of cancer that causes death in the male population is prostate cancer. This disease occurs only in men because in women they do not have a prostate appearance. The aim of this study was to compare the accuracy of the model with the predictions of prostate cancer specialists. Prediction is made based on prostate specific antigen data, age, and patient prostate volume. The independent variables in this study were prostate specific antigen, age, and prostate volume. The dependent variable is the risk of prostate cancer using a fuzzy model. The novelty of this study is that the model has a low, moderate, high, and very high prostate cancer risk level output. In the previous article only PCR values were produced. The results show that the proposed fuzzy model provides a PCR value that is within the PCR interval predicted by a specialist doctor can be used properly to help diagnose and analyze the possibility of prostate cancer and is one of the considerations for doctors to decide whether or not a biopsy is needed for these patients.

Keyword: fuzzy expert system, prostate specific antigen, age, patient prostate volume, and prostate cancer risk

1. Introduction
The main cause of death in the world is cancer. Prostate cancer is the second type of cancer worldwide [1]. One type of cancer that causes death in the male population is prostate cancer. The prostate gland is owned by men not women so that cancer is only found in men aged between 65 and 75 years [2]. Prostate abnormalities can occur in patients who have a normal PSA value (<4 ng / mL) and more than normal (> 4 ng / mL), with the age at which the prostate abnormality is 50-93 years [3]. As the patient ages, prostate cancer will increase [4]. Approximately 31,620 deaths out of 174,650 prostate cancer cases occurred in the United States based on 2019 data [5]. In 2018 the number of new cases of prostate cancer in Indonesia reached 11,361 cases, and the death rate from this disease was 5,007 patients (Globocan, 2018). The risk factors for cancer that should be preventable are closely related to the high number of new cases of cancer, which is about 40% of cancer deaths [6]. Important modifiable risk factors for cancer are smoking, being overweight, excessive alcohol consumption, air pollution, and casinogens in the work environment [7].

The development of medical technology helps make medical decisions, especially in predicting the determination of the type of disease, recognizing the symptoms of the disease, and making decisions for therapeutic actions for a disease by combining the signs and symptoms of the disease with the history of the disease, physical examination and laboratory findings [8] [9]. Artificial Intelligence (AI) is a sub-field of computer science which is the process of designing intelligent computers (hardware / software) that have intelligent behavior that is taken by people who are considered smar [10]. Soft computing as a computing system that gives space to the obscurity of the real world and
using the human brain as a model has been applied to develop computational systems for diagnosis and prognosis in medicine [11]. Soft computing basically consists of artificial neural networks, fuzzy logic and genetic algorithms [12]. The use of fuzzy logic and other AI methods provides positive results to solve various problems in the medical field, one of which is the application of fuzzy logic to predict prostate cancer which can be used as a decision support tool in medical diagnosis [13]. The use of soft computing techniques based on fuzzy set theory with fuzzy rules and an adjusted membership function based on a genetic algorithm can provide good results for predicting prostate cancer stage based on fuzzy genetic algorithms [8]. The neuro-fuzzy system uses a fuzzy system to represent and process knowledge in a clear way with easy interpretation and takes advantage of the artificial neural network (ANN) learning capacity used to classify prostate cancer [14] [15].

This research is a repetition of research [16] who researched at the Department of Urology, Meram Medical Faculty, Necmettin Erbakan University, Konya, Turkey with the title Application of Soft Sets to Diagnose the Prostate Cancer Risk, with a sample of 78 patients. Input variables used were prostate specific antigen (PSA), prostate volume (PV) and patient age, while the output variable was the risk of prostate cancer. As for foreign and domestic research, there have been studies previously [14] resulted in a predictive accuracy of the neuro-fuzzy system superior to tPSA and% PSA in increasing specificity and sensitivity. Research [8] shows that the use of soft computing techniques can provide good results for predicting prostate cancer stage based on fuzzy genetic algorithms. While research [13] produce a fuzzy expert system (FES) to predict prostate cancer which can be used as a decision support tool in medical diagnosis. A domestic [3] with the results that prostate abnormalities can occur in patients who have a normal PSA value (<4 ng / mL) and more than normal (> 4 ng / mL), with the age of the prostate abnormality being 50-93 year.

The difference between this study and previous research is that this study developed a model with the fuzzy logic of the mamdani method to classify prostate cancer risk (low, middle, high, and very high) based on PSA, age and PV data. This study describes the making of a model equipped with the membership function of each fuzzy variable and all the required fuzzy rules. Model testing uses some patient data at a private hospital in Bandar Lampung.

2. Method
2.1 Research Design
Prostate cancer risk prediction research design can be seen in the following figure.

![Figure 1 Research design](image)

2.2 Objects, Variables, Populations and Research Samples
This study used the fuzzy function of the Mamdani method with the object of the study being a male prostate patient. Independent variables used in the study were prostate specific antigen (PSA), prostate volume (PV) and patient age.
The dependent variable is the risk of prostate cancer. The data collection method was performed using a database of prostate patients, with a population of 5 male patients.

2.3 Fuzzy Logic

As one of the building blocks of soft computing, fuzzy set theory was first introduced by Lotfi A. Zadeh in 1965. The theory of fuzzy sets is the basis of fuzzy logic. Membership value is the main characteristic of fuzzy logic reasoning [17]. Fuzzy logic with a truth level of value between black and white (gray) replaces boolean truth. The representation of the meaning of black and white can use a crisp set. The elements in the set are defined as a crisp set A. If \( a \in A \), then \( a = 1 \), and if \( a \notin A \), then \( a = 0 \). The notation \( A = \{(x, P_x)\} \) indicates that A contains element x with properties P is correct. P(x) can be said to be true if and only if \( X_A(x) = 1 \) assuming \( X_A \) is a function of characteristic A with properties P [18]. The extended range of characteristic functions in a crisp set becomes the basis for a fuzzy set that includes real numbers with intervals \([0,1]\). Membership values are not only at 0 and 1, but also the values that lie between them [19]. In another sense, the truth value of a statement is not only true (1) or false (0), but there are still values that lie between true and false [20].

The application of neuro fuzzy in the health sector has been carried out by several studies including Benecci's [14] research, the development of a neuro-fuzzy system has been carried out to improve the performance of tPSA as a differentiator for prostate cancer based on serum data, namely tPSA and% fPSA, and clinical data, namely patient age. A fuzzy-based system using a 4-tuple record consisting of a blood urea test sample, urea clearance test, creatinine clearance test and Estimated Filtrate Glomerular rate (eGFR) was used in developing a predictive model for chronic kidney disease and failure using MATLAB software [21].

2.4 Metode Mamdani

The fuzzy inference system used in this study uses Mamdani. The mamdani method or the max-min method was first introduced by Ebrahim Mamdani in 1975. The stages to get the output are: formation of fuzzy sets, application of implication functions, composition of rules, and affirmation (defuzzy) [17].

2.5 Prostat Cancer

Prostate cancer is the second most common cause of cancer death among men in some industrialized countries. Factors that cause prostate cancer include family history of cancer, age, ethnic background, and the level of prostate specific antigen (PSA) in the blood [22]. A very important method of predicting baseline for patients is the PSA level in the blood [23]. Prostate specific antigen (PSA) is a glycoprotein produced by prostate epithelial cells [24]. PSA production is increased in men with prostate cancer and more PSA is released into the serum due to disruption of the tissue barrier between the lumen of the prostate gland and capillaries, which will result in increased PSA levels [25]. PSA is widely used in diagnosis, post-prostate cancer treatment planning follow-up process. PSA has a specific organ character, not a disease due to the presence of cancer cells, PSA levels can be increased in all clinical conditions of the prostate [26]. Serum PSA can be used to predict prostate cancer [27]. If the PSA level is high, the prostate volume growth rate (VP) is faster [28]. VP growth rates averaged 0.7 ml/year (PSA levels 0.2-1.3 ng/dl), 2.1 ml/year (PSA levels 1.4-3.2 ng/dl), 3.3 ml/year (PSA level 3.3-9.9 ng/dl) [29]. Apart from PSA levels, age and body mass index (BMI) were significant predictive factors for PV. The rate of change in PV according to age was 0.68 ml/year (age 40s), 0.84 ml/year (age 50s), 1.09 ml/year (age 60s), and 0.50 ml/year (age >70 years) [30].

3. Evaluation

3.1 Variables

This fuzzy model for prostate cancer diagnosis is used to determine the percentage of Prostate Cancer Risk (PCR) based on PSA, age, and PV data. This system has limitations, namely the system design is made with fuzzy reasoning using the Mamdani method (system input and output in the form of fuzzy sets), input variables (PSA, Age, and PV) and output variables (PCR), separate arrangements for specific policies in outside the variables used, and making rules in the knowledge base based on the views of experts related to this field. The designed fuzzy model is shown in the following Tables 1 and Figure 2.
Table 1. Fuzzy variables

| I/O  | Variabel                                      | Domain |
|------|-----------------------------------------------|--------|
| Input| Prostate Specific Antigen/PSA (ng/ml)         | [0, 9] |
|      | Age (tahun)                                  | [0, 100] |
|      | Prostate Volume/PV (ml)                      | [0, 50] |
| Output| Prostate Cancer Risk/PCR                     | [0, 3]  |

Table 2. Fuzzy input set

| Fuzzy Variables | Fuzzy Sets | Domain |
|-----------------|------------|--------|
| **PSA**         | Very Low  | VL     |
|                 | Low       | L      |
|                 | Middle    | M      |
|                 | High      | H      |
| **Age**         | Middle Age| MA     |
|                 | Elderly   | E      |
|                 | Old       | O      |
| **PV**          | Very Old  | VO     |
|                 | Small     | S      |
|                 | Middle    | M      |
|                 | Big       | B      |
|                 | Very Big  | VB     |

Figure 2. Input and output variables

The fuzzy set used for each variable for the fuzzy input set and the fuzzy output set is in Table 2 and Figures 3-5.

The triangular membership function is used to represent the PSA variable in the Very Low, Low, Middle, and High fuzzy sets, while the trapezoidal membership function is used for the Very High fuzzy set.

Table 3. Fuzzy output set

| Model | \( \text{PSA} \) |
|-------|------------------|
| The triangular membership function is used to represent the PSA variable in the Very Low, Low, Middle, and High fuzzy sets, while the trapezoidal membership function is used for the Very High fuzzy set. |
Age
The triangular membership function is used to represent the age variable in the Elderly and Old fuzzy sets, while the trapezoidal membership function is used for Middle Age and Very Old fuzzy sets.

PV
The triangular membership function is used to represent the PV variable in Middle and Big fuzzy sets, while the trapezoidal membership function is used for Small and Very Big fuzzy sets.

The output model for displaying the analysis results using fuzzy mamdani is adjusted to the following rules.

| Fuzzy Variables | Fuzzy Sets | Domain |
|-----------------|------------|--------|
| PCR             | Low        | VL     | [0, 0.85] |
|                 | Middle     | M      | [0.67, 1.5] |
|                 | High       | H      | [1.4, 2.25] |
|                 | Very High  | VH     | [2, 3] |

The output model is presented in Figure 6.
The triangular membership function is used to represent the PCR variable for Middle and High fuzzy sets, while the trapezoidal membership function is used for Low and Very High fuzzy sets.

Figure 6. Representation of the membership function for the PCR variable

3.2 Fuzzy Rule

The ability to make decisions from a fuzzy system is contained in a set of rules. In general, these rules are intuitive and in the form of qualitative statements written in the form of if then, so that they are easy to understand. The rules of the fuzzy system for prostate cancer diagnosis are derived from intuition, the views of experts in the field of internal medicine, especially those dealing with prostate cancer and based on literature. Based on the combination of the existing input variables, 64 rules can be formed. For example, the following rules can be written.

Rule 1: IF PSA = Very Low AND age = Middle Age AND PV = Small THEN PCR = Middle
Rule 33: IF PSA = Low AND age = Old AND PV = Big THEN PCR = High

3.3 Fuzzy System Inference

The set operation used in the fuzzy system for prostate cancer diagnosis is AND (minimum method) the use of the minimum method in the fuzzy system for prostate cancer diagnosis can be defined μPSA age PV = (μPSA ∩ μage ∩ μPV) = (μPSA ∩ μage ,, min μPV). The minimum method used for Rule 1 and Rule 33 can be written as follows.

\[ \alpha_1 = \mu_{VL}(PSA) \land \mu_{MA}(age) \land \mu S(PV) = \min(\mu_{VL}(PSA), \mu_{MA}(age), \mu S(PV)) \]

\[ \alpha_{33} = \mu_{L}(PSA) \land \mu O(age) \land \mu B(PV) = \min(\mu_{L}(PSA), \mu O(age), \mu B(PV)) \]

4. Results and Discussion

The study used patient data which is presented in Table 4.

Table 4 Test problem

| Patients | PSA (ng/ml) | Usia (year) | PV (ml) |
|----------|-------------|-------------|---------|
| 1        | 9           | 71          | 41.0    |
| 2        | 7           | 63          | 37.7    |
| 3        | 4.7         | 52          | 26.3    |
| 4        | 2.9         | 47          | 36.0    |
| 5        | 3.4         | 55          | 47.2    |

Model testing uses 3 variables from 5 patient data. The first data was a patient whose PSA level = 9 ng / ml, was 71 years old with PV = 41.0. Based on the analysis results obtained fuzzy value = 0.41 so that the classification of the risk of prostate cancer is low. Prostate cancer risk calculation as shown in Figures 7 and 8.
The results of the analysis of the third patient who had PSA levels = 2.9 ng / ml, aged 47 years with PV = 36.0 obtained a fuzzy value = 2.53 so that the classification of the risk of prostate cancer is classified as Very High.

The test results of the five data are presented in Table 5.

| No | Variables | Value of Fuzzy | FES PCR | Expert Judgement PCR | Result |
|----|-----------|----------------|---------|----------------------|--------|
| 1  | 9         | 71             | 41      | Low Risk             | Low Risk | Correct |
| 2  | 7         | 63             | 37.7    | Low Risk             | Low Risk | Correct |
| 3  | 4.7       | 52             | 26.3    | Low Risk             | Low Risk | Correct |
| 4  | 2.9       | 47             | 36.0    | Very High Risk       | Very High Risk | Correct |
| 5  | 3.4       | 55             | 47.2    | Low Risk             | Low Risk | Correct |
The results of testing the data on 5 patients showed that the model developed was in accordance with the opinion of a urologist in the prostate field.

5. Conclusion

The results showed that the proposed fuzzy model could be used properly by specialist doctors to help diagnose and analyze the possibility of prostate cancer. The results of the calculation provide a PCR value that is within the PCR interval predicted by a specialist, which can be one of the considerations for doctors to make a decision whether or not a prostate biopsy is needed for this patient. Henceforth, in order to obtain a more optimal level of accuracy, it is necessary to test the model using more data and adding rule-based knowledge.

6. References

[1] L. Rahib, B. D. Smith, R. Aizenberg, A. B. Rosenzweig, J. M. Fleshman and L. M. Matrisian, "Projecting cancer incidence and deaths to 2030: The unexpected burden of thyroid, liver, and pancreas cancer in the United States," Cancer Res, vol. 74, no. 11, pp. 2913-2921, 2014.
[2] V. Kumar, A. Abbas and J. Aster, Buku Ajar Patolog Robbins, 9th Edition, Singapura: Elsevier, 2013.
[3] N. S. Wulansari and M. Marindawati, "Profil Prostate Spesific Antigen (PSA) pada Penyakit Prostat di Rumah Sakit Umum Daerah Cengkareng Jakarta Barat," Muhammadiyah Journal of Geriatric, vol. 1, no. 1, pp. 18-22, 2020.
[4] A. Jemal, R. Siegel, E. Ward, T. Murray, J. Xu, C. Smigal and M. J. Thun, "Cancer statistics," CA Cancer J Clin, vol. 56, no. 2, pp. 106-130, 2006.
[5] R. L. Siegel, K. D. Miller and A. Jemal, "Cancer Statistics, 2019," CA Cancer J Clin, vol. 69, no. 1, pp. 7-34, 2019.
[6] Pusat Data dan Informasi, Situasi Penyakit Kanker, Jakarta: Kementerian Kesehatan RI, 2015.
[7] G. Danaei, S. V. Hoorn, A. D. Lopez and C. J. Murray, "Causes of cancer in the world: Comparative risk assessment of nine behavioural and environmental risk factors," Lancet, vol. 366, pp. 1784-1793, 2005.
[8] M. J. d. P. Castanho, F. Hernandes, A. M. De Re, S. Rautenberg and A. Bilis, "Fuzzy expert system for predicting pathological stage of prostate cancer," Expert System with Applications, Elsevier, vol. 40, no. 2, pp. 466-470, 2013.
[9] N. Allahverdi, "Fuzzy Logical Its Application in Medicine," In Press, 2019.
[10] N. Allahverdi, "Application of Fuzzy Approach in Medicine. Problems and Perspectives," 3rd International Symposium on Multidisciplinary Studies and Innovative Technologies (ISMSIT), pp. 1-8, 2019.
[11] F. Susilo, Pengantar Himpunan & Logika Kabur serta Aplikasinya, Yogyakarta: Universitas Sanata Dharma, 2003.
[12] O. F. B. Al Hassani and S. A. Kareem, "The use of Soft Computing Approaches "FL" Models for Medical Prognosis "NPC"," in Proceedings of iiWAS, Linz, Austria, 2008.
[13] I. Saritas, N. Allahverdi and I. U. Sert, "A Fuzzy Expert System Design for Diagnosis of Prostate Cancer," in International Conference on Computer-Systems and Technologies - Comp SysTech, 2003.
[14] L. Benecchi, "Neuro-Fuzzy System for Prostate Cancer Diagnosis," Urology, Elsevier, vol. 68, no. 2, pp. 357-361, 2006.
[15] A. Keles, A. Keles and U. Yavuz, "Expert system based on neuro-fuzzy rules for diagnosis breast cancer," Expert Systems with Application, vol. 38, no. 5, pp. 5719-5726, 2011.
[16] S. Yuksel, T. Dizman, G. Yildizdan and U. Sert, "Application of Soft Sets to Diagnose the Prostate Cancer Risk," Journal of Inequalities and Applications, vol. 229, pp. 1-16, 2013.
[17] S. Kusumadewi and H. Purnomo, Aplikasi Logika Fuzzy untuk Pendukung Keputusan, Yogyakarta: Graha Ilmu, 2010.

[18] J. Yan, M. Ryan and J. Power, Using Fuzzy Logic: Towards Intelligent Systems, New Jersey: Prentice Hall, 1994.

[19] PERSI, I. Saritas, N. Allahverdi and L. Sert, "A Fuzzy Expert System Design for Diagnosis of Prostate Cancer," in International Conference on Computer Systems and Technologies, CompSysTech, 2003.

[20] J.-S. R. Jang, C.-T. Sun and E. Mizutani, Neuro-Fuzzy and Soft Computing: Computational Approach to Learning and Machine Intelligence, India: Pearson Education Pte.Ltd, 1997.

[21] A. Michael and A. Olayinka, "Predictive Model for Likelihood of Detecting Chronic Kidney Failure and Disease Using Fuzzy Logic," The International Journal of Computational Science, Information Technology and Control Engineering, vol. 5, no. 2, pp. 1-29, 2018.

[22] W. J. Catalona, A. W. Partin, K. M. Slawin, M. K. Brawer, R. C. Flanigan, A. Patel, J. P. Richie, J. B. deKernion, P. C. Walsh, P. T. Scardino, P. H. Lange, E. N. Subong, R. C. Parson, G. H. Gasior, K. G. Loveland and P. C. Southwick, "Use of the Percentage of Free Prostate-Specific Antigen to Enhance Differentiationof Prostate Cancer from Benign Prostatic Disease," Journal American Medical Association, vol. 279, no. 19, pp. 1542-1547, 1998.

[23] S. Egawa, S. Soh, M. Ohori, T. Uchida, K. Gohji, A. Fuji, S. Kuwao and K. Koshiba, "The Ratio of Free to Total Serum Prostate Specific Antigen and Its Use in Differential Diagnosis of Prostate Carcinoma in Japan," Journal American Cancer Society, vol. 79, no. 1, pp. 90-98, 1996.

[24] P. J. V. Cangh, P. D. Nayer, L. D. Vischer, P. Sauvage, B. Tombal, F. Lorge, F. X. Wese and R. Opsomer, "Free to Total Prostate-Specific Antigen (PSA) Ration Improves The Discrimination Between Prostate Cancer and Benign Prosttic Hyperplasia (BPH) in The Diagnostic Gray Zone of 1.8 to 10 ng/mL Total PSA," Journal of Urology, Elsevier Inc., vol. 48, no. 6A, pp. 67-70, 1996.

[25] R. M. Hoffman, "Screening for Prostate Cancer," Uptodate.com, 02 Mar 2020. [Online]. Available: https://www.uptodate.com/contents/screening-for-prostate-cancer. [Accessed 02 Sep 2020].

[26] K. Miller, P. Abrahamsson, K. Akakura, F. Debryune, C. Evans and I. Klotz, "The Continuing Role of PSA in the Detection and Management of Prostate Cancer," European Urology Supplements, pp. 327-333, 2007.

[27] K. A. D'Silva, P. Dahm and C. L. Wong, "Does This Man With Lower Urinary Tract Symptoms Have Bladder Outlet Obstruction? The Rational Clinical Examination: A Systematic Review," JAMA, vol. 12, no. 5, pp. 535-542, 2014.

[28] C. Roehrborn, J. M. Mc Connell, J. Bonilla, S. Rosenblatt, P. Hudson, G. Malek, P. Schellhammer, R. Bruskewitz, A. Matsumoto, L. Harrison, H. Fuselier, P. Walsh, J. Roy, G. Andriole, M. Resnick and J. Waldstreicher, "Serum Prostate Specific Antigen is a Strong Predictor of Future Prostate Growth in Men With Benign Prostatic Hyperplasia. PROSCAR Long-Term Efficacy and Safety Study," J Urol, vol. 163, no. 1, pp. 13-20, 2000.

[29] S. Wijanarko, G. W. S. Hardjowijoto and et al, "Studi Analitik Pengaruh Pemasangan Kateter terhadap kadar Antigen Spesifik Prostat Dalam Darah Pada Pasien Hiperplasia Prostat Jinak Dengan Retensi Urine," JURI, vol. 10, pp. 1-8, 2003.

[30] T. Jinsung, D.-G. Lee, B. Suh, S. Y. Cho, D. H. Chang, S. H. Paick and H. L. Lee, "Establishment of Reference Range for Prostate Volume and Annual Prostate Volume Change Rate in Korean Adult Men: Anlyses of a Nationwide Screening Population," Journal of Korean Medical Science, vol. 30, pp. 1136-1142, 2015.