

An Intelligent System for Computer-Aided Ovarian Tumor Diagnosis

Krzysztof Dyczkowski¹, Andrzej Wójtowicz¹,
Patrik Żywica¹, Anna Stachowiak¹,
Rafał Moszyński² and Sebastian Szubert²

¹Faculty of Mathematics and Computer Science
Adam Mickiewicz University
Umultowska 87, 61-614 Poznań, Poland
chris@amu.edu.pl

²Division of Gynecological Surgery
Poznan University of Medical Sciences
Polna 33, 60-535 Poznań, Poland
rafalmoszynski@gmail.com

Abstract. This article describes the fundamentals of an intelligent decision support system for the diagnosis of ovarian tumors. The system is designed to support diagnosis by less experienced gynecologists, and to gather data for continuous improvement of the quality of diagnosis. The theoretical basis for the construction of the system is the IF-sets framework, used to aggregate multiple decision-making methods, and simultaneously providing information about positive and negative diagnosis of a given tumor type.

1 Introduction

Recent statistics on ovarian tumors indicate that incidence and mortality rates are intolerably high. Estimated numbers of patients newly diagnosed with the condition, and of deaths, in all member countries of the European Union in 2012, stand at 45,000 and 30,000 respectively. In some countries the problem has already taken on dramatic proportions. For instance, in Poland the European age-standardized mortality rate per 100,000 stands at 10.3, which is significantly higher than the European Union average of 7.4 [1].

There are several factors preventing a significant improve prognosis of ovarian cancer patients. Most of tumors are diagnosed in an advanced stage, which is due to the absence of symptoms at the beginning of the disease and the lack of effective screening. This leads to the fundamental issue which is deficiency in highly skilled gynecologists, especially in the field of ultrasonography. Recent research shows that in rural area, where the availability of such gynecologists is low, the number of difficult to diagnose cases is the same as in urbanized area [2]. The result of distinguishing between malignant and benign tumors provides answers to two significant questions: whether the patient needs surgery, and if so,

who should perform it – a gynecological oncologist or a general gynecologist [3]. If a tumor is difficult to diagnose, the patient is referred to an external center. In such cases a precautionary laparotomy is performed, which could be avoided in favor of less invasive laparoscopy if the diagnosis were more certain. An initial misdiagnosis may lead to delayed diagnosis or to an operation by an inexperienced surgeon.

For this reason, there is a need to develop an effective preoperative model for inexperienced gynecologists. Two approaches have emerged in the last two decades, which aim to provide an approximate model of a subjective assessment [4]. The first approach is based on scoring systems, where points are assigned for the presence of certain features in the patient. If the total number of points exceeds a certain threshold, then malignancy of the tumor is indicated. This approach has resulted in a wide range of scoring systems [5–7].

The second approach involves the use of formal mathematical models. Many algorithms have been developed under the rule-based approach: they use not only sophisticated concepts such as rough sets [8] but also simpler schemes of reasoning [9]. By the use of machine learning techniques, researchers have developed solutions which take advantage of logistic regression [10, 11], artificial neural networks [12, 13], support vector machines and Bayesian networks [14, 15]. Some attempts have also been made to use neuro-fuzzy networks in ovarian tumor diagnosis [16].

Intermediate approaches have been proposed in the form of the RMI model, which is a combination of a scoring system and a formal model [17], and in GI-RADS, which is a rule-based scoring system [18].

The authors of the above-mentioned scoring systems and models claim high overall prognostic accuracy for their predictive models, reaching as high as 95% and even 100% [6, 19]. Unfortunately, when these assumptions are subjected to external evaluation, it is found that in reality the efficacy of predictions rarely exceeds 90%, in case of either sensitivity or specificity [20, 21]. If we wish to achieve a significant decrease in the mortality rate, then results such as these will not be sufficient.

In this paper we present the detailed concept of OvaExpert – a complex system that is being developed by specialists in computer-aided decision making systems in cooperation with scientists from the Division of Gynecological Surgery at Poznan University of Medical Sciences. The system is intended to address the need for a highly reliable tool supporting less experienced gynecologists in the entire diagnostic process. Details of the motivations, functionality and architecture of this system will be presented in the following sections of this paper. We end by stating some conclusions and describing plans for future work.

2 Motivation

The need to improve the efficacy of preoperative differentiation of tumors is inspiring studies at many research centers. The most widely exploited approach is to develop new models using recent techniques from the fields of computa-

tional intelligence and machine learning. This is a very challenging task, because the conventional methods seem already to have attained their maximum performance. In our research we approach the problem differently. The main idea is to integrate all present knowledge about ovarian tumors (models, scoring systems, reasoning schemes, etc.) into a single computer-aided system. Access to a set of testing data and to extensive expert knowledge was our main motivation to take advantage of this experience and to integrate it so as to achieve a synergy effect.

It can be observed that there is a need to create a tool that can not only support a gynecologist in the final diagnosis, but can also assist him or her during the whole diagnostic process, beginning with collecting data about the patient, and moreover can connect the medical community in the exchange of experience and verification of knowledge. To the best of our knowledge such a system does not yet exist.

One of the main objectives of the proposed system would therefore be to provide an easy, convenient and coherent way of gathering data about patients and final diagnoses. At present, the absence of a common data format leads to a lack of cooperation between physicians and loss of data. Our system, by providing a convenient interface and a standardized data schema, enables the collection of data in a common database which can be browsed, reported and analyzed, and which will become a valuable resource for the entire medical community.

A core feature of the system is its modular architecture, described in detail in the next section. All existing and new methods for supporting ovarian tumor diagnosis can be plugged into the system as modules and then integrated to increase the reliability of diagnosis. One of the key modules would be a knowledge base of rules obtained directly from experts. By that means a knowledge repository would be created, and would then be continuously supplemented and updated by users of the system. Importantly, the system would also have the ability to learn through generating rules from the collected data.

The main issue with past solutions is their insensitivity to uncertainty of the input data. We have carried out research on uncertainty in ovarian tumor diagnosis and on the construction of classifiers on such data, and the results are very promising [22, 23]. We have found that consideration of an uncertainty factor has a crucial influence on the final diagnosis. Hence the next objective of the OvaExpert system is to properly grasp and process the uncertainty of the information received, and moreover, to present the results in the bipolar form. This makes it possible to preserve full information about the amount of uncertainty. More information about a mathematical model that includes uncertainty can be found in the next section.

3 System overview

A standard approach to medical diagnosis involves the construction of criteria which allow one to identify the most adequate diagnosis. It is also possible to have criteria that exclude certain diagnoses. It is apparent that the diagnostic process can be modeled in bipolar fashion. On the one hand, the patient's condition

can be modeled towards indication of a specific diagnosis, and on the other towards the exclusion of diagnoses that are certainly incorrect. In current medical applications the first approach is more frequently used, being by far the more natural (a physician is expected to make a diagnosis and begin treatment). For comprehensive computer-aided diagnosis support systems, evidence of the second type may also be important.

OvaExpert will use fuzzy logic and Atanassov's intuitionistic fuzzy sets [24–26] to model bipolarity in the diagnostic process as well as subjectivity, imprecision, uncertainty and even lack of knowledge about the results of diagnostic tests. These concepts are innovative in medicine, their use in the diagnosis having only been indicated as a possibility [16, 27, 28]. Their primary advantages are transparency and ease of comprehension of the principles, the ability to take into account knowledge derived both from experts and from data, and the built-in possibility of representation of uncertain information.

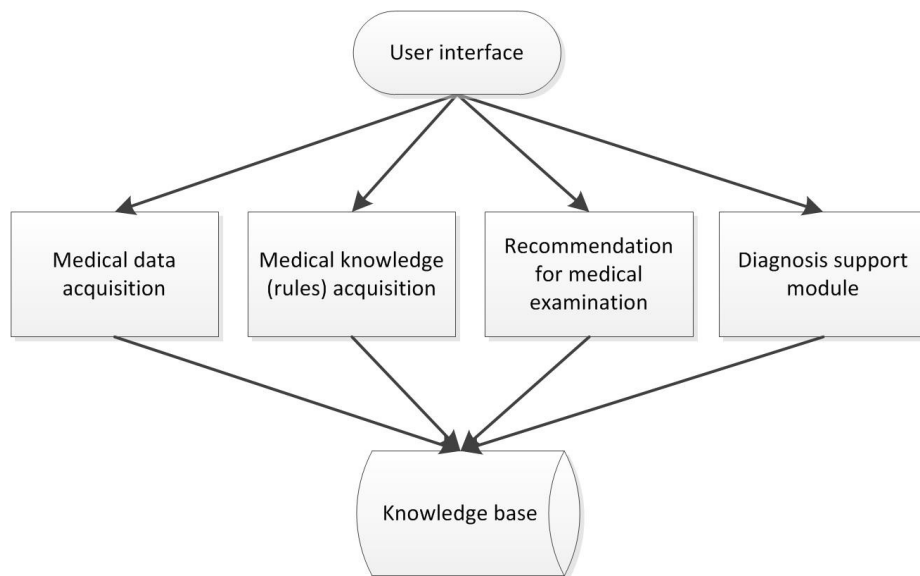


Fig. 1. The main components of the OvaExpert system.

We briefly introduce the principles of the system and its main elements. The system covers four main areas (see Figure 1):

- Medical data acquisition;
- Gathering medical knowledge;
- Decision support in the process of selecting the optimal diagnostic path;
- Decision support in a making a final diagnosis.

3.1 Medical data acquisition

The system gathers knowledge about symptoms, results of medical examinations and final diagnoses for different types of tumors. These data are the basis for the whole diagnostic process. The system enables the entry of such data concerning patients via an online Web interface. This solution makes it possible to centralize the medical data entered by many experts from different centers, and thus to build a knowledge base about different medical cases and set up a continuous learning system. This also enables quality assessment of the diagnostic decisions taken by the system, performed by specialists from different medical centers.

3.2 Gathering medical knowledge

OvaExpert enables a user to enter his or her own diagnostic rules derived from personal experience. These rules take the form of IF-THEN clauses with both numerical (e.g. based on the level of a particular blood marker) and linguistic terms. This means that an individual specialist is able to modify the behavior of the system, which may lead to expansion of the knowledge contained in the system. Potentially this can lead to an increase in the effectiveness of diagnoses.

3.3 Decision support in the process of selecting the optimal diagnostic path

The diagnostic process begins with a medical history entered by the doctor. It then continues through several stages, where further medical examinations are made. Each of them provides additional knowledge for the diagnostic process (e.g. levels of blood markers, ultrasound descriptions, etc). The process runs iteratively. At each stage OvaExpert computes a bipolar recommendation for diagnosis. On the basis of that recommendation the doctor must decide what further tests should be carried out to substantiate the final diagnosis. The system supports the selection of the optimal diagnostic path. This is done by utilizing knowledge from retrospective data (e.g. statistical methods such as decision trees) as well as from fuzzy rules introduced into the system by experts. Interaction with the physician is presented in Figure 2.

3.4 Decision support in making a final diagnosis

The system is designed so that it is possible to add new diagnostic modules at any time. In order to provide a physician with the best recommendation of a final diagnosis, the system synthesizes various methods (modules) such as statistical, fuzzy, diagnostic scales, etc. The system utilizes the IF-sets framework, hence it is possible to aggregate the results of many models into a single diagnosis represented in the form of bipolar information. Dealing with such information requires use of appropriate tools such as similarity measures for incompletely known fuzzy sets [29]. A gynecologist, at each stage of the diagnostic process, will receive a set of possible diagnoses for a particular type of tumor, with an

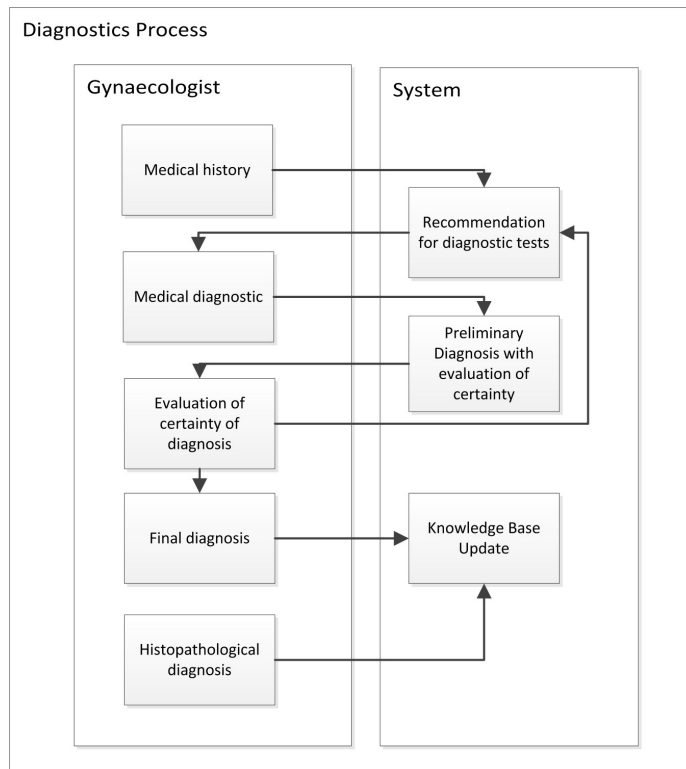


Fig. 2. Diagram of interaction between a physician and OvaExpert.

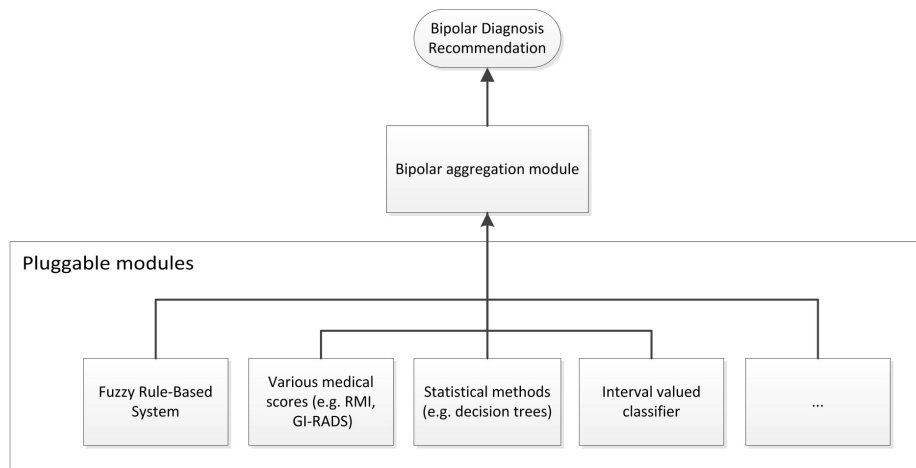


Fig. 3. Modular architecture of the OvaExpert diagnosis support component.

indication of how probable it is that the diagnosis is correct and how probable that it is not. A diagram of the support module is shown in Figure 3. The diagnostic process will be visualized in a readable form (see Figure 4).

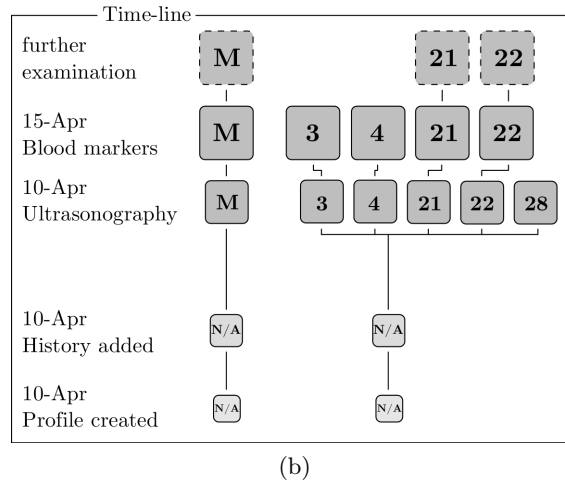
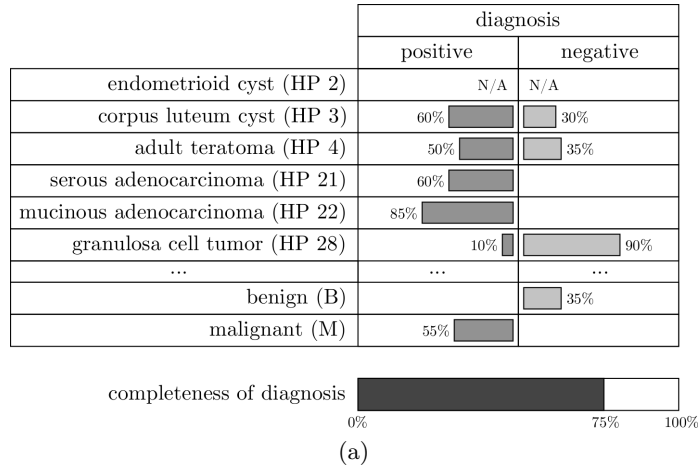


Fig. 4. A visualization of running preliminary diagnosis. (a) A current state of the bipolar prediction together with the completeness of the diagnosis. (b) A time-line graph with short-coded possible diagnoses at given state and possible diagnoses which may be achieved with further examinations.

4 Conclusions

In this project we take advantage of all of the benefits of computational intelligence, which are complementary to the methods of machine learning (see [30]). We plan to give a broader context to the parameters which describe the patient. OvaExpert will consider the subjectivity, imprecision, uncertainty and even lack of knowledge about the results of diagnostic tests obtained from a gynecologist.

The resulting system will set a new pioneering in the development of ovarian tumor diagnosis. We believe that work on the problem of ovarian tumor diagnosis should use not only machine learning techniques, but also computational intelligence and data mining. The project is part of the current trend in interdisciplinary research, producing results that will be of interest to both physicians and mathematicians.

References

- [1] Ferlay, J., Steliarova-Foucher, E., Lortet-Tieulent, J., Rosso, S., Coebergh, J., Comber, H., Forman, D., Bray, F.: Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. *European Journal of Cancer* **49**(6) (2013) 1374–1403
- [2] Szperek, D., Moszyński, R., Szubert, S., Sajdak, S.: Urban and rural differences in characteristics of ovarian cancer patients. *Annals of Agricultural and Environmental Medicine* **20**(2) (2013) 390–394
- [3] du Bois, A., Rochon, J., Pfisterer, J., Hoskins, W.J.: Variations in institutional infrastructure, physician specialization and experience, and outcome in ovarian cancer: A systematic review. *Gynecologic Oncology* **112**(2) (2009) 422–436
- [4] Timmerman, D., Schwärzler, P., Collins, W., Claerhout, F., Coenen, M., Amant, F., Vergote, I., Bourne, T.: Subjective assessment of adnexal masses with the use of ultrasonography: an analysis of interobserver variability and experience. *Ultrasound in Obstetrics & Gynecology* **13**(1) (1999) 11–16
- [5] DePriest, P., Shenson, D., Fried, A., Hunter, J., Andrews, S., Gallion, H., Pavlik, E., Kryscio, R., et al.: A morphology index based on sonographic findings in ovarian cancer. *Gynecologic Oncology* **51**(1) (1993) 7–11
- [6] Alcázar, J.L., Mercé, L.T., Laparte, C., Jurado, M., López-García, G.: A new scoring system to differentiate benign from malignant adnexal masses. *Obstetrical & Gynecological Survey* **58**(7) (2003) 462–463
- [7] Szperek, D., Moszyński, R., Ziętkowiak, W., Spaczyński, M., Sajdak, S.: An ultrasonographic morphological index for prediction of ovarian tumor malignancy. *European Journal of Gynaecological Oncology* **26**(1) (2005) 51–54
- [8] Moszyński, R.: Evaluation of usefulness of rough set theory in diagnostics of ovarian tumors (2003) Doctoral thesis at the Poznan University of Medical Sciences.
- [9] Timmerman, D., Testa, A.C., Bourne, T., Ameye, L., Jurkovic, D., Van Holsbeke, C., Paladini, D., Van Calster, B., Vergote, I., Van Huffel, S., et al.: Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound in Obstetrics & Gynecology* **31**(6) (2008) 681–690
- [10] Timmerman, D., Testa, A.C., Bourne, T., Ferrazzi, E., Ameye, L., Konstantinovic, M.L., Van Calster, B., Collins, W.P., Vergote, I., Van Huffel, S., et al.: Logistic regression model to distinguish between the benign and malignant adnexal mass

- before surgery: a multicenter study by the International Ovarian Tumor Analysis Group. *Journal of Clinical Oncology* **23**(34) (2005) 8794–8801
- [11] Moore, R.G., McMeekin, D.S., Brown, A.K., DiSilvestro, P., Miller, M.C., Allard, W.J., Gajewski, W., Kurman, R., Bast Jr, R.C., Skates, S.J.: A novel multiple marker bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a pelvic mass. *Gynecologic Oncology* **112**(1) (2009) 40–46
- [12] Taylor, A., Jurkovic, D., Bourne, T.H., Collins, W.P., Campbell, S.: Sonographic prediction of malignancy in adnexal masses using an artificial neural network. *BJOG: An International Journal of Obstetrics & Gynaecology* **106**(1) (1999) 21–30
- [13] Smoleń, A., Czekierdowski, A., Stachowicz, N., Kotarski, J.: Use of multilayer perception artificial neural networks for the prediction of the probability of malignancy in adnexal tumors. *Ginekologia Polska* **74**(9) (2003) 855–862
- [14] Van Calster, B., Timmerman, D., Lu, C., Suykens, J.A., Valentin, L., Van Holsbeke, C., Amant, F., Vergote, I., Van Huffel, S.: Preoperative diagnosis of ovarian tumors using Bayesian kernel-based methods. *Ultrasound in Obstetrics & Gynecology* **29**(5) (2007) 496–504
- [15] Van Calster, B., Timmerman, D., Nabney, I.T., Valentin, L., Testa, A.C., Van Holsbeke, C., Vergote, I., Van Huffel, S.: Using Bayesian neural networks with ARD input selection to detect malignant ovarian masses prior to surgery. *Neural Computing and Applications* **17**(5-6) (2008) 489–500
- [16] Madu, E., Stalbovskaia, V., Hamadicharef, B., Ifeachor, E., Van Huffel, S., Timmerman, D.: Preoperative ovarian cancer diagnosis using neuro-fuzzy approach. In: *European Conference on Emergent Aspects on Clinical Data Analysis*. (2005)
- [17] Tingulstad, S., Hagen, B., Skjeldestad, F.E., Onsrud, M., Kiserud, T., Halvorsen, T., Nustad, K.: Evaluation of a risk of malignancy index based on serum CA125, ultrasound findings and menopausal status in the pre-operative diagnosis of pelvic masses. *BJOG: An International Journal of Obstetrics & Gynaecology* **103**(8) (1996) 826–831
- [18] Amor, F., Vaccaro, H., Alcázar, J.L., León, M., Craig, J.M., Martinez, J.: Gynecologic imaging reporting and data system a new proposal for classifying adnexal masses on the basis of sonographic findings. *Journal of Ultrasound in Medicine* **28**(3) (2009) 285–291
- [19] Timmerman, D., Bourne, T.H., Taylor, A., Collins, W.P., Verrelst, H., Vandenberghe, K., Vergote, I.: A comparison of methods for preoperative discrimination between malignant and benign adnexal masses: the development of a new logistic regression model. *American Journal of Obstetrics and Gynecology* **181**(1) (1999) 57–65
- [20] Valentin, L., Hagen, B., Tingulstad, S., Eik-Nes, S.: Comparison of 'pattern recognition' and logistic regression models for discrimination between benign and malignant pelvic masses: a prospective cross validation. *Ultrasound in Obstetrics & Gynecology* **18**(4) (2001) 357–365
- [21] Van Holsbeke, C., Van Calster, B., Valentin, L., Testa, A.C., Ferrazzi, E., Dimou, I., Lu, C., Moerman, P., Van Huffel, S., Vergote, I., et al.: External validation of mathematical models to distinguish between benign and malignant adnexal tumors: a multicenter study by the International Ovarian Tumor Analysis Group. *Clinical Cancer Research* **13**(15) (2007) 4440–4447
- [22] Wójtowicz, A., Żywica, P., Szarzyński, K., Moszyński, R., Szubert, S., Dyczkowski, K., Stachowiak, A., Szperek, D., Wygralak, M.: *Dealing with Uncertainty in Ovarian Tumor Diagnosis* (2014) to appear.

- [23] Stachowiak, A., Żywica, P., Dyczkowski, K., Wójtowicz, A.: An Interval-Valued Fuzzy Classifier Based on an Uncertainty-Aware Similarity Measure. In: *Advances in Intelligent Systems and Computing*. (2014) to appear.
- [24] Zadeh, L.A.: Fuzzy logic and approximate reasoning. *Synthese* **30**(3-4) (1975) 407–428
- [25] Wygralak, M.: *Intelligent Counting under Information Imprecision: Applications to Intelligent Systems and Decision Support*. Springer (2013)
- [26] Atanassov, K.T.: *Intuitionistic fuzzy sets*. Springer (1999)
- [27] De, S.K., Biswas, R., Roy, A.R.: An application of intuitionistic fuzzy sets in medical diagnosis. *Fuzzy Sets and Systems* **117**(2) (2001) 209–213
- [28] Szmidt, E., Kacprzyk, J.: An intuitionistic fuzzy set based approach to intelligent data analysis: an application to medical diagnosis. In: *Recent advances in intelligent paradigms and applications*. Springer (2003) 57–70
- [29] Stachowiak, A., Dyczkowski, K.: A similarity measure with uncertainty for incompletely known fuzzy sets. In: *IFSA World Congress and NAFIPS Annual Meeting (IFSA/NAFIPS), 2013 Joint, IEEE* (2013) 390–394
- [30] Kruse, R., Borgelt, C., Klawonn, F., Moewes, C., Steinbrecher, M., Held, P.: *Computational Intelligence: A Methodological Introduction*. Springer (2013)