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# Combining case-based reasoning with Bee Colony Optimization for dose planning in well differentiated thyroid cancer treatment

Dušan Teodorović [a], Milica Šelmić [a,*], Ljiljana Mijatović-Teodorović [b]

[a] University of Belgrade, Faculty of Transport and Traffic Engineering, Vojvode Stepe 305, 11000 Belgrade, Serbia
[b] University of Kragujevac, Medical Faculty, Clinical Center Kragujevac, Svetozara Markovica 69, 34000 Kragujevac, Serbia

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ABSTRACT

Thyroid cancers are the most common endocrine carcinomas. Case-based reasoning (CBR) is used in this paper to describe a physician's expertise, intuition and experience when treating patients with well differentiated thyroid cancer. Various clinical parameters (the patient's diagnosis, the patient's age, the tumor size, the existence of metastases in the lymph nodes and the existence of distant metastases) influence a physician's decision-making in dose planning. The weights (importance) of these parameters are determined here with the Bee Colony Optimization (BCO) meta-heuristic. The proposed CBR–BCO model suggests the I-131 iodine dose in radioactive iodine therapy. This approach is tested on real data from patients treated in the Department of Nuclear Medicine, Clinical Center Kragujevac, Serbia. By comparing the results that are obtained through the developed CBR–BCO model with those resulting from the physician's decision, it has been found that the developed model is highly reflective of reality.



## 1. Introduction

Thyroid cancers are the most common endocrine carcinomas. They are also among the ten most common cancers in women. Among thyroid malignancies, more than 95% are well differentiated thyroid cancers (WDTCs) of follicular cell origin, papillary and follicular carcinomas. Malignant transformation of thyroid epithelial cells (follicular and parafollicular), followed by their division and accumulation, leads to the development of malignant tumors of the thyroid gland. Well differentiated thyroid cancers are more common in younger patients; papillary carcinoma is usually diagnosed in the third decade of life, and follicular carcinoma is usually diagnosed in the fourth decade. All types of thyroid cancer occur 1.5–4 times more often in women than in men.

The incidence of WDTC has increased in several European countries since the Chernobyl nuclear disaster. The most important risk factors that increase the probability of WDTC are: age, female sex, radiation exposure of the neck region (especially in childhood) and the positive familiar anamnesis of other malignancies.

The disproportion between the number of patients with carcinoma of the thyroid gland and the number of deaths (95% vs. 65.9%, respectively) indicates that the malignant disease has a relatively indolent nature, and thus applied therapies are likely to be successful. The aim of the application of radioactive iodine in patients with well differentiated thyroid carcinoma is the ablation of normal thyroid tissue or cancer cell therapy after thyroidectomy. The dosing decision that is made by an experienced physician is based on the clinical stage of the disease, its risk factors and the TNM classification (T – Tumor size, N – metastases in the lymph nodes and M – distant metastases). Although WDTC has a very good prognosis in the vast majority of patients, there are still patients who have high risk factors and who require, even after a total or near total thyroidectomy, radioactive iodine therapy (Riesco-Eizaguirre & Santisteban, 2007; Savin, Cvejic, Mijatovic, & Zivancevic Simonovic, 2010; Vrndic et al., 2011). The ability of the thyroid follicular cells to take up iodine via a sodium iodide symporter at the basolateral cell membrane enables the use of radioiodine for the therapy of WDTC.

The choice of dose proposed by a physician cannot be easily described by precise rules and/or mathematical algorithms. There is a trade-off between the benefit and the risk of radioiodine (I-131) therapy. In this paper, we developed a case-based reasoning (CBR) model Aamondt & Plaza, 1994; Burkhard & Wess, 1998; Kolodner, 1993 for the prescription of the I-131 iodine dose in WDTC treatment. The case-based reasoning is used in this paper to describe a physician's expertise, intuition, and experience. Various clinical parameters (patient's diagnosis, age, and TNM classification) influence a physician's decision-making in dose planning. These parameters do not have the same importance and influence on proposed doses in the physician's decision-making process. The

* Corresponding author. Tel.: +381 11 3091207; fax: +381 11 2638912.
*E-mail addresses:* duteodor@vt.edu (D. Teodorović), m.selmic@sf.bg.ac.rs (M. Šelmić), lili@medf.kg.ac.rs (L. Mijatović-Teodorović).

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weights (importance) of these parameters are determined in this paper by the Bee Colony Optimization (BCO) meta-heuristic (Lučić & Teodorović, 2001, 2002, 2003).

The main objective of this paper is to research the possibility of developing a new model that could improve the quality of the decisions made by young physicians who study WDTC. In other words, our intention is to use the CBR–BCO model mainly for educational purposes. Our key interest is to develop a model that helps students to test their acquired knowledge and to learn how to reach an appropriate decision.

This paper is organized as follows. Section 2 presents a brief literature survey. CBR for a radioiodine (I-131) dose decision is given in Section 3. The BCO meta-heuristic is described in Section 4. BCO application on the weight determination process is given in Section 5. The results and discussion are presented in Section 6. Section 7 contains the conclusions.

## 2. Literature survey

Case-based reasoning (CBR) is the process of solving new problems based on the solutions of similar past problems. Many papers and books related to this technique have appeared in the last two decades (Aamodt, Gundersen, Loge, Wasteson, & Szczepanski, 2010; Aamondt & Plaza, 1994; Burkhard & Wess, 1998; Juarez, Guil, Palma, & Marin, 2009; Kolodner, 1993; McGovern, Samson, & Wirth, 1994). CBR has been applied in various scientific fields, one of which is medicine.

The authors of Bichindaritza and Marlingb (2011) provided an excellent survey of CBR in the health sciences. The authors described the current trends and issues, and projected the future directions for research in this area. Current research in CBR in the health sciences is varied, highlighted by work in bioinformatics, support to the elderly and people with disabilities, and the formalization of CBR in biomedicine.

In the study of Song, Petrovic, and Sundar (2007), the determination of a dose plan for prostate cancer in radiotherapy is considered. The determination of the dose plan is based on the analysis of a trade-off between the expected benefits in terms of the cancer control and the risk in terms of the side effects to the rectum caused by the radiation. The CBR approach to dose planning is proposed, in which a fuzzy set theory is applied in the analysis of similarity measures.

The paper of Juan, Rodríguez, Bajo, and Corchado (2009) presented a CBR system for the automatic classification of leukemia patients from microarray data. This system incorporates novel algorithms from data mining that allow filtering, classification, and knowledge extraction. The system has been tested, and the results obtained are presented in the paper.

The authors of Kumar, Singh, and Sanyal (2009) presented a hybrid approach of case-based reasoning and rule-based reasoning to build a clinical decision support system for an Intensive Care Unit (ICU). Experiments with real ICU data as well as simulated data clearly demonstrate the efficacy of the proposed method.

The goal of the paper (Aamodt et al., 2010) was to create a computational framework and system architecture for clinical decision support in palliative care. The application considered was the classification of depression. System architecture was described and exemplified through an implemented prototype.

A CBR system for generating dose plans for prostate cancer patients was developed in Petrovic, Mishra, and Sundarb (2011). The proposed approach captures the expertise and experience of oncologists when treating previous patients and recommends a dose in phase I and phase II of the treatment of a new patient, also considering the success rate of the treatment. To mimic the continuous learning characteristic of oncologists, the weights corresponding to each feature used in the retrieval process are updated automatically each time after generating a treatment plan for a new patient.

In recent literature, computational intelligence methods are used in combination with the CBR concept. Genetic algorithms, one of the most popular search techniques, belong to the class of evolutionary algorithms and are used to determine weights for the CBR approach in the personnel rostering problem (Beddoe & Petrovic, 2006).

The authors of Kuo, Cha, and Chou (2006) integrated both the clustering method and CBR for developing a diagnostic system for maintenance. The reason for this integration is that searching similar cases with CBR is time-consuming if the case base is fairly large. Thus, it is necessary to cluster the cases into groups and then to perform a search for the most appropriate possible group. A novel approach, the ant colony system clustering algorithm (ASCA), is employed for this purpose.

An integrated framework based on multi-agent collaboration and CBR that can resolve various collaboration issues in the supply chain is proposed in Ohbyung, Ghi, and Kun (2008).

In last 2 years, researchers started to use Swarm Intelligence techniques in medicine. The authors of Chen et al. (2011) developed a three-stage expert system approach to diagnose thyroid disease. Part of the system is based on the Particle Swarm Optimization (PSO) technique. In the paper (Davidović, Ramljak, Šelmić, & Teodorović, 2011), a PSO technique is used in breast cancer diagnosis. The same technique is used in the process of knowledge extraction in the paper (Du, Jiang, Diao, & Yao, 2011). The authors of Rizk and Arnaout (2011) proposed Ant Colony Optimization (ACO) for solving the surgical cases assignment problem, while in Kavitha and Ramakrishnan (2010), an ACO was used to identify the optic disk in the human retina.

In this paper, we propose Bee Colony Optimization as a tool for parameter weight determinations in the CBR approach. BCO was among the first of the bee-inspired algorithms (Lučić & Teodorović, 2001, 2002, 2003). Among other algorithms that were inspired by honey bees, we note the following: The collective intelligence based on bees' behavior is analyzed in Yonezawa and Kikuchi (1995). Sato & Hagiwara (1997) proposed a modified genetic algorithm named the bee system. In essence, this algorithm belongs to the class of genetic algorithms. Abbass (2001) developed the MBO model, which is based on the marriage process in honeybees. BeeHive (Wedde, Farooq, & Zhang, 2004), Artificial Bee Colony (ABC) algorithm Karaboga, 2005 and Bees Algorithm (Pham, Ghanbarzadeh, Koc, Otri, & Zaidi, 2006), as well as BCO, are based on the foraging behavior of honeybees, but all of them use different concepts for the algorithm development. An interesting survey of algorithms that are inspired by bees' behavior can be found in Karaboga and Akay (2009), Teodorović (2009).

Lučić & Teodorović (2001, 2002, 2003) introduced Bee Colony Optimization (BCO) and tested it on the case of the Traveling Salesman Problem. The authors of Teodorović and Dell'Orco (2005) used BCO to solve the Ride-Matching Problem. This meta-heuristic is used to solve the Routing and Wavelength Assignment (RWA) problem Markovic, Teodorovic, & Acimovic-Raspopovic, 2007, while the Maximal Covering Location Problem was solved in Dimitrijević, Teodorović, Simić, and Šelmić (2012). In addition, BCO was applied to solving the problem of inspection station locations in transport networks (Šelmić, Teodorović, & Vukadinović, 2010) and the *p*-center location problem (Karaboga & Akay, 2009).

To the best of our knowledge, the present research represents the first attempt to apply the CBR–BCO concept in WDTC therapy. Recently, the authors of this paper published a paper in which they proposed a model based on neural networks for I-131 iodine dose prediction (Teodorović, Šelmić, & Mijatović-Teodorović, 2011).