Multi-objective genetic algorithms for scheduling of radiotherapy treatments for categorised cancer patients

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Multi-objective Genetic Algorithms for Scheduling of Radiotherapy Treatments for Categorised Cancer Patients

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Abstract. This paper presents a multi-objective optimisation model and algorithms for scheduling of radiotherapy treatments for categorised cancer patients. The model is developed considering real life radiotherapy treatment processes at Arden Cancer Centre, in the UK. The scheduling model considers various real life constraints, such as doctors' rota, machine availability, patient's category, waiting time targets, (i.e., the time when a patient should receive the first treatment fraction), and so on. Two objectives are defined: minimisation of the Average patient's waiting time and minimisation of Average length of breaches of waiting time targets. Three Genetic Algorithms (GAs) are developed and implemented which treat radiotherapy patient categories, namely emergency, palliative and radical patients in different ways: (1) Standard-GA, which considers all patient categories equally, (2) KB-GA, which has an embedded knowledge on the scheduling of emergency patient category and (3) Weighted-GA, which operates with different weights given to the patient categories. The performance of schedules generated by using the three GAs is compared using the statistical analyses. The results show that KB-GA generated the schedules with best performance considering emergency patients and slightly outperforms the other two GAs when all patient categories are considered simultaneously. KB-GA and Standard-GA generated better performance schedules for emergency and palliative patients than Standard-GA.

Keywords: Scheduling, Genetic Algorithms, Radiotherapy, Waiting Times

1. Introduction

The number of patients diagnosed with cancer in the UK is constantly increasing; according to NRAG (2007) the increase is estimated to be 8% and 16% in 2010 and 2016, respectively. The cancer mortality rate is also increasing. The long waiting times and delays in treatments are widespread in radiotherapy cancer departments in the UK. Consequences of delays in starting radiotherapy treatments, which permit spreading of the cancers beyond the treatment volume or reduce the prospect of local control, were discussed in (Recht, 2004). In a recent paper, Mackillop (2007) analysed the direct and indirect clinical evidence of treatment delays in radiotherapy.

The aim of this paper is to propose and analyse suitable scheduling techniques which will reduce delays and patient waiting times for cancer treatments. Research in scheduling theory has evolved over the years and has been the subject of much literature elaborating various techniques ranging from dispatching rules to highly sophisticated optimisation algorithms and heuristics (Jain & Meeran 1999, Pinedo 2002). Application of exact optimisation methods, such as linear programming, mixed integer programming, or Lagrangian relaxation to scheduling problems may not always be possible as the time to find solutions increases exponentially with increases in the problem sizes. Heuristics methods do not guarantee achieving optimal solutions; rather they are able to attain near optimal solutions. Various metaheuristics such as evolutionary computation, tabu search, simulated annealing, and ant search have found their place in the scheduling theory for handling complex, large size scheduling problems (Reeves 1995, Nowicki & Smutnicki 1996, Podgorelec & Kokol 1997).

Scheduling patients in the health care domain has attracted considerable researchers' attention; for example, scheduling of radiotherapy departments, health examinations, surgeries and outpatient departments were presented in (Conforti *et al*., 2008, Chern *et al*., 2008, Pham & Klinkert, 2008, and Cayirli & Veral 2003), respectively. Larson (1993) was among the first authors who studied radiotherapy patient scheduling. His system was based on formulae used to organise patient waiting times queue and was implemented on a personal computer. In a more recent study, Petrovic *et al.* (2006) considered a treatment stage of the radiotherapy process and developed algorithms for booking treatments for radiotherapy patients. Effects of changing a number of parameters relevant for radiotherapy scheduling on the schedule performance were discussed in (Petrovic & Leite, 2008). Discrete event simulation models that measure performance of radiotherapy treatment schedules were presented in (Proctor *et al*., 2007 and Kapamara *et al*., 2007).

Exact methods cannot be applied to generic radiotherapy treatment scheduling problems due to the complexity of constraints and the size of the problems. Novel multi-objective GAs have been proposed in this paper to handle a patient scheduling problem identified in Arden Cancer Centre, University Hospitals Coventry and Warwickshire, NHS Trust, in the UK. Based on the intent of radiotherapy treatments, patients are categorised into three categories including radical (intent is to cure cancer), palliative (intent is to alleviate pain) and emergency (typically to relieve intense pain). The developed GAs treat patient categories in different ways: (1) Standard GA considers all the patient categories equally, (2) KB-GA has an embedded knowledge on the scheduling of emergency patient category and (3) Weighted-GA operates with different weights given to the patient categories. We considered two objectives simultaneously, including minimisation of Average patients waiting times, where the waiting time is defined as the time that elapses from the moment when the decision to treat the patient is made until the time of the first treatment fraction administration, and minimisation of Average length of breaches of waiting time targets.

This paper is organised in the following way. In Section 2, the radiotherapy treatment process under consideration is defined. In Section 3, the scheduling problem statement and a scheduling model are presented. Section 4 is dedicated to descriptions of the developed multi-objective GAs: Standard-GA, KB-GA and Weighted-GA. Section 5 discusses the tuning of GAs parameters and results obtained by using the three GAs and presents a comparison of their performance based on statistical analyses. Section 6 provides the conclusion and directions for future work.

2. Radiotherapy Treatment Process

Radiotherapy involves use of ionising radiation targeting the cancer cells while minimising damage to a healthy tissue. There are three major types of radiotherapy including external beam therapy, brachytherapy and unsealed source therapy. In this paper, we focus on scheduling of external beam therapy patients. A patient diagnosed with cancer and recommended for radiotherapy should start the treatment within the waiting times recommended by JCCO (Joint Collegiate Council for Oncology) (JCCO 1993). There are three categories of cancer patients under consideration, namely radical, palliative and emergency patients with waiting time targets set to 28, 14 and 2 days, respectively.

The radiotherapy treatment process in the Arden Cancer Centre is carried out in four units: Planning, Physics, Pre-treatment and Treatment, as illustrated in Fig. 1. Each patient follows a treatment path that usually depends on the cancer site and is determined by an assigned doctor. In the remaining part of the paper, we will refer to servicing of a patient on a machine or facility as an operation. Therefore, a treatment path consists of a series of operations.

Doctors work on a rota and their availability is limited. Machines and a facility in the Planning unit consist of a simulator, a computed axial tomography (CT) scanner, and a mould room. A patient undergoes processing on at least one of these machines and facility. The simulator and scanner are used to determine the location and magnitude of advancement of the cancer. In order to obtain a precise image of the cancer, some patients, for example, those with cancers close to delicate organs, may require a mask to immobilise them during the planning and, later on, during their treatment. The immobilisation mask is moulded in the mould room. Once the mask has been moulded, the patients should undergo planning on the scanner and simulator on the same day. This means, there are precedence constraints to all the operations on the planning machines or facility. The assigned doctor has to be available to approve and sign the treatment plan for each patient in the planning stage. The patients' images and all documents are passed to the Physics unit or directly to the Pre-treatment unit, depending on the complexity of the cancer. Dosimetry calculations for complex cases are carried out in the Physics unit and rechecked in the Pre-treatment unit. Simple cases are considered directly in the Pre-treatment unit. Each patient is then booked for a prescribed treatment machine for a specified number of fractions. The Treatment unit contains 7 machines including 3 high energy linear accelerators (linacs), 2 low energy linacs, 1 Deep X-Ray and 1 Beta-tron.

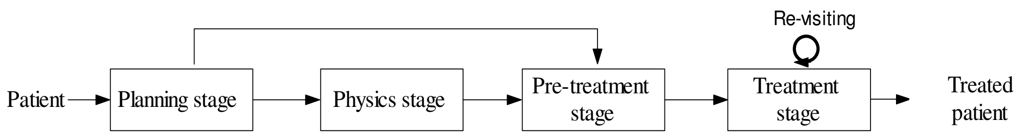


Fig. 1. The radiotherapy treatment process

3. Problem Statement

3.1 Notation

The following are the symbols used in the formulation of the problem.

N : number of patients received within a scheduling horizon

j : patient, $j = 1,2.., N$

M : set of machines and facilities

k : machine or facility, $k \in M$

H : total number of doctors

h : doctor, $h = 1,2,\ldots, H$

h_j : doctor allocated to patient j

H_h : availability of doctor h in the hospital rota

(i, j, k) : operation i of patient j on machine or facility k

(i^f, j, k) : the first treatment fraction i^f of patient j on machine k

$s_{(i, j, k)}$: time when operation i for patient j on machine or facility k starts

$\tau_{(i,, j, k)}$: processing time of operation i of patient j on machine of facility k

$c_{(i, j, k)}$: the completion time of operation i of patient j on machine or facility k

$$c_{(i, j, k)} = s_{(i, j, k)} + \tau_{(i,, j, k)}$$

r_j : time when decision to treat by radiotherapy for patient j is made

d_j : waiting time target for the first treatment fraction of patient j; will be referred to as "due date", in the remaining part of the paper

E : emergency patient category

P : palliative patient category

R : radical patient category

C_j : category of patient j

w_j : weight given to patient j based on the patient category

$RTM(k)$: existing schedule of machine or facility k

$RTM(k) = \{ [s_{(i,\ j,\ k)},\ c_{(i,\ j,\ k)}] \mid$ starting and completion times of all operations of all patients scheduled on machine or facility $k\}$

$RTD(h)$: existing schedule of doctors

$RTM(h) = \{ [s_{(i,\ j,\ h)},\ c_{(i,\ j,\ h)}] \mid$ set of starting and completion times of all operations of all patients allocated to doctor $h\}$

L_j : lateness in starting time of the first fraction of patient j with respect to the due date

$$L_j = s_{(if,\ j,\ k)} - d_j$$

T_j : length of breaches of waiting time targets; will be referred to as "delay in treatment of patient j", in the remaining part of the paper

$$T_j = \max(L_j, 0)$$

Delay in treatment is defined to be zero if the patient starts his/her first fraction before or on the due date, otherwise it is a time difference between the start time of the first fraction and the due date.

$\overline{T}$: average delay in treatments of N patients serviced within a scheduling horizon

$$\overline{T} = \frac{1}{N} \sum_{j=1}^{N} T_j$$

$\overline{T}_w$: average weighted delay in treatments of N patients serviced within a scheduling horizon

$$\overline{T}_w = \frac{1}{N} \sum_{j=1}^{N} w_j T_j$$

F_j : flowtime from the Planning to the Treatment unit of patient j (waiting time of patient j)

$$F_j = s_{(if,\ j,\ k)} - r_j$$

$\overline{F}$: average flowtime of N patients serviced within a scheduling horizon (average waiting time)

$$\overline{F} = \frac{1}{N} \sum_{j=1}^{N} F_j$$

$\overline{F}_w$: average weighted flowtime of N patients serviced within a scheduling horizon

$$\overline{F}_w = \frac{1}{N} \sum_{j=1}^{N} w_j F_j$$

3.2 Assumptions

The assumptions applied in this model are listed as follows:

1. The radiotherapy facilities strictly follow a five day working week, i.e. from Monday to Friday.
2. Only one patient can be serviced on a machine at a time.
3. No pre-emption is allowed, i.e. once the operation starts on a machine or facility, it cannot be interrupted.
4. All the operations for patients are known in advance and they are ready to start processing at the beginning of the time horizon under consideration.
5. The processing times of all the operations and precedence constraints are deterministic and known in advance.
6. The processing time of each operation does not depend on the sequence in which the operations are processed.
7. The times when the patients are available to start the radiotherapy processes are known.
8. Patient are categorised into 3 categories: radical, palliative and emergency with waiting time targets - due dates of 28, 14 and 2 days, respectively.

9. Machine or facility set-up times and transfer times between machines or facilities are considered negligible compared to the processing times.
10. There are no recycles on machines and facilities, except on linacs; a patient visits a machine or facility once, which means there is a single operation to be carried out on a machine or facility for each patient.
11. The machines and facilities are always available during the shift. Break down and maintenance operations are not considered. Man power of uniform ability is available.
12. Doctors are available on a rota of the hospital.
13. Once a delivery of fractions starts, it has to be continued on each day except weekends and holidays until completed.

3.3 Objectives and constraints

The objectives are to minimise the Average flow time (waiting time) $\overline{F}$ and Average delay in treatments of all patients $\overline{T}$ in the radiotherapy treatment process:

minimise $\overline{F}$

minimise $\overline{T}$

subject to the following constraints:

Capacity restriction of machine or facility k

$RTM(k) = \{\, [s_{(i,j,k)}, c_{(i,j,k)}] \mid \text{time intervals } [s_{(i,j,k)}, c_{(i,j,k)}] \text{ do not overlap}\}$ for all i, j

Capacity restriction of doctor h

$RTD(h) = \{\, [s_{(i,j,h)}, c_{(i,j,h)}] \mid \text{time intervals } [s_{(i,j,h)}, c_{(i,j,h)}] \text{ do not overlap}\}$ for all i, j

Time lags of consecutive operations i and $(i+1)$ of patient j for any machine or facility k and k', where $k, k' \in M$

$s_{(i,j,k)} - s_{(i+1,j,k')} + \tau_{(i,j,k)} \leq 0$, where $k \neq k'$

$s_{(i, j, k)} \geq 0$

$\tau_{(i,, j, k)} \geq 0$

$k = 1, 2, \ldots, |M|, j = 1, 2, \ldots, N, h = 1, 2, \ldots, H$

4. Multi-objective GA

Three different types of GA are developed for the multi-objective scheduling problem defined in Section 3: Standard–GA, KB–GA and Weighted–GA. They include basic GA techniques and an additional domain knowledge, in KB-GA, and weights for categorised patients, in Weighted-GA.

A GA is a search algorithm inspired by natural selection and genetics (Goldberg 1989). It uses a population of candidate (possible) solutions represented as strings which are evaluated by a fitness (objective) function. Search for a near optimal solution is carried out iteratively through the selection process, which considers fitness of each candidate solution. New solutions are generated using two operators: **crossover**, which combines two solutions and generates a new solution by replacing a part of one string, usually randomly selected, with a corresponding part of another string, and **mutation**, which is used to alter one or more, usually randomly selected parts of one string.

4.1 Standard-GA

String representation. In this GA, we use a modification of an Operation based string representation, which indirectly represents a schedule (Gen *et al.*, 1984). For example, in the case of four patients and four machines the string can have the following form [2-2-4-4-3-3-1-2-4-4-3-1-1-1-2-3], where all operations for a patient are named using the patient-id. The positions of the patient-id in the string determine the sequence of patient operations. In the given example, the first operation to be scheduled is the first operation of patient 2, then the second operation of patient 2, first operation of patient 4, second operation of patient 4, and so on. The last operation assigned to each patient is the administration of the first fraction on the prescribed treatment machine. The strings are of the equal size that is (number of patients) × (maximum number of operations of any patient). The machines or facilities on which the operations are carried on are specified for each patient in a matrix, and hence the dimension of the matrix is (number of patient) × (maximum number of operations). An additional matrix is used to record processing times of all the operations of each patient. The dimension of the matrix is also (number of patient) × (maximum number of operations). In case when patient does not require the maximum number of operations, the remaining operations are still specified in the string with the patient-id, but the corresponding operation processing times are set to 0.

The generated string needs to be decoded into a schedule. A good feature of this string representation is that it always represents a feasible solution, i.e., schedule. The operations are scheduled according to their sequence in the string in such a way that each operation is allocated the earliest available time on the machine or facility the operation requires. The time of the first fraction is scheduled in such a way as to enable delivery of the prescribed number of fractions on consecutive days (excluding weekends and holidays). Decoding of the above string is given in Fig. 2, using the machines that operations require and corresponding processing times given in Table 1 and Table 2.

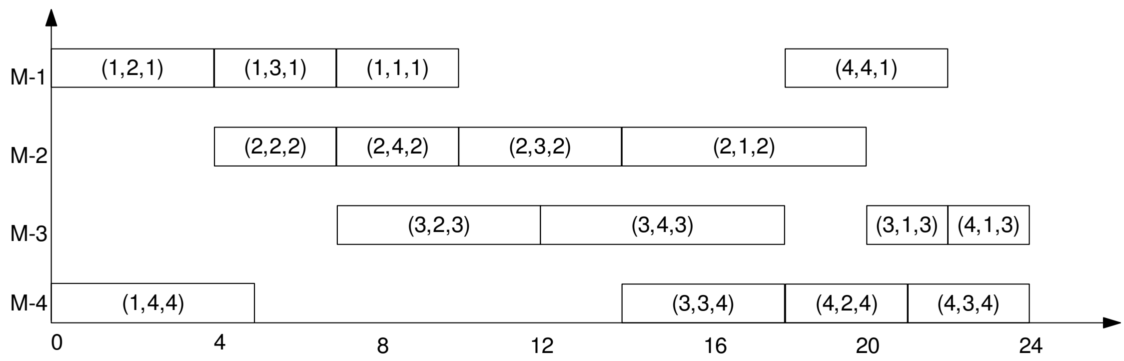


Fig. 2. Decoding of a 'four patient-four machines' string to a schedule

(i,j,k) represents operation i of patient j on machine or facility k

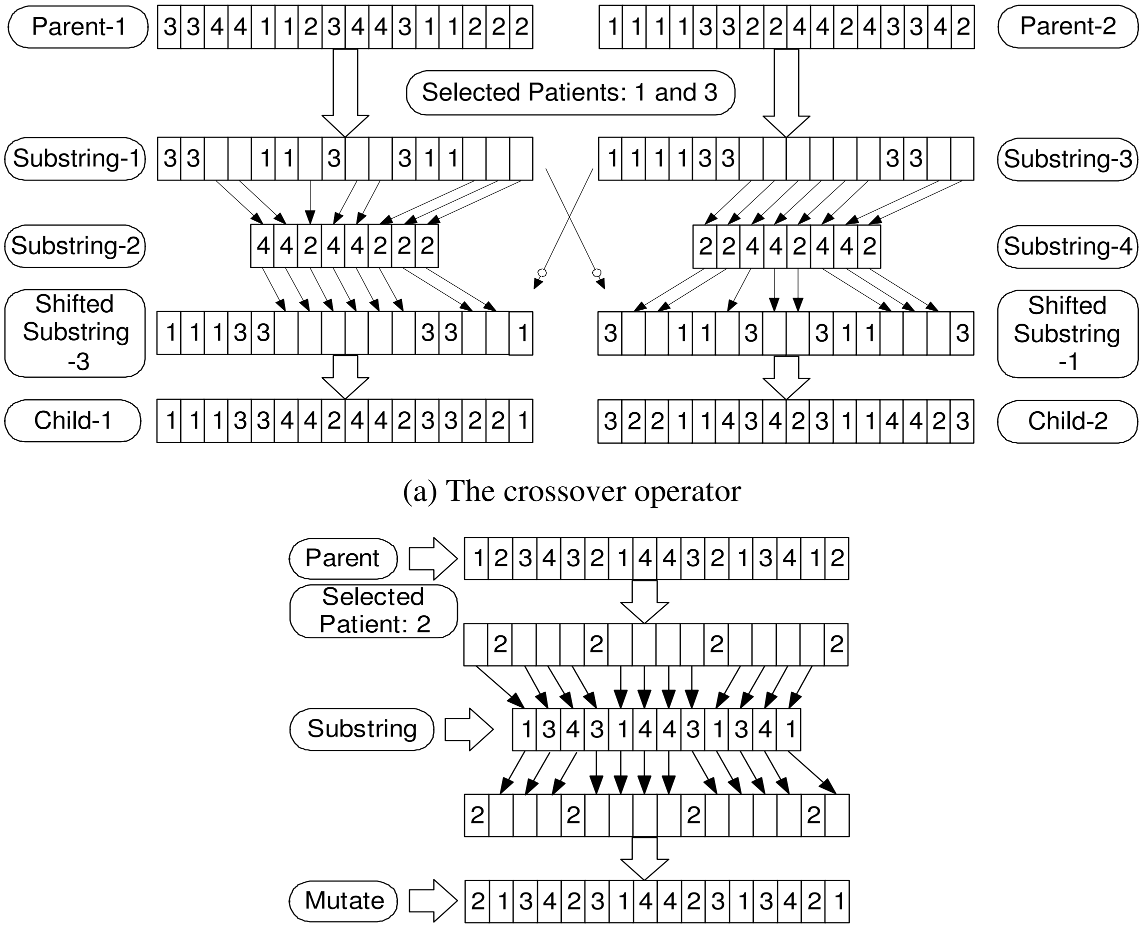
Table 1: Operations Machines

	Operations			
Patients	*1*	*2*	*3*	*4*
1	1	2	3	3
2	1	2	3	4
3	1	2	4	4
4	4	2	3	1

Table 2: Processing Times

	Operations			
Patients	*1*	*2*	*3*	*4*
1	3	6	2	2
2	4	3	5	3
3	3	4	4	3
4	5	3	6	4

GA operators. The crossover and mutation operators applied to the strings preserve the number of operations for each patient and, therefore, newly generated strings remain feasible. The crossover operator applied is Linear order crossover (Gen *et al.*, 1994). It is defined in such a way as to keep the relative positions of operations of the selected patients in two parent strings and to swap it among the parent strings, while the remaining parts of the parent strings are modified by shifting the string one position to the left. In this way, the child string does not have substantial changes compared to the parents' strings in the sense that it keeps relative positions of some of the operations. Similarly, the mutation is defined in such a way as to keep the relative positions of operations of the selected patient, while shifting operations by one position to the left. Example of the crossover and mutation operators is illustrated in Fig. 3.



(a) The crossover operator

(b) The mutation operator

Fig. 3. Examples of the GA operators

Fitness function. The fitness function is defined considering two objective functions: Average waiting time and Average delay in treatments of the patients. However, the waiting time and delay in treatment have different scales (a waiting time is always longer than a delay in treatment), and, therefore, the values of the corresponding two objectives have to be normalized, before they are summed to form a single fitness value of a string. Normalisation is carried out as a linear mapping of the interval formed by the minimum and the maximum values of all achieved values of the objective function in one iteration, on the interval

[0, 1]. The fitness function is used wherever evaluation of a string takes place. Before the string can be evaluated, it needs to be decoded into the corresponding schedule.

Initialisation. The population of initial strings is created using some simple techniques, e.g., sequence all operations of the patient 1 first, then patient 2, etc, or sequence the first operation of all patients, then second operations of all patients, and so on. Finally, strings are generated randomly, until the whole population of the specified size is created.

Selection. In each iteration, we apply the elitist strategy, i.e., a certain number of the strings with highest achieved values of the fitness function are directly input into the population of the subsequent iteration. After applying the GA operators, crossover and mutation, the strings are evaluated and ranked, and the remaining part of the population is filled with strings with highest fitness.

The flow chart given in Fig. 4 illustrates the steps taken to generate a near optimal schedule.

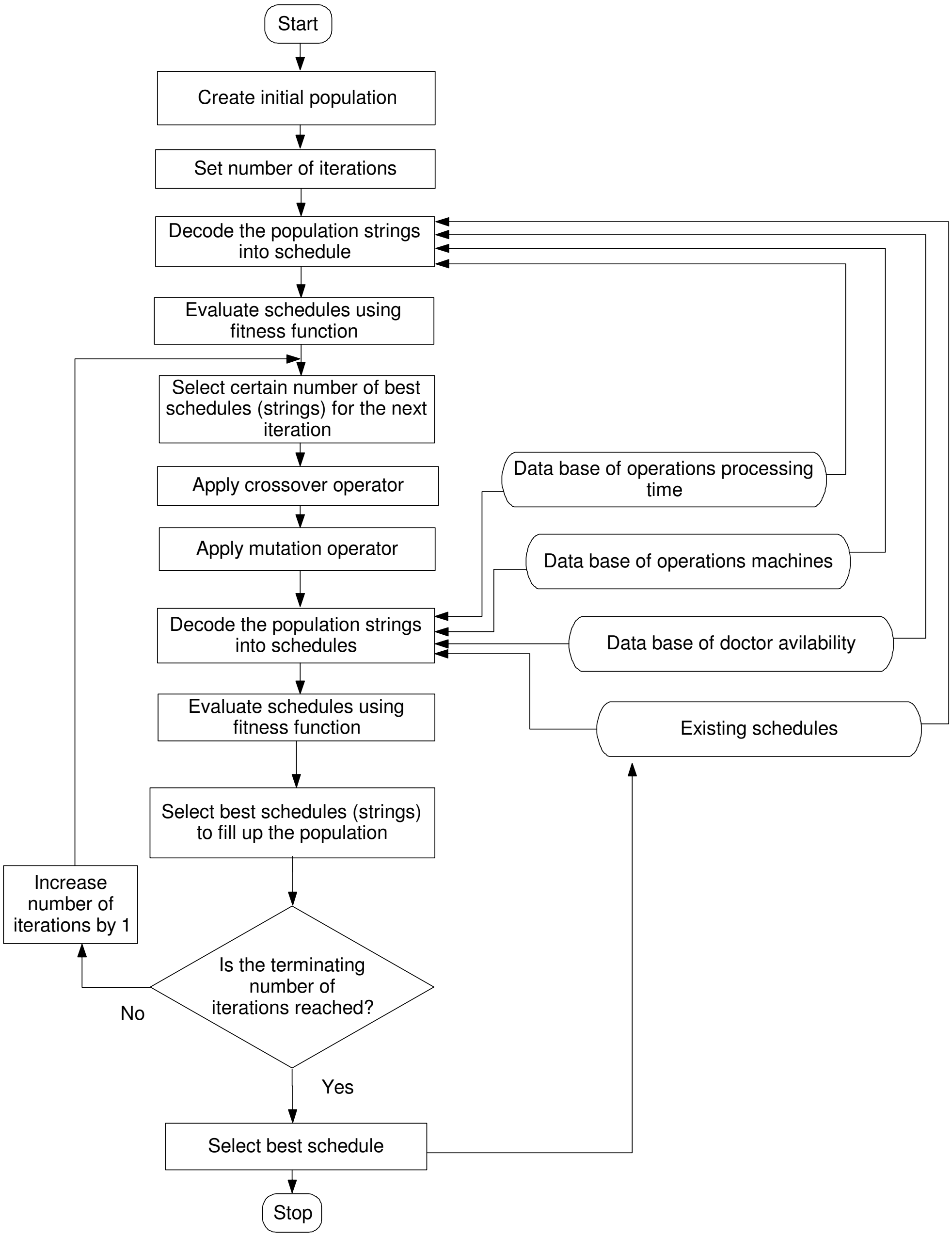


Fig. 4. The flow chart of the developed GA

4.2 KB-GA

Standard-GA constructs a schedule by considering the generated sequence of patient operations and by booking the first available time slots on the requested machines and facilities. Generally, this approach where all the patients are treated equally, does not lead to satisfactory waiting times for emergency patients. It is often the case that all slots of the requested machines or facilities are already booked, during a certain day, preventing emergency patients to have their treatment appointments booked within their two days target. Therefore, we introduce a domain knowledge into the Standard-GA, i.e., into the population initialisation, crossover and mutation operations, and selection of the best solutions for the following iteration.

In order to give priority to emergency patients, different techniques are defined to generate the initial population of strings; for example, all operations of the emergency patients are randomly sequenced at the beginning of the string, followed by randomly sequenced operations of all remaining patients; or all emergency patients are randomly sequenced at the beginning, followed by a random sequence of the remaining patients, and, then, the string is generated by setting all the operations of the 1^{st} patient in the sequence, followed by all the operations of the 2^{nd} patient in the sequence etc.

The crossover and mutation operators are modified in such a way as to select strings where operations of the emergency patients are at the beginning and to keep these operations at the beginning of the strings, while changing the sequence of remaining operations. In order to achieve this, both crossover and mutation operators select emergency patients and keep relative positions of the emergency patient operations.

In order to keep some of the strings in which operations of the emergency patients are set at the beginning, certain numbers of these strings with best fitness function values are input into the population for the next iteration.

4.3 Weighted-GA

Weighted-GA gives different weights to patient categories. These weights are used in the string evaluation. The fitness function is defined as the sum of average weighted waiting times and average weighted delays in treatments. As in the case of Standard-GA, the values of patient waiting times and delay in treatments need to be normalised first. All other steps remain the same as in the Standard-GA.

5. Analyses of the Results

This section describes how the GAs parameters were set and presents results of performance comparison of Standard-GA, KB-GA and Weighted-GA. Results of statistical testing of hypothesis on the GAs performance are presented as well.

5.1 Setting the GA parameters

The multi-objective GA models described above are applied to generate schedules for radiotherapy patients at Arden Cancer Centre. There are 13 resources available including 3 machines and doctors in the Planning unit, 1 Physics unit, 1 Pre-treatment unit, and 7 machines in the Treatment unit. Scheduling is done on daily basis.

Real data collected from the Arden Cancer Centre in the period September, 2005 and January, 2007 were used to develop a simulation model for the radiotherapy processes within the centre (Kapamara *et al.*, 2007). We used this simulation model to generate data about each newly arriving patent such as the category of the patient, the date of the patient arrival to the Cancer Centre, allocated doctor, sequence of patients' operations in his/her pathway, and the treatment machine prescribed by the doctor. Based on the historical data, it is estimated that the daily number of newly arrived patients has a Poisson distribution with the expected rates 8.88, 7.76, 7.47, 6.59 and 11.6 for 5 days in a week, Monday to Friday, respectively.

Probabilities that a patient belongs to the radical, palliative or emergency category are 0.67, 0.31 and 0.02, respectively. Probabilities that a patient of a certain category will require each of the machines and facilities were also determined by the simulation model.

The initial parameters for the GAs and the relevant weights for patient categories were carefully chosen by carrying out experiments on data generated by the simulation model and using different settings of the parameters as follows (parameter values are given in the parenthesis with a chosen value underlined): Number of generations: {30,50}, Population size: {30,50,100}, Crossover rate: {0.6,0.8}, Mutation rate: {0.01,0.02,0.03}, and Number of elite solutions, i.e., the number of strings directly input into the population of the subsequent iteration: {3,5}. The experiments were repeated using different sets of daily patients and average values of the fitness function were considered. Weights given to different patients' categories in Weighted-GA were determined empirically. The weights considered were (3,2,1), (10,8,5), (15,7,1), (18,5,3), (20,10,5), (30,10,1), (35,10,8), (25,8,3), and (50,30,5) for emergency, palliative and radical patients, respectively. The weights (30,10,1) performed best for both objective functions the Average of weighted waiting times and the Average of weighted delays in treatments. They were used in the further analyses.

Once the GA parameters were selected, the quality of schedules generated by Standard-GA was analysed. First, the Standard-GA was used to generate a schedule for the machines and facilities, RTM, and a schedule for doctors, RTD, for "a warming up period" of 60 days. Initially, all the machines, facilities and doctors were available and during "the worming up period" they become partially booked. It was empirically concluded that period of 60 days was long enough for "warming up" and the percentage of machines', facilities' and doctors' available time slots became reasonable stable after this period. Then, Standard-GA was used to schedule newly arrived patients on one day, taking into consideration the machines', facilities' and doctors' bookings generated during "the warming up" period. The scheduling performance was evaluated considering only newly arrived patients.

Due to the stochastic nature of the GAs, we run Standard-GA 10 times for the same set of daily patients. In each run, a new initial population was created. However, in order to take into account uncertainty in the daily number of newly arrived patients, their categories and treatment plans, we used Standard-GA to generate schedules for 10 different sets of daily arrived patients. The obtained results are given in Table 3, including the average of the first and second objective values (i.e., Average waiting times and Average delay in treatments, respectively), and the best and worst values of the first and second objectives obtained in 10 runs for each of the 10 daily sets of patients. As one can see, the ranges of the obtained values for both objectives are not wide, for all 10 daily sets of patients. Therefore, in the tests presented in the following section, we used the GAs parameters as identified above.

Table 3. Scheduling performance of 10 runs of 10 different daily sets of patients

Test sets	1	2	3	4	5	6	7	8	9	10
Average$^{\Delta}$	12.35	13.68	15.36	12.70	15.72	14.53	13.97	15.11	11.18	19.52
Best$^{\Delta}$	9.34	11.16	13.84	11.16	14.86	13.65	13.42	14.70	10.65	18.25
Worst$^{\Delta}$	14.46	16.38	17.11	15.35	16.28	15.32	15.02	16.42	12.69	21.86
Average*	2.29	0.98	0.96	0.83	0.67	1.61	0.98	0.91	0.82	2.01
Best*	1.96	0.72	0.91	0.72	0.31	1.53	0.82	0.32	0.31	1.94
Worst*	4.01	1.94	1.04	0.92	1.27	1.87	1.03	0.94	0.95	3.54
	$^{\Delta}$Average Waiting times					*Average Tardiness				

5.2 Comparison of Standard-GA, KB-GA and Weighted-GA

The performance of the three GAs developed was compared using 20 different problem sets, i.e., daily sets of patients where all three categories of patients were present. The averages of Average waiting time recorded for different patient categories are presented in Fig. 5.

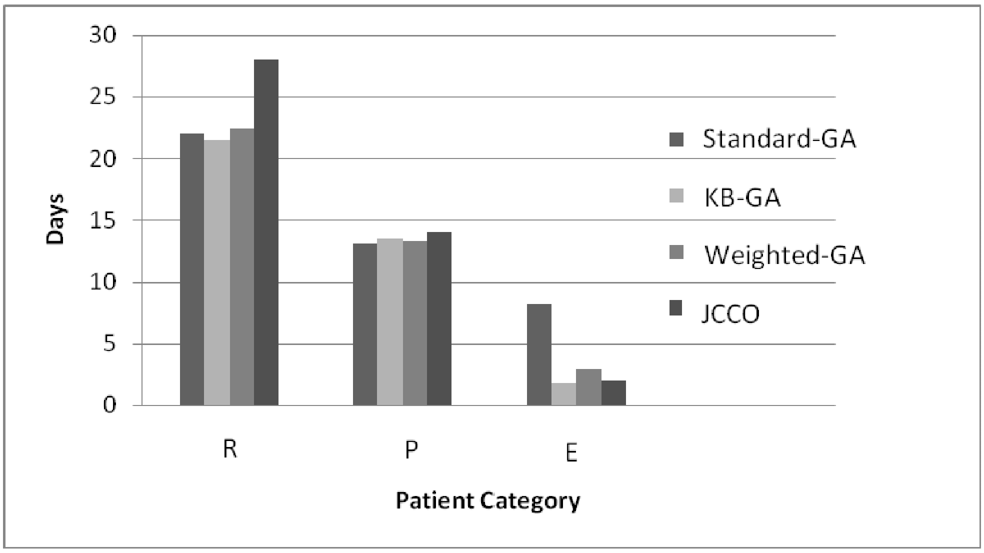


Fig. 5. Comparison of averages of Average waiting times obtained for different patient categories: R - radical, P – palliative and E - emergency

The obtained results showed that performance of KB-GA with respect to the waiting time was better compared to Standard-GA and Weighted-GA for emergency and radical patients. The average of Average waiting time achieved in 20 days using Standard-GA was 22.01, 13.10, 8.23 days, using KB-GA, 21.48, 13.49, 1.78 days and using Weighted-GA, 22.4, 13.26, 2.89 days for radical, palliative and emergency patients, respectively. The Average waiting times for radical and palliative patients obtained using all three GAs were within the JCCO recommendation. The Average waiting time for emergency patients within the JCCO target was obtained by using KB-GA only, while in the case of Standard-GA and Weighted-GA the waiting time was prolonged by 311.8% and 44.06%, respectively, compared to the JCCO target.

The box diagram (Fig. 6) gives a statistical picture of the waiting times obtained. The Standard-GA performed well for radical and palliative patients, but badly for emergency patients, e.g., all the emergency patients had their treatment booked well beyond the target waiting time for all 20 daily sets of patients. The KB-GA was able to schedule all three patients' categories within the JCCO targets. The Weighted-GA performed moderately well for all the three categories, but was unable to schedule all the emergency patients in 20 daily sets of patients within the JCCO target waiting times; still it outperformed the Standard-GA with respect to the waiting times of the emergency patients.

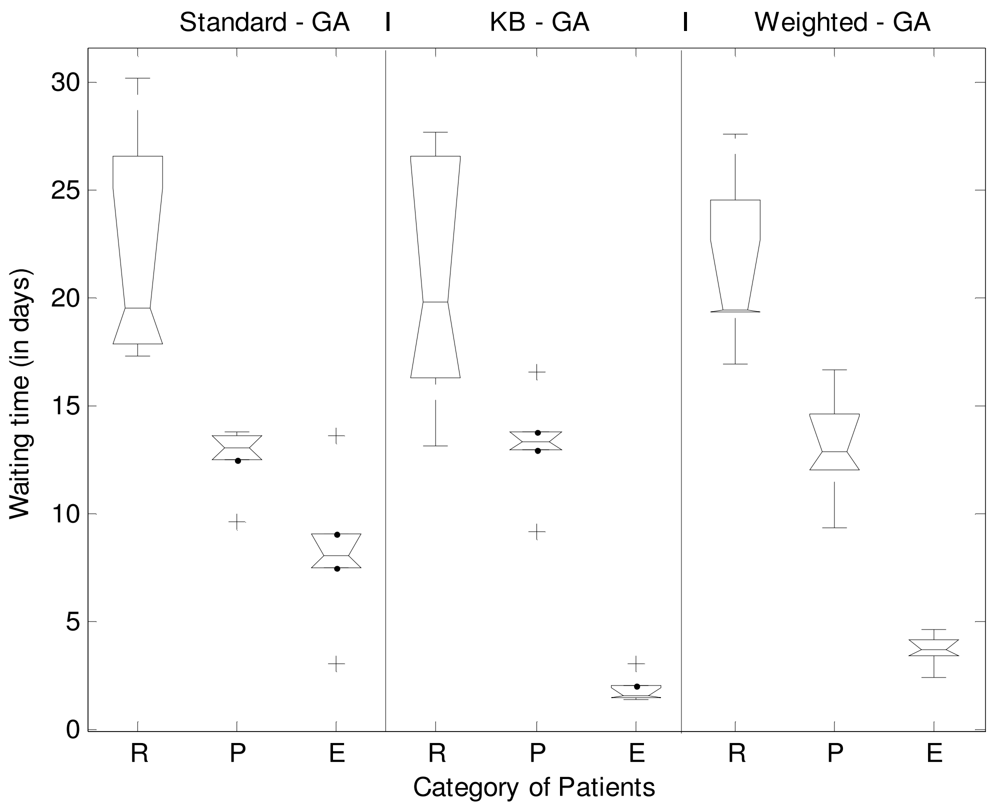


Fig. 6. Comparison of the waiting times of all patient categories obtained by the three GAs

The averages of Average delay in treatments obtained using the 20 daily sets of patients are presented in Fig. 7. The averages recorded for radical, palliative and emergency patients were 0.61, 1.08, 5.85 days, respectively, when Standard-GA was applied, 0.85, 1.16, 0.29 days when KB-GA was applied and 0.62, 0.88, 1.15 days when Weighted-GA was applied. The emergency patients had considerably higher average delay in treatments obtained by using Standard-GA and Weighted-GA, compared to KB-GA.

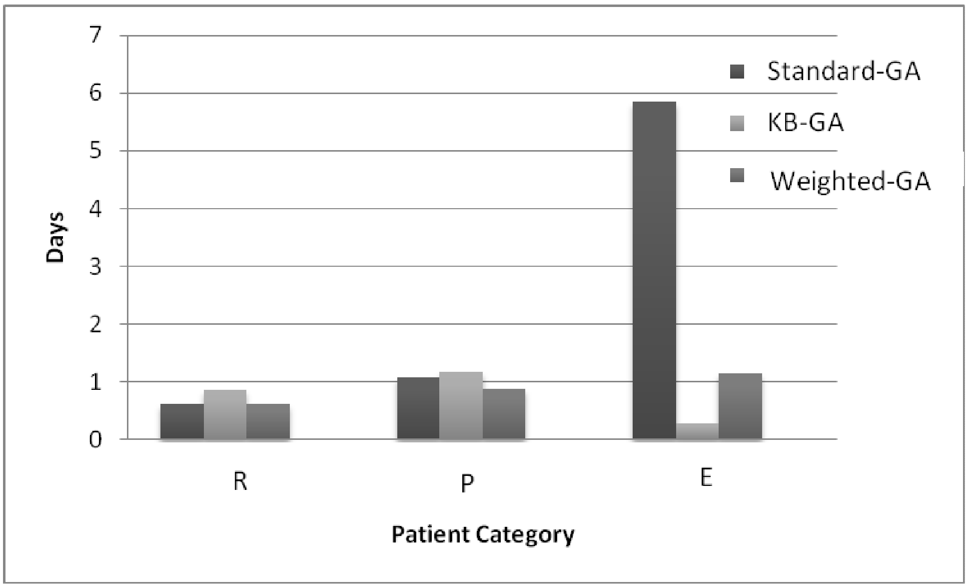


Fig.7. Comparison of averages of Average delay in treatments obtained for different patient catagories

It is interesting to notice that by using all three GAs the average of Average waiting times achieved in all 20 days for radical and palliative patients were better than the current average waiting times recorded using the real hospital data, collected in 2008, that were 35 and 15 days for radical and palliative patients, respectively. However, it is not the case for emergency patients for which the average waiting time in the hospital was 2 days only. KB-GA was able to generate schedules which met the target waiting times for emergency patients. We should point out that the hospital does not operate during holidays, certain machines do not work when undergoing maintenance and the hospital used overtime working hours, in special situations. These assumptions were not considered in the developed GAs.

5.3 Hypothesis Testing

The one-way ANOVA and two-way ANOVA statistical tests were carried out to analyse two hypothesis regarding the performance of the three GAs: (1) "there is no significant difference between waiting times for each patient category considered separately, achieved by the three GAs" and (2) "there is no significant difference between waiting times achieved for all patient categories considered simultaneously, achieved by the three GAs ". The acceptance significant level (α) was 0.05, acceptable absolute error was 0.50 and the sample size was 20, that corresponds to 20 runs of the three GAs, each run for a different set of daily arrived patients. The results obtained are given in Table 4.

Table 4. Results of the hypothesis tests

Test	***P-Value***	***Remarks***
Hypothesis (1) for Radical patients	0.77354	Little or no evidence against the null hypothesis
Hypothesis (1) for Palliative patients	0.77025	Little or no evidence against the null hypothesis
Hypothesis (1) for Emergency patients	0.00050	Very strong evidence against the null hypothesis
Hypothesis (2) for Radical, Palliative and Emergency patients	0.55699	Little or weak evidence against the null hypothesis
Hypothesis (2) for Palliative and Emergency patients	0.01887	Moderate evidence against the null hypothesis.
Hypothesis (2) for Radical and Emergency patients	0.24705	Little or weak evidences against the null hypothesis
Hypothesis (2) for Radical and Palliative patients	0.95150	Little or no real evidences against the null hypothesis

The results showed that there was a strong evidence in favour of KB-GA, in scheduling emergency patients. Analysing the results presented in Fig. 6., and ANOVA test results in Table 4, we concluded that there was a little or weak evidence that KB-GA outperformed Standard-GA and Weighted-GA considering waiting times of all the patient categories simultaneously. In addition, KB-GA and Weighted-GA moderately outperformed Standard-GA considering palliative and emergency patients simultaneously.

6. Conclusions

The three multi-objective GAs for scheduling of radiotherapy patients, namely Standard-GA, KB-GA and Weighted-GA are developed. The three GAs handle the patient categories in different ways: Standard-GA treats all patient categories equally, KB-GA gives priority to scheduling of emergency patients and Weighted-GA gives different weights to the patient categories corresponding to their target waiting times. The GAs are applied to a real life radiotherapy problem. Two objectives relevant to radiotherapy scheduling optimisation are defined: (1) minimisation of Average waiting time and (2) minimisation of Average delay in treatments which compares the starting day of administering the first fraction and the target waiting time, set by JCCO. The performance of generated radiotherapy schedules using the GAs are measured and compared for all categories of patients. The obtained results proved that KB-GA performs well for all categories of cancer patients with waiting times obtained within the targets, and in particular, for emergency patients. The ANOVA tests showed that KB-GA performed better than the other two GAs namely Weighted-GA and Standard-GA with respect to waiting times of emergency patients, and achieved slightly better performance considering all the three patient categories simultaneously. Both KB-GA and Weighted-GA achieved better performance of scheduling palliative and emergency patients considered simultaneously.

The future work will be carried out in different directions as follows:

- New objectives relevant for measuring the performance of a radiotherapy schedule will be included, such as to minimise the number of breaches of target waiting times, to minimise the number of weighted delays in treatments, to minimise the maximum delay in order to ensure that there is no patient with unacceptably long waiting time, etc.

- Different experiments will be carried out, for example, to analyse the effects of reserving certain time slots on the treatment machines for the emergency patients, to investigate the impact of including an additional treatment machine, to evaluate the impact of overtime working hours on the schedule performance, etc.

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