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The Kidney Transplant Problem: an approach to evolutionary computing

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Abstract: *This work addresses the Kidney Transplant Problem (KTP) with priority in the care of organ receptor patients and proposes a resolution methodology based on operational research techniques. In this case, the main objective is to perform as many transplants as possible with the lowest surgical and mobility costs, considering the geographical positions of donors, recipients and hospitals, as well as surgical costs accredited hospitals to perform kidney transplant surgeries. The problem meets the characteristics imposed by the Unified Health System (SUS) of the Health Ministry from the Federative Republic of Brazil. Thus, our work aims to reduce the waiting time of the queue of these patients who need a kidney transplant and give an optimized planning to perform this task. A literature review was made for the specific problem and we found the Kidney Exchange Problem (KEP) with different characteristics from the KTP. It developed for the specific problem: a mathematical model; a set of instances; and a metaheuristic, based on Genetic Algorithm (AG), applies it to solving the problem. The results of the AGare presented with great degree of satisfaction.*

Keywords: *Genetic Algorithm, Kidney Transplant, Metaheuristic, Combinatorial Optimization.*

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I. INTRODUCTION

According to the Brazilian Institute of Geography and Statistics (IBGE in Portuguese) [1], on July 1, 2017, the Brazilian population was 207,660,929 of which10,565 people entered the waiting list for kidney transplantation that year. Unfortunately, 1,176 of these individuals died, either due to complications directly linked to the organ in question or by other causes. The year ended by accounting for 21,059 active patients within the waiting list for organ transplantation under analysis. This year, only 5,929 kidney transplants performed [2]. The low number of donors in contrast to those of recipients can be considered an indicator of social taboo among the various countries. It can be mentioned China, which even with more than 18% of the world's population, is not among the top on the list of countries with the highest rates of organ donations as can be seen in [3-5]. In the case of this country, it is believed that this is due to religious beliefs. On the other hand, countries such as France, Spain, Belgium and Portugal, after experiencing the deaths of hundreds of their inhabitants due to the lack of donors, perceived the alarming state that is the scenario and the discrepancy between the high number of inhabitants in contrast to number of effective donors. To resolve this problem, new laws arose, unlike Brazil, indicating that every person becomes organ donor after his death from brain death. Thus, the need for the person to inform the family his willingness to become a donor. If the person does not want to be a donor, he should inform the non-interest in the donation ([6-7]).

It is known that in Brazil, several people die in the waiting line of the Unified Health System (SUS in Portuguese) due to the slowness to perform transplantation. The Brazilian government realized that some transplants were not done by geospatial logistical difficulty between donors and compatible recipients in a timely manner. Thus, he sanctioned a law that determines a support of the Brazilian Air Force (FAB in Portuguese) in the logistics of interstate transplants [8]. Although the number of donors has increased over the years, the difference between the number of effective donors and receivers still makes the scenario alarming. However, it is positive to see that some countries have been uneasy about organ donation. Thus, the scientific community has studied methods to increase the quality of life of patients who are in the final stage of the disease and who need organ donation. However, one of the main methods of solving this problem is still transplantation, as shown in [9-14]. It is important to emphasize that thanks to scientific advances, when comparing the drugs used for post-transplants of 1987 with the current ones, an average survival of 10 years of the transplanted organ in the patient was compared, as can be seen in [9]. Thus, if before the transplanted patient lived on average 5 years with the same graft, today, one lives on average 15 years. The organ taken from a living donor provides significantly longer-term survival when compared to the organ from a deceased donor, according to [10].

One of the main motivations for solving the problem is to exchange donor-recipient pairs and lower costs for public coffers. This particular problem, in the way we are proposing its resolution, is little addressed on the national scene. It is interesting to create insight into how the process of renal transplantation can impact public coffers. For this, it is important to highlight that the Brazilian transplant program is one of the largest in the world, 95% of which is funded by the SUS and has a logistics of organ allocation that does not take into account social, racial privileges, etc., as described in [9-15].In Portugal, an average of 25,000 EUR per patient is spent per year [16]. In the USA, 85,000 USD per year is spent on dialysis per patient, while 120,000 USD is spent on transplants with an additional 20,000 USD per year on immunosuppressive drugs, according to [17]. Also, in Brazil, according to [18], renal transplantation of the deceased donor generates an economy per patient of 37,000 BRL and 74,000 BRL in relation to hemodialysis and peritoneal dialysis, respectively. Regarding renal transplantation of living donor, the savings are even greater: 46,000 BRL and 82,000 BRL in relation to hemodialysis and peritoneal dialysis, respectively. This result, combined with survival and quality of life analyses, can characterize kidney transplantation as the best alternative from a financial and clinical point of view, assisting in the formulation of public policies related to organ transplants in the Brazil.

It is important to emphasize that in Brazil, in case of chronic disease or failure of one or more organs, Brazilian laws of nº. 9,434 and 10,211 and Art. 13 of the Civil Code provide for the possibility of organ and tissue transplantation. Still in case of jurisprudence, it is interesting to know that, in case of family affinity between donor and recipient, there may only be transplantation in case of consanguineous kinship up to fourth degree, even if the donor and recipient are compatible. However, in order to have this procedure, a judicial authorization must be requested to proceed with the surgery, because the law only provides, for this case, the possibility of the spouse. Thus, an authorization will be requested from the Ethics Committee of the hospital where the surgery will be performed. It is also necessary for a law judge and the State Transplant Center to release the procedure. These are measures that, from an analytical point of view, tend to increase the waiting time in the transplant queue of the Unified Health System. Thus, to minimize the waiting time and relieve the SUS, a new methodology was proposed for optimizing the logistics of kidney transplantation in Brazil, where, a priori, the present work can also be applied to other types of organs for transplants.

As shown above, it is perceived that the problem is worldwide not only in health, but at an economic level, also described in [17]. The population growth determines an increase in demand for transplants. If the country does not have public policies that further stimulate dialysis transplantation, this will directly impact its economy with a view to high spending to keep a person on dialysis in favor of transplantation. Thus, with the population increase over time, some countries will tend to need more transplantation. Some continents, such as Europe, because they have greater ease of communication between member countries, may even send a patient or donor to a member country for transplantation, with the benefit of reducing costs of public coffers. Thus, a logistical problem is created that can be solved with clear knowledge and objectives of the operational research area.

The current ways of solving the problem do not meet the great demands. Current mathematical formulations cannot find the best donor for the patient in very long chains in a timely manner. With the time of ischemia being a constant for each type of organ and with the growth of the number of patients following the tendency to be higher than the number of donors. Finding the best donor for the patient in a timely manner is a major challenge and will be one of the focuses of this work. Therefore, in view of the above and the negotiations to resolve the consequences of the low number of donors in a given spatial region, a resolution method for the specific problem of finding the best donor-recipient pair taking into account their spatial location and surgical operating costs, priority care and blood compatibility, based on existing information and registered in a database.

The main objective of this work is to present and characterize the problem of specific kidney transplants with a resolution methodology, where it is intended to find the best sequence of recipients compatible with available donors respecting the restrictions of the problem, such as geographic proximity linked to cost, priorities in service and other restrictions. For this to happen, a simulation of the location of hospitals, donors and recipients was randomly done in certain regions of the Brazilian territory. Although the actual data have been unsuccessfully requested. With this data, we hope to find the best donors for kidney recipients in a timely manner, checking the shortest distances, costs and expenses to be traveled to perform transplants.

II. DESCRIPTION OF THE PROBLEM

Brazil, like other countries, has laws regulating organ transplantation. However, there are only two donation methods: deceased donor or living donor. In case the graft comes from a deceased donor and has his brain death proven, by at least two different doctors and specific tests, the deceased donor will be placed on the SUS list. In case you are a living donor, you will undergo tests that attest to your pre- and post-transplant health. In case of end-stage kidney disease, the recipient must register on the official waiting list for a transplant and, after the compatible donor is found, the transplant is performed. In addition to the difficulties provided for in Brazilian legislation as previously stated, there are technical incompatibilities that will be addressed below.

2.1 Blood

It is important to realize that there are three main conditions for organ transplantation. One of them is blood typing. Blood typing is one of the main factors that influence the compatibility between donor-recipient. A better view can be seen in Table 1. In this table, the compatibility of each donor-recipient pair with their blood type can be visualized. For example, a blood type "A" person can receive blood from people type "0" and "A" and can donate to "A" and "AB".

Table 1. Blood transplant groups (donation and reception).

Blood groups	Can receive organ of type	Can donate to type person
O	O	O, A, B, AB
A	O, A	A, AB
B	O, B	B, AB
AB	O, A, B, AB	AB

Another condition is the typing of Human Leukocyte Antigens (HLA) or Histocompatibility Antigens. These antigens, which stay in leukocytes, read every cell in our body to know if that cell really is from our organism or not. If it isn't, she'll be attacked. Each person's HLA system is a combination of six antigens: 2 HLA-A antigens, 2 HLA-B antigens and 2 HLA-DR antigens. The last primary condition is the Lymphocyte Cross-test or also called Cross-Match. In this test, the donor and recipient's blood is mixed to verify the possibility of a possible rejection of the organ to be transplanted. If the test is positive, there are receptor antibodies that will act against donor antigens. This means that the organ will be rejected after transplant. These last two conditions were not taken into account in our study due to lack of consistent information.

2.2 Logistic

The problem of paired kidney transplantation has a logistical difficulty, as described in [13,19-20]. Surgery is required of 4 rooms in a hospital. One for the removal of the donor organ of the pair i and the other for the implantation of the graft in the patient of the pair j, while in two other rooms are done simultaneously the same procedures with the other donor-recipient group. Surgeries have to be done simultaneously. In this way you have the Kidney Paired Donation (KPD) or cross-transplant of kidneys, where the concurrency of events is mandatory. In [2], it was reported that there are cities with a higher number of patients and few donors, others with a higher number of donors, but that they do not require a high demand from donors. Due to the great territorial extension of Brazil, there are organs that do not find the most compatible receiver. For this, the Brazilian government promulgated the authorization of aircraft for transplantation as described earlier in Section 1, given the distances to be traveled by donors and recipients in a continental country.

The following are described several models found of the problem with their own characteristics: *2-way KPD*, suggests that donor 1 donate to receptor 2 and donor 2 donates to receptor 1; *k-way KPD*, suggests the same procedure as the above item, but with higher numbers of chains; *Domino Paired Donation* (DPD) suggests the inclusion of an altruistic A donor in the system and penultimate pairing of the cycle provide an inclusion in a W receiver from the SUS waiting list; *Non Simultaneous Extended Altruistic Donor* (NEAD), suggests the beginning of the chain provided by the insertion of altruistic donor to the cycle and, at the end of this first round of combinations, the last donor begins a new cycle. This last donor is called the "bridge donor" because it will be the connection between chain n with chain *n*+1; *listex change*, indicates that the patient in the KEP program will have priority to receive the organ, which would initially go to the SUS receiver and will be used for the beginning of a new chain with the obligation to return to the SUS at the end of the chain; *Altruisticallyunbalanced 2-way KPD*, indicates that pair 1 has compatibility, par 2 has incompatibility, however, as donor 1 is compatible with receptor 2 and donor 2 is compatible with receptor 1, transplants can be performed; *Desensitization in 2-way KPD*, suggests that receptor 2 will undergo a desensitization process to receive donor organ 1 and, as well as a "Simple Cycle Chain", donor 2 will donate to receiver 1.

The main focus of our work is the search not only of the most compatible donor, but that it is also the closest donor to the surgery hospital along with its recipient, and with the lowest surgical cost. Thus, unlike existing literature, we propose an innovative method that aims to revolutionize the "modus operandi" of the SUS and we named *Kidney Transplant Problem* (KTP), where an instance of this problem takes into account: a set D of donors; an R set of receivers; and an H set of hospitals. All these sets with their georeferenced locations. The purpose of the specific problem is to look for the recipient-donor-hospital triad that has the lowest operational cost (surgical and mobility), and which generates the largest number of transplants.

Here, the data are described to represent an instance of the specific problem: H={1, 2, 3, ..., *nh*} is the whole of hospitals, where *nh* is the total number of existing hospitals; R={1, 2, 3, ..., *r*} is the set of receptors, where r is the total receivers; D={1, 2, 3, ..., *d*} is the total donors, where *d* is the total donors; DH_{ih} is the distance from donor *i* to hospital *h*; RH_{jh} is the distance from receiver *j* to hospital *h*; CH_h is the surgical cost of transplantation in hospital *h*; W = Max(CH_h) + Max(DH_{ih}) + Max (RH_{jh}) represents the highest transplant cost; Z_p is the total receivers with priority type p=1, 2, 3, ..., *k*; W_p represents the weight of the transplant for the priority recipients of the type p=1, 2, 3, ..., *k*, calculated as follows: $W_k = W$; $W_p = (Z_{p+1} + 1) \times W_{p+1}$, para $p=(k-1), (k-2), ..., 3, 2, 1$.

Receptors with priority in the care of type *p*=1 indicates that they have priority in transplants to be performed on the other recipients with priority other than 1. Similarly, receptors with *p*=2 have priority in transplants in relation to type 3, 4, ..., *k*, and so on. In this type of problem, the tendency is to allocate first donors to receivers with priority 1, then those with priority 2, and so follows. Suppose we have an instance with 10 receivers, *p* ranging from 1 to 3 and W=100:

Receptor	1	2	3	4	5	6	7	8	9	10
Priority	1	1	2	2	2	3	3	3	3	3

Therefore, the weight of transplantation for each recipient with their proper priority is given by: $W_3=W=100$; $W_2=(Z_3 + 1) \times W_3 = (5 + 1) \times 100=600$; $W_1=(Z_2 + 1) \times W_2 = (3 + 1) \times 600=2400$. The distance DH_{ih} e RH_{jh} are calculated based on the georeferenced positions of donors, recipients and hospitals. The following mathematical model for KTP was developed by us:

$$\text{Max} \quad F(X) = \sum_{i\in D, j\in R, h\in H} [W_{P(j)} - (RH_{jh} + DH_{ih} + CH_h)]X_{ijh} \tag{1}$$

Subject to:

$$\sum_{i\,\in\, D_0} \sum_{h\,\in\, H} X_{ijh} \leq 1, \forall\, j\, \in R_O \tag{2}$$

$$\sum_{i\,\in\, D_0 \cup D_A} \sum_{h\,\in\, H} X_{ijh} \leq 1, \forall\, j\, \in R_A \tag{3}$$

$$\sum_{i\,\in\, D_0 \cup D_B} \sum_{h\,\in\, H} X_{ijh} \leq 1, \forall\, j\, \in R_B \tag{4}$$

$$\sum_{i\,\in\, D} \sum_{h\,\in\, H} X_{ijh} \leq 1, \forall\, j\, \in R_{AB} \tag{5}$$

$$\sum_{j\,\in\, R} \sum_{h\,\in\, H} X_{ijh} \leq 1, \forall\, i\, \in D_O \tag{6}$$

$$\sum_{j\,\in\, R_A \cup R_{AB}} \sum_{h\,\in\, H} X_{ijh} \leq 1, \forall\, i\, \in D_A \tag{7}$$

$$\sum_{j\,\in\, R_B \cup R_{AB}} \sum_{h\,\in\, H} X_{ijh} \leq 1, \forall\, i\, \in D_B \tag{8}$$

$$\sum_{j\,\in\, R_{AB}} \sum_{h\,\in\, H} X_{ijh} \leq 1, \forall\, i \in D_{AB} \tag{9}$$

$$X_{ijh} \in \{0,1\}, \forall\, i\, \in\, D, j\, \in R\ e\ h\, \in H \tag{10}$$

$$\text{whit } X_{ijh} = \begin{cases} 1, \mathit{if\ the\ donor\ i\ donate\ a\ kidney\ to\ the\ receiver\ j\ in\ the\ hospital\ h} \\ 0, \mathit{otherwise} \end{cases}$$

The objective function of the mathematical model, described in (1), determines the maximum value for performing the highest number of transplants to be performed, respecting the compatibility and priority of care, with the lowest surgical cost and mobility of donors and recipients to hospitals for transplants. The best donor and the best hospital are defined for each recipient, who will do the transplant, based on the lower value we want to subtract from the first sum. This value represents exactly the surgical cost and mobility costs of the recipient and donor to the hospital where the transplant will be carried out. The groups of restrictions of types (2) to (5) represent the blood donation compatibility for each blood type of each receptor. Additionally, these restrictions determine that each receiver can only receive a maximum of one donation. The sets R_0, R_A, R_B e R_{AB} form a partition of the R set based on the blood type of each receptor. Similarly, set D was partitioned into D_0, D_A, D_B e D_{AB}. The groups of restrictions of types (6) to (9) represent the blood donation compatibility for each blood type of each donor. In addition, these restrictions determine that each donor can only make a maximum of one kidney donation. In (10) you have the range of values for the problem decision variables according to their definitions. The mathematical model has $r \times d \times nr$ variables and $r+d$ restrictions, that is, it is a complex model in the number of variables and simple regarding the number of restrictions, when compared to the total number of variables. The following is the genetic algorithm proposed to be applied in solving the problem without making the use of mathematical programming.

III. THE GENETIC ALGORITHM

The algorithm proposed in this work aims to find the best sequence of receptors that takes into account their geographical locality, priority of care, blood compatibility with the donor, geographical location of donors and hospitals and the surgical costs of hospitals. The components used in the construction of our genetic algorithm are given as follows:

i) The structure of a solution *s* is given as a permutation of set R, where the order of individuals in the permutation determines the allocation of a compatible donor that is still available to it. In this structure, generally the first positions must be constituted by the receivers of priority 1, then the receptors of priority 2, and so on. Not taking into account this fact generates solutions with technical unfeasibility of the specific problem, where a higher priority receiver may be moving ahead of another with better priority than his. Leaving this receiver without a transplant when he should be met by his priority.

ii) The individuals are all evaluated by using Equation (1), where to calculate the cost of a solution s takes into account the weight of the transplant, the lower cost of the operation of the transplant and the distances traveled by the recipients and donors to the hospitals where the transplants will be performed. Based on the solution s, initially an available and compatible donor is sought in set D, these donors found that donor *b* and hospital *t* had the lowest operational cost to perform for transplanting the recipient *s*(1). Select this donor and the hospital for the *s*(1) receptor let and the b donor unavailable for future donations. Compute the cost of this operation in variable *f*(*s*), conform the objective function of the mathematical model, and also compute the actual problem cost of the specific in a variable $v(s)=RH_{s(1)t} + DH_{bt} + CH_t$. The allocation proceeds in the same way for the other receivers in the solution s, from the second position, following the order given in *s*. The process stops when this procedure was also performed for the last receiver in the solution *s*, in this case the receiver *s(r)*. In the end, the suits (recipient, donor, hospital) are included, indicating who is the donor who will participate in the recipient's transplant in the specified hospital; the real value of transplants; and the value of the objective function of the problem specific to the solution presented. The best solution to be presented by the method is the one with the highest value in the objective function.

iii) The generation of the initial population is the main criterion to deal with the diversification. A set of *NPOP* initial individuals or chromosomes form an initial population, where *NPOP* represents the population size and this value was egual to 50 individuals. The initial population was composed of each individual starting with i=1, 2, ..., *r* and then this individual is transformed into his symmetrical. For example, for *r*=4, one individual <3214> has its symmetric being <2341>.That is, the sum of each position of the two individuals is equal to *r*+1.The initial population takes the best individual *NPOP* from the 2*r* generated.

iv) The selection strategy for crossover and mutation is made with all individuals of the population.

v) Crossover is a genetic operation to generate a new sequence (i.e., child) from its parent strings. It has a great influence on the performance of genetic algorithm. The crossover operator exchanges the information of the selected parents to generate promising offspring or sequences. It can be used to generate a set of new solutions or offspring between two solutions from the set. The idea behind crossover is that the new chromosome may be better than both of the parents if it takes the best characteristics from each of the parents. The crossover operator is applied to all individuals in the population, making (*NPOP* × (*NPOP*-1))/2 applications for each type of crossover operator. Four crossover operators were used in GA: order crossover with one-point (1P), order crossover with two-point (2P), partially mapped crossover (PM), and order crossover with two blocks (2B). The operators 1P, 2P and PM are widely used in evolutionary computation and can be found in [20, 21]. We developed the 2B operator. The two cutting points *c1* and *c2* used in 2P, PM and 2B are given as *c1*=*r*/3+1 and *c2*=2×*r*/3 + 1. The cutting point *c1* used in 1P is given as *c1*=*r*/2. We did not use the random generation of these points for the algorithm proposed because we want to split the chromosome in approximately three equal parts when we used 2P, PM and 2B, and in approximately two equal parts, when used 1P. We developed the 2B operator on the idea of replicating the good built blocks. In addition, it increases the number of solutions generated and evaluated by GA, diversifying the search to find the optimal solution of the problem. The Figure 1 illustrates this procedure, where each parent D_1 and D_2 is divided into three blocks. The cutting points that generate the blocks are *c1* and *c2*, specified above. Taking D_1 as the base, the blocks b_1, b_2 and b_3 generate four offspring (children): F_1=<b_1 b_2>, F_2= <b_1 b_3>, F_3= <b_2 b_1>, and F_4= <b_3 b_1>. The block b_1 is the part between the two cutting points (central block D_1 – gray color). The block b_2 is formed by elements that are not in b_1 and they are placed in the order of their appearance in D_2. The block b_3 consists of the elements of block b_2, with their order reversed. The same procedure is repeated for D_2 being the base, generating more four children. In this work, a new mutation operator is proposed in order to intensify the search, regenerating the solutions considered worse quality. The purpose of this operator is to build good solutions from a particular solution combined with the best solution found up to that moment of the search. The mutation operator used in the GA works as follows. Figure 1 shows an application of the mutation operator with *r*=8, *k*=2, *sopt*=<3 5 8 6 1 7 2 4> (solution defined as the regeneration solution), and *s*=<7 3 1 5 2 6 8 4> (a solution of the current population to be regenerated), it produces the solution *sr*=<7 2 4 3 5 8 1 6> (solution regenerated by the application of the mutation operator). Initially, *k* adjacent positions of the regeneration solution are copied for the solution regenerated. Thereafter, the copies can be alternate positions of the regeneration solution, if certain receptors of *k* adjacent positions have already been copied to the solution regenerated. Furthermore, the copy can also be made with *v* positions of the regeneration solution ($v<k$). This happens when the number of receptors, from a certain position of the regeneration solution, yet not copied from the regeneration solution is less than *k*. In the example, the regenerate solution was obtained as follows. Let s_1 be the first receptor of the solution *s* (s_1=7). Insert s_1 into first position of solution *sr* (*sr* = <7>). Find the position *j* of the receptor s_1 in solution *sopt* (*j*=6). Let $b=(b_{j+1}, b_{j+2}, ..., b_{j+k})$ be a partial sequence of *sopt* with *k* adjacent positions, after position *j*(*b*=(2, 4)). Insert *b* into *sr* (*sr*=<7 2 4>). This process is repeated for other receptors of the solution *s*, checking which of them are not in *sr*. Thus, the next iterations show the following results {s_2=3, *j*=1, *b*=(5, 8), *sr*=<7 2 4 3 5 8>}, {s_3=1, *j*=5, *b*=(), *sr*=<7 2 4 3 5 8 1>}, {s_6=6, *j*=4, *b*=(), *sr*=<7 2 4 3 5 8 1 6>}. Another important feature of this technique is that the regeneration solution can be updated whenever a better solution is found. After several tests, the GA is running with k=1, 2, ..., *r*/2.

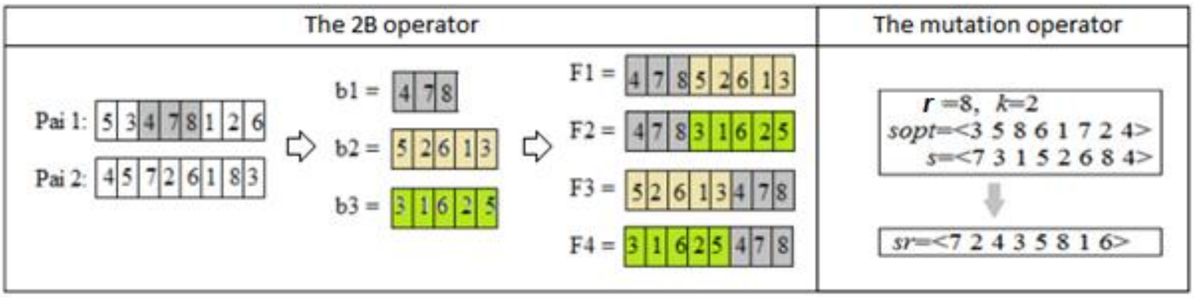

Figure 1. The crossover (2B) and mutation operator.

vi) The replacement strategy is responsible for controlling the replacement of individuals from one generation to the next in the population. The size of the population is constant (*NPOP*). The proposed strategy for our GA is fully replacing all individuals of the population by the best individuals found in the application of the crossover and mutation operators. Acting this way, the GA intends to diversify and intensify further the search to find the optimal solution of the problem.

```
Procedure GA
  stop=0;
  InitialPopulation();
  avg1= ∑_{v=1}^{NPop} I(v,0)/NPop;
 while (stop==0) do
    Crossover_1P(); Crossover_2P();
    Crossover_PM(); Crossover_2B();
    Mutation();
    avg2 = ∑_{v=1}^{NPop} ICM (v,0)/NPop;
    I=ICM;
    if (avg1==avg2) then stop=1;
    avg1= avg2;
 endwhile
 Output: s_opt (The best solution found);
```

Figure 2. Pseudocode of the Genetic Algorithm.

vii) Many stopping criteria based on the evolution of a population may be used. Some of them use the following conditions to determine when to stop: generations (when the number of generations reaches the value of generations), time limit (after running for an amount of time in seconds equal to time limit), fitness limit (when the value of the fitness function for the best point in the current population is less than or equal to fitness limit), stall generations (when the average relative change in the fitness function value over stall generations is less than function tolerance), function tolerance (The algorithm runs until the average relative change in the fitness function value over stall generations is less than function tolerance), among other conditions. The algorithm stops when any one of these conditions is met. Initially, the GA used the following criteria:

generations, time limit and stall generations. Several analyzes were performed with the execution of the algorithm applied to different instances of the problem, where it was observed that the algorithm never stopped for the values of the first two variables (generations=r and time limit=3600). The average value of fitness of individuals of the current population was used for the third variable. It was compared with the average value of the immediately preceding population. When these values are equal to at least 2 consecutive iterations, the algorithm stops and presents the best solution found to the problem. This feature prevents the evaluation of solutions that can be distinct from those already generated and analyzed, but with the same performance. This greatly reduced the algorithm runtime. The Figure 2 shows o pseudocode of the GA, where the crossover and mutation population is allocated to array *ICM*. The fitness of the individual v is stored in its first component ($I_{v(0)}$ and $ICM_{v(0)}$). The components of avg1 and avg2 contain the average fitness of the populations *I* and *ICM*. These values are calculated for individuals of the current population and immediately preceding population.

The GA algorithm is based in the DGA algorithm used for Silva, Viana and Silva [22, 23]. They used the DGA algorithm in the resolution of the No-wait and Permutational Flowshop Scheduling Problem (NWFSP and PFSP) with makespan as performance criteria.

Table 2. Instances of the problem with relation to the blood type.

Instance	PATIENT					DONOR				
	A	B	AB	O	***r***	A	B	AB	O	***d***
i1	24	12	12	12	60	8	8	8	8	32
i2	12	24	12	12	60	8	8	8	8	32
i3	12	12	12	24	60	8	8	8	8	32
i4	12	12	24	12	60	8	8	8	8	32
i5	24	12	12	12	60	15	15	15	15	60
i6	12	24	12	12	60	15	15	15	15	60
i7	12	12	12	24	60	15	15	15	15	60
i8	12	12	24	12	60	15	15	15	15	60
i9	24	12	12	12	60	23	23	23	23	92
i10	12	24	12	12	60	23	23	23	23	92
i11	12	12	12	24	60	23	23	23	23	92
i12	12	12	24	12	60	23	23	23	23	92
i13	40	20	20	20	100	19	19	19	19	76
i14	20	40	20	20	100	19	19	19	19	76
i15	20	20	20	40	100	19	19	19	19	76
i16	20	20	40	20	100	19	19	19	19	76
i17	40	20	20	20	100	25	25	25	25	100
i18	20	40	20	20	100	25	25	25	25	100
i19	20	20	20	40	100	25	25	25	25	100
i20	20	20	40	20	100	25	25	25	25	100
i21	40	20	20	20	100	31	31	31	31	124
i22	20	40	20	20	100	31	31	31	31	124
i23	20	20	20	40	100	31	31	31	31	124
i24	20	20	40	20	100	31	31	31	31	124
i25	80	40	40	40	200	45	45	45	45	180
i26	40	40	80	40	200	45	45	45	45	180
i27	40	80	40	40	200	45	45	45	45	180
i28	40	40	40	80	200	45	45	45	45	180
i29	80	40	40	40	200	50	50	50	50	200
i30	40	40	80	40	200	50	50	50	50	200
i31	40	80	40	40	200	50	50	50	50	200
i32	40	40	40	80	200	50	50	50	50	200

IV. COMPUTATIONAL EXPERIMENTS

The computational experiments carried out to observe the performance of GA was executed in a PC with a clock of 3.2 GHz and 8Gbytes of RAM and the source program is in ANSI C. Table 2 shows how the proportion of donors and patients was divided by blood type, in the instances used of the problem. Table 3 present the performance of the GA for each crossover operator, with the F(s) values and the execution time given in seconds. In Table 4, a comparation of performances is made for each crossover operator with the

Number of Transplants Operationalized (NTO) for each instance. The *Rate of Transplants not Operationalized* (RTnO), in relation to the minimum number of *d* and *r*, is presented.

The Table 3 shows that operators 2B (media of 76,87 seconds) and 2P (media of 20,96 seconds) spent the most execution time when compared to operators 1P and PM.In both tables, the bold values represent the best performances for each instance. The GA with operator 2B had much more significant gains than with the others crossover operator. Importantly, operator 2B obtained the best RTnO media (1.34%), followed by 2P (4.50%), PM (4.91%) and 1P (5.00%). Therefore, our GA will work with the operator 2B.

Table 3. Performance of GA with the F(s) values and execution time.

Instance	**F(s)**				**Time (s)**			
	1P	**2P**	**PM**	**2B**	**1P**	**2P**	**PM**	**2B**
i1	375971392	375974656	296789888	**375977056**	0,94	2,36	0,25	2,48
i2	380108800	380108608	289108928	**380115264**	1,67	2,75	0,61	2,91
i3	499019616	**499030592**	303650720	469163168	0,97	2,62	0,31	0,89
i4	455595712	**455607424**	306297760	414877568	0,70	1,39	0,14	50,64
i5	625057856	705236416	308996768	**809690048**	2,91	9,01	0,58	11,36
i6	624338880	660730176	289641696	**757348224**	3,78	7,06	0,58	23,43
i7	528530464	664025088	297601856	**895008192**	3,77	5,44	0,48	244,93
i8	661609728	696268992	295694880	**772859456**	3,73	12,04	0,59	658,25
i9	447667616	497541376	247947632	**513912896**	3,98	12,54	0,53	13,68
i10	598313728	802425920	295512256	**888207232**	2,08	24,31	0,41	80,18
i11	**620999040**	618782848	295097536	599256000	3,14	7,59	0,83	327,10
i12	905636032	841415552	295124384	**985618816**	6,05	6,73	0,92	24,99
i13	2740048128	2851913984	1306548224	**2926460672**	5,22	31,48	1,97	24,21
i14	2236011520	2459238912	1288857216	**2459267584**	6,12	26,07	1,89	26,44
i15	2568841728	2861829632	1308437888	**2861859584**	19,47	29,49	1,58	19,11
i16	1302843392	**2608352000**	1302845440	2608344832	1,14	20,82	1,14	37,53
i17	1299054720	3216861440	1299042304	**3420923648**	2,17	11,53	1,83	31,00
i18	1254173184	3731561216	1254174592	**4483395072**	2,62	41,74	1,27	47,89
i19	1286382080	3160828160	1286385408	**3323138560**	1,36	50,57	1,28	74,80
i20	1291543680	3165678592	1291563776	**3401385216**	2,67	57,00	2,23	50,77
i21	1276906112	3086192384	1276907904	**3116426240**	1,14	56,51	2,38	53,51
i22	1239856768	3589917184	1239858432	**4772630528**	2,28	49,69	3,09	48,36
i23	1266229248	2879570432	1266247296	**3090384640**	1,17	26,63	1,64	159,84
i24	1242726784	3976840960	1242727168	**4607013888**	1,17	22,84	1,17	20,48
i25	10216656896	10216659968	10216660992	**24202844160**	6,30	16,45	6,31	119,90
i26	10249030656	10249035776	10249031680	**27540625408**	6,03	24,17	4,75	83,16
i27	10105809920	10105809920	10105812992	**27156402176**	4,25	8,37	6,47	156,56
i28	10105738240	10105747456	10105763840	**27156402176**	6,25	8,25	4,81	10,45
i29	10122449920	**10122458112**	10122456064	10122446848	4,72	32,68	9,01	8,50
i30	10097202176	**10097214464**	10097211392	10097212416	4,80	23,46	7,19	16,77
i31	10064220160	10062018560	**10064230400**	10064224256	7,09	19,91	9,08	12,69
i32	10010795008	10010816512	**10010839040**	10010835968	4,91	19,18	9,03	17,15
				Time Media	**3,89**	**20,96**	**2,64**	**76,87**

Table 4. Performance of GA with the NTO and RTnO values.

Instance	NTO					Min	RTnO				
	1P	2P	PM	2B	Best	(r,d)	1P	2P	PM	2B	Best
i1	**32**	**32**	**32**	**32**	32	32	0,0	0,0	0,0	0,0	0,0
i2	**32**	**32**	**32**	**32**	32	32	0,0	0,0	0,0	0,0	0,0
i3	**32**	**32**	**32**	**32**	32	32	0,0	0,0	0,0	0,0	0,0
i4	**32**	**32**	**32**	**32**	32	32	0,0	0,0	0,0	0,0	0,0
i5	52	51	52	**60**	60	60	13,3	15,0	13,3	0,0	0,0
i6	52	49	52	**60**	60	60	13,3	18,3	13,3	0,0	0,0
i7	49	49	51	**59**	59	60	18,3	18,3	15,0	1,7	1,7
i8	56	57	**58**	57	58	60	6,7	5,0	3,3	5,0	3,3
i9	**60**	**60**	**60**	**60**	60	60	0,0	0,0	0,0	0,0	0,0
i10	**60**	**60**	**60**	**60**	60	60	0,0	0,0	0,0	0,0	0,0
i11	**60**	**60**	58	**60**	60	60	0,0	0,0	3,3	0,0	0,0
i12	55	**60**	**60**	**60**	60	60	8,3	0,0	0,0	0,0	0,0
i13	**76**	71	72	**76**	76	76	0,0	6,6	5,3	0,0	0,0
i14	**76**	**76**	75	**76**	76	76	0,0	0,0	1,3	0,0	0,0
i15	**76**	73	73	**76**	76	76	0,0	3,9	3,9	0,0	0,0
i16	**76**	**76**	**76**	**76**	76	76	0,0	0,0	0,0	0,0	0,0
i17	99	**100**	97	**100**	100	100	1,0	0,0	3,0	0,0	0,0
i18	90	92	90	**100**	100	100	10,0	8,0	10,0	0,0	0,0
i19	85	96	85	**100**	100	100	15,0	4,0	15,0	0,0	0,0
i20	94	97	94	**100**	100	100	6,0	3,0	6,0	0,0	0,0
i21	**100**	**100**	**100**	**100**	100	100	0,0	0,0	0,0	0,0	0,0
i22	99	**100**	**98**	**100**	100	100	1,0	0,0	2,0	0,0	0,0
i23	99	98	**100**	**100**	100	100	1,0	2,0	0,0	0,0	0,0
i24	89	100	91	**100**	100	100	11,0	0,0	9,0	0,0	0,0
i25	170	170	170	**180**	180	180	5,6	5,6	5,6	0,0	0,0
i26	**180**	**180**	**180**	**180**	180	180	0,0	0,0	0,0	0,0	0,0
i27	169	166	170	**180**	180	180	6,1	7,8	5,6	0,0	0,0
i28	167	162	167	**178**	178	180	7,2	10,0	7,2	1,1	1,1
i29	**180**	**180**	**180**	**180**	180	200	10,0	10,0	10,0	10,0	10,0
i30	**200**	199	**200**	**200**	200	200	0,0	0,5	0,0	0,0	0,0
i31	**170**	169	**170**	**170**	170	200	15,0	15,5	15,0	15,0	15,0
i32	178	179	**180**	**180**	180	200	11,0	10,5	10,0	10,0	10,0
					RTnO	**media**	**5,00**	**4,50**	**4,91**	**1,34**	**1,28**

V. CONCLUSION

This work showed that the results obtained with the computational experiments of the genetic algorithm proposed to solve the kidney transplantation problem, suitable for the Brazilian system, were efficient and effective in the search for good quality solutions, when compared to the initial solutions generated for the problem, in the initial population of the method used. The proposed GA behaved very well in response to the problem, and it is clear that its computational implementation is very simple.

After several tests, it was noticed that the crossing operator 2B performed better than the other genetic operators when compared to the objective function and the number of transplants operationalized, followed by the performance of crossing operators 2P, PM and 1P. As for the computational time, the crossing operator PM had more speed in presenting its good solutions than the others, while the operator 1P had the worst performance in the generation of good solutions. This is due to the fact that this operator generates more crossbreeding solutions than the other genetic operators used in our GA.

It is worth noting that, no description of this specific problem has been found in the literature. Given that our problem contemplates a real situation from Brazil. Other structures different from other problems similar to ours were incorporated into the problem such as surgical cost and geographic data containing latitudes and longitudes of patients, donors and hospitals. These values were simulated on the map of Brazil in different Brazilian states. An attempt was made to get closer to reality. In addition, the priority of care that each patient has in the list of patients to be transplanted was also introduced.

Moreover, it was noticed that Brazil, being a continental country, does not have facility of a mobility exchange of donors and recipients to hospitals in order to perform the transplants. This requirement is met in our proposed mathematical model for problem solving and which our problem-solving method has also incorporated.

As future recommendations, it would be very interesting to verify the application of the mathematical model in the instances described in the computational experiments in order to compare with the solutions presented by our genetic algorithm. See the possibility of developing an exact algorithm or apply the Egon Balas algorithm to the problem to know the optimal solutions of each instance. Other recommendations would be to apply GA with *NPOP* = 100, 150 and 200. Use other genetic operators of crossing, mutation and a heuristic to generate the initial population in the genetic algorithm and analyze their performances.

Our next job will be to use the best solution from the GA algorithm and apply it to the TG algorithm, in [24], as an initial solution. Thus, TG accelerates the tree search to determine the optimal solution for the specific problem. In addition, we will also use the SH algorithm, in [25], to populate the initial DGA population and speed up the search for the optimal solution. The DGA was successfully applied to the No-Wait and Permutational Flowshop Scheduling Problem, *cf.* [22, 23].

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