

DECISION ALGORITHM FOR HEURISTIC DONOR-RECIPIENT MATCHING

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Abstract: *This paper introduces the application of artificial intelligence paradigm towards precision medicine in renal transplantation. The match of the optimal donor-recipient pair in kidney transplantation in Latvian Transplant Centre (LTC) has been constrained by the lack of prediction models and algorithms. Consequently, LTC seeks for practical intelligent computing solution to assist the clinical setting decision-makers during their search for the optimal donor-recipient match. Therefore, by optimizing both the donor and recipient profiles, prioritizing importance of the features, and based on greedy algorithm approach, advanced decision algorithm has been created. The strength of proposed algorithm lies in identification of suitable donors for a specific recipient based on evaluation of criteria by points principle. Experimental study demonstrates that the decision algorithm for heuristic donor-recipient matching integrated in machine learning approach improves the ability of optimal allocation of renal in LTC. It is an important step towards personalized medicine in clinical settings.*

Keywords: *machine learning, greedy algorithm, evaluation criteria by points, precision medicine*

1 Introduction

Artificial intelligence (AI) is a general term that implies the use of a computer, techniques and algorithms to control system and model processes with minimal human intervention. Fields that are most notably influenced by AI are computer science, theory of organizations, biology, logistics, manufacturing, security, and medicine and healthcare. In medicine this approach allows physicians and analysts in the clinical setting to predict more accurately which treatment and transplantation strategy for a particular disease or graft will work in which groups of patients. Moreover, artificial neural networks, evolutionary computing, support vector machines, fuzzy and rough sets, integrating into precision medicine approach can be capable to solve many today existing medical and healthcare problems.

According to the [1], precision medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person. Genetic studies associated with multiscale omics datasets from tissue and cell types could offer new avenues for novel diagnostic, prognostic and targeted therapeutics development [2]. In precision medicine, diagnostic testing as well as allocation of organs for transplantation should be employed for selecting suitable and optimal methods based on the framework of a patient's genetic content or other molecular or cellular analysis. Tools engaged in precision medicine can include gene diagnostics, imaging, analytics, and applicable algorithms. For instance, the donor's human leukocyte antigen (HLA) complex is matched to the recipient to reduce the risk of compatibility. Although examples can be found in several areas of medicine, the role of precision medicine in day-to-day healthcare is relatively limited.

There are two main branches of AI in medicine: virtual and physical. The virtual approach encompasses informative approach from machine learning (ML) including health management systems, health records, and active guidance of physician in their treatment decisions [3]. It is well known that there are three types of ML algorithms: (i) supervised (classification and prediction algorithms), (ii) unsupervised (ability to find patterns without external information during its learning process), and (iii) graded or reinforcement learning (give "grade" or "score" for overall performance of its output) [4]. Today, it is considered that knowledge-discovery and decision-making in organ transplantation for creating comprehensive algorithm for intelligent computation in precision medicine consists of two aspects: (i) appearance of the problems to be solved and (ii) on the underlying mechanism for organ transplantation processes. Twisting both assumptions together is a difficult subject without using ML.

There are many examples of the ML methodologies used for medicine and health care. Such examples can include novel adaptive algorithms, evolutionary Markov clustering, genome-wide analysis and more. AI for personal use is going to stay with us as much as genetics will continue to provide personal service. For instance, Kido and Swan [5] evaluated the prediction abilities of 7 ML algorithms: adaboost, deep learning, bagging, CART, neural networks, random forest and support vector shaping the personalized and participative health care of the future. Shaikhina et al. [6] describe ML algorithms to predict successfully biomedical outcomes despite small datasets for biomedical engineering.

This paper is organized as follows: Section 2 describes the organ allocation rules in context of selection and matching of kidney transplantation based on literature review. Section 3 outlines the methodological and mathematical

background and design of decision algorithm for kidney donor-recipient matching. Section 4 shows the experiment study that was performed accordingly to proposed algorithm, with data available in the Latvian Transplant Centre (LTC). Finally, conclusions and future research have been addressed.

2 Organ Allocation Rules

This section contains a brief description of organ allocation systems, emphasized on kidney donor and recipient evaluation and pre-transplantation graft allocation that is currently in use. For kidney allocation, there are different systems of so called allocation criteria systems, established according to the characteristics required for the match between the donor and the recipient. Having known the kidney allocation characteristics, the sequence of importance and weights as an input for intelligence system, the best outcome in terms of donor-recipient matching can be realized.

2.1 Kidney allocation

Recently, there are a number of studies conducted using data-driven analytics on various organ transplantation datasets. A number of authors, generally with mathematical methods, have tried to match the best allocation of the transplant candidates (clinical efficiency), indicating a strong variability in the quality of the datasets and chosen classes for matching. The origin of the data, the number of samples, a few extra features and the chosen outcome make up most of the difference [7]. One of the features in medical care still existing today is the need of intelligent diagnostic tools for transplant specialists to assess donor-recipient matching as well as personalized monitoring of transplant patient. There are systems which mainly focus on selecting recipients for a donor (recipient-donor pair) and systems (applications) for clinical predictive modelling based on statistical approach. Systems, which can function slightly different by requires different MK algorithms which are based on learning methods. Nevertheless, ML algorithms help the transplantation team speeding up their decisions.

Renal transplantation has emerged as the definitive treatment for end-stage renal disease (ESRD) with an increasing waiting list. The expansion of the waiting list over-exceeds the number of available donor organs, contributing to the stress on allocation system. From above it be can reasoned that pre-transplant donor and recipient attributes to which it can be considered as a network to be an objective tool to optimize donor-recipient match. As evidence-based medicine becomes the standard of care, clinicians look toward prognostic tools to assist in decision making. Nomograms, neural networks, and decision trees have become popular transplant methods for creating more objective ways to predict transplant outcomes [8]. Wolfe [9] proposed a conceptual procedure for imputing a recipient's pre-transplant life years by matching his/her medical conditions at the time of kidney offer to a "similar" candidate in the waitlist.

Generally, matching donors to recipients is a two-step process. The first step involves comparing the tissue type of the donor to the recipient. The second step of the process involves a blood type that determines whether the candidate exhibits antibodies to the proteins of the donor. Currently, renal transplantation is allocated based on HLA type matching and time on list, using computational schemes [10]. Another study has been declared a donor's age, and recipient body mass index, gender, race amongst the pretransplant variables with strongest association to outcome. Yahav and Shmel [11] explicated that kidneys are allocated to patients primary through a combination of tissues matching, sensitization level, the level of sensitization to donor antigens, measured by Panel Reactive Antibody (PRA), and waiting time. Salvioli [12] noted ABO blood group, HLA, PRA have been identified as having a greater influence on the immune response, the closer the match, the lower the likelihood of rejection of the graft [13]. In general, due to recent trends in medicine, shortfall of kidney supply, some systems do better, but some systems fail to match donors and recipients well.

Today more and more ML can enable the development of predictive models that incorporate multiple variables for a system approach to organ allocation. Brown et al. [14] reported the principle of Bayesian Belief Network (BBN) to determine whether a predictive model of graft survival can be derived using pre-transplant variables. Briceno et al. [15] reported the use of ANN for donor-recipient matching by using the Neural Net Evolutionary Programming algorithm.

2.2 Selection of Donor-Recipient Candidates

The donor-recipient selection and matching for renal transplantation are complicated problem that require expert decisions. Finding a good donor is not a straightforward task because a complex network of relations exists between the immunological, demographic and physiological features that influence the recipient's acceptance of the transplanted organ. It is therefore necessary to find a donor who has the highest possible compatibility with recipient, and thus reduce rejection. It is identified that the kidney allocation problem is the trade-of between clinical efficiency and equity. The allocation systems available today focus on to determine action of suitable kidney for recipient. It is important to select the authentic donor with recipient, find matched donor-recipient kidney specification.

There are different kidney allocation systems, policies and simulators worldwide which are based on different methods and point systems. For instance, the European Best Practice Guideline group has been issued guidelines on the evaluation and selection of kidney donor and recipient transplantation candidates, United Network of Organ Sharing point system, Kidney Allocation Score. The Kidney-Pancreas Simulated Allocation Model (KPSAM) simulator,

developed by Scientific Registry of Transplant Recipients, for simulating the allocation of organs to waitlist candidates accordingly to the current Priority Points allocation policy. KPSAM is based on even-sequence Monte Carlo technique.

In the proposed donor-kidney matching virtual medical expert model the algorithm has been considered by: (i) LTC guidelines [16], (ii) the careful study by clinical transplant team (expert knowledge) of the LTC, (iii) ML and precision medicine approach. Virtual medical expert algorithm was created by taken into consideration those attributes which the most influenced the donor-recipient candidates. It is also based on paired matching principles and priority setting.

3 Donor-Recipient Algorithm Design

Section 3 outlines methodological and mathematical aspects as the platform for proposed decision algorithm. Using multi attribute decision making methodology is the best possible way to recognize the donor-recipient matching process. From the mathematical point of view the principle of similarity has been applied, but the logic of intelligent algorithm is based on evaluation of criteria by points.

3.1 Methodological and Mathematical Aspects

ML technologies have become one of the major factors influencing the decision-making process in medicine in a global context. The types of decisions facing donor-recipient matching problem vary considerably from structural, repetitive to non-routine, unstructural. Data mining and AI technique are essential tools for identifying the trends and evaluations. It means to consider the best kidney allocation process management notation for LTC.

Multi criteria decision analysis (MCDA) provides the foundation for making such evaluations in decision-making. The idea behind MCDA is that the problem has been divided into smaller parts, analysed each part and integrating parts to provide logical, consistent decision [17]. It is known that MCDA can be classified into two main categories: (i) multi objective decision making (MODM) and (ii) multi attribute decision making (MADM). There are several methods in each category. For both categories the common ground is mathematical techniques, focus on a list of chosen criteria, its parameters and attributes which one wishes to examine in the decision making process. Based on medical experts conclusion for donor-recipient matching the MADM has been chosen as a platform for creating proposed algorithm.

From a mathematical point of view, a kidney allocation problem consists of a finding the kidney of the donor which is compatible to the recipient, and this can be done through a priority mechanism. A kidney allocation problem can be modelled through undirected graph, where each node indicates a compatible donor-recipient pair or indicates an incompatible donor-recipient pair from the patient pool.

The assumptions for decision making on creating the algorithm for heuristic donor-recipient match is based on the following: (i) the matching process can involve only one pair (pair matching), one from donor set and another from recipient set; (ii) the matching process should include symmetry assumption; (iii) compatibility of the pair can be considered by using preference relation based on matching point system, and (iv) overall ranking of the recipients candidates are made for the donor by applying MADM process.

The kidney allocation intelligent system means a computational system capable of dealing with several forms of reasoning. It is clear that such system should be also equipped to represent knowledge. As a result, evaluation of criteria by points and mathematical logic has led to solve the donor kidney allocation matching problem.

3.2 Donor-Recipient Algorithm design

The problem of matching has been studied under various topics including microsimulation modelling, entity resolution [18], record detection [19], record linkage [20], etc.

The proposed matching algorithms is based on understanding the donor and recipient compatibility using pair matching. We assumed that there is a matching pool of patients P , where the argument P_i is the total number of all patients:

$$P = \sum_{i=1}^N P_i, \tag{1}$$

The pool P is matched into pairs or we deal with an even numbers. The patients are divided into N categories on the basis of factors ABO Blood type, crossmatch, HLA, age, etc. The number of selections into one category or between different categories can be expected rather large. Thus, based on equation (1) our aim is to find the real numbers $x_{i,k}$ ($i = \overline{1, n}, k = \overline{1, n}$) such that:

$$\sum_{i=1}^n x_{ik} = P_k, k = 1, \dots, n, \tag{2}$$

where

$$x_{ik} = x_{ki}, i = 1, \dots, n, k = 1, \dots, n. \quad (3)$$

As a result (Equations 2, 3), the symmetry assumption has been defined. The variable x_{ik} indicates the number of patients of category i that are paired with patients of type k , and vice versa. If a patient of category i is paired with a patient of type k then there is the opposite also, patient of category k is paired with a patient of category i .

After we declared the assumption of symmetry the next step must be the donor-recipient candidates selection. We have two datasets D of donor data and R of recipient data, represented as structural records. Structural records of $d \in D$ and $r \in R$ consists of the same category C and attributes a . The attributes can be numerical or categorical. The objective is to match d to one or more structured records in R . Each $d \in D$ has been matched to one structural record in $r \in R$, creating a matched dataset M^+ Dataset M^- provides mismatched records of every $d \in D$.

Another objective of matching is to match the specific donor, d_i to the specific recipient, r_k that has the largest matching points. To obtain the best candidate, the recipient needs to agree with the donor, especially on the value of the attributes that contribute large points to the matching function. It means, further reduce the candidate set by identifying those top pointed attributes that can potentially give matching points. The maximum matching point system p^{max} approach has been taken to find the optimal recipient $r \in R$ that has the largest points of match to given donor offer, d . Each attribute a has k_a values, then there is $\prod_a k_a$ logical useful match in the donor offer. When donor d_i is paired with the recipient r_k , we determine the maximal number of attributes and their corresponding points of d_i in which the maximum number of attributes and their corresponding points agree in their values with r_k . This is the case of optimal match. Generally, optimal definition of the donor with respect to the recipient $T_{d,r}$ can be defined:

$$T_{d,r} = \{(a_n, p_n) \in T_d \text{ AND } ((a_n, p_n) \in T_r \text{ AND } a \text{ is numeric OR } r.point(a_i) > \lambda)\}, \quad (4)$$

where $r.point(a_i)$ is the points of attribute a_i in recipient r , and λ the threshold level for transplantation.

We can mark those attribute (name, points) pairs, a_n, p_n in d that match with attribute (name, points) pairs in r , we also retain those attribute (name, points) pairs for which there is no corresponding pair in r . The similarity between donor and recipient is characterized by the values of the attributes present in them. Let $T_{d,r}$ produce the optimal match of donor d_i with respect to recipient r_k . As a result, for the pair d_i, r_k the similarity feature vector \mathbf{f} can be calculated by considering similarity levels based on point system between d_i and r_j for each attribute $a_i \in A$, where A is set of all attributes. Therefore, form methodological and mathematical assumptions the algorithm for heuristic donor-recipient matching is following, see below.

Algorithm Heuristic Donor-Recipient Matching

Input:

$D = \{d_1, \dots, d_n\}$ – a set of donors.

$R = \{r_1, \dots, r_m\}$ – a set of recipients.

Definition:

$C = \{C_1 \dots C_i\}$ – a set of categories.

$C_q = \{c_{1i}, \dots, c_{qi}\}$ – a category attribute set.

P – matching point system.

$M^+ = \{(d_i, r_k)\}_{i=1}^N, (d_i \in \mathcal{D}, r_k \in \mathcal{R})$ – pairs of matched records, one for every d_i .

$M^- = \{(d_i, r_k)\}_{i=1}^N, (d_i \in \mathcal{D}, r_k \in \mathcal{R})$ – pairs of mismatched records.

Output:

r^* - best matching recipient $r \in R$.

$d \Leftarrow$ optimal match attributes with largest points.

Blocking:

$a_i \Leftarrow$ attributes with largest points.

$R^* \Leftarrow$ subset of R with $\cup_i (d.points(a_i)) = (r.points(a_i))$

for all $r_i \in R^*$ do

P (match(r_i, d_i)) = best matching score of a pair.

end for

Return: $r^* \arg \max_{r_i} p(\text{match}(d, r))$ best matching point score of all pairs.

For evaluation purposes of proposed decision algorithm the test set of recipients, $r \in T_R$ and the test set of donors, $d \in T_D$ has been accessed. The best matched pair mean that there is no other r that can match d with a higher matching points. We require the match points to be at least some $\lambda \in [\min_{match}, \max_{match}]$. The system has no knowledge about the medical features, but instead predicts the best matched recipient r^* with the sum of points p^* for every donor d . We define precision (5) and recall (6) at threshold level λ :

$$\text{Precision}(\lambda) = \frac{\sum_{d \in D} I[(p^* > \lambda) \text{ AND } (r^* = r)]}{\sum_{d \in D} I[p^* > \lambda]}, \tag{5}$$

$$\text{Recall}(\lambda) = \frac{\sum_{d \in D} I[(p^* > \lambda) \text{ AND } (r^* = r)]}{|T|}, \tag{6}$$

where $I[x]$ is the indicator function. Combining precision and recall we can get balanced F-score (7), as following:

$$F(\lambda) = \frac{2 \text{ precision}(\lambda) \text{ recall}(\lambda)}{\text{precision}(\lambda) + \text{recall}(\lambda)} \tag{7}$$

The precision and recall values should be calculated for deployed categories. To better evaluate categories and attributes within category which have been exhibited by the proposed algorithm the transplantation matrix and the transplantation match graphics have been offered for transplantation team for the decision-making. The commitment of the evaluation of the proposed greedy algorithm was realized through practical experimental study by matching the donors' kidney to recipients at LTC.

4 Experimental Study

The first kidney transplant operation was performed in world in 1954, but in Latvia at the end of 2013 there were done 1724 kidney transplantations [16]. Donors and recipients data were obtained from the LTC database using all the features available at the time of allocation. An algorithm was developed to simulate the matching of the two different datasets as the input. The recipient dataset was on the day of testing comprised of 57 patients, who are ESRD's. There were 5 donors available on the moment of the testing.

A. Definition of donor-recipient categories

Generation the initial configurations, i.e. identification of donor-recipient attributes is the first matching step in the environmental donor-recipient assessment of compatibility. In accordance with expertise as well as with combination of existing data, 9 attributes have been defined. These are the major attributes affected the donor graft to be chosen for recipient. The attributes may also be divided into four categories. All the attributes are designed and presented in Table 1, where the categories of attributes are designed as $C = \{C_1, C_2, C_3, C_4\}$, where C_1 represents a category of immunology, C_2 – demography, C_3 – physiology, C_4 – relevant category. Each category of the above 4 categories also represents one category attribute set.

B. Definition of matching point system

The matching point system based on evaluation of kidney transplantation experts for the category of immunology see Table 1:

Table 1: Matching point system for the category of immunology.

Attribute type	Data profile	Matching Points
ABO Blood Type, ABO	R profile D profile	100 points for identical blood type; 25 points for compatible blood type; 0 points mismatch, => no transplantation.
Crossmatching, Crossmatch	R profile D profile	50 points for negative test; 0 points for positive test => no transplantation.
HLA, HLA	R profile D profile	50 + 50 points if DR1 and DR2 matches; 50 points if one DR1 or DR1 matches; 40 + 40 points if DQ1 and DQ2 matches; 40 points if DQ1 or DQ2 matches; 20 + 20 points if A1 and A2 matches; 20 points if A1 or A2 matches; 20 + 20 points if B1 and B2 matches; 20 points if B1 or B2 matches; 5 + 5 points if Cw1 and Cw2 matches; 5 points if Cw1 or Cw2 matches; no match 0 points.
Antibodies, Anti	R profile	50 x 5 = 250 points, if 80-100% and crossmatching test negative (CMTN); 50 x 4 = 200 points, if 50-79% and CMTN; 50 x 3 = 150 points, if 40-49% and CMNT; 50 x 2 = 100 points, if 20-39% and CMNT; <20% = 50 points.
Children, Ch	R profile	<15 age => priority; >15 age => continue.
Age difference, AD	R profile D profile	<5 years, 50 points; 5 to 10 years, 40 points; 10 to 20 years, 20 points; 20 to 30 years, 10 points; > 30 years => no transplantation.
Weight difference,	R profile	+/- 10 kg, 50 points; +/- 20 kg,

WD	D profile	25 points; +/- 30 kg, 0 points.
Waiting time, WT	R profile	<1 year, 0 points; 2 years, 25 points; 3 years, 35 points; >3 years, 50 points.
	R profile	
Ischemia time, Isch	R profile	8/16/24 hours => transplantation; >30 hours =>no transplantation.

As was mentioned before the population is divided into 4 distinct categories based on immunological (ABO Blood Type, crossmatching, HLA, antibodies), demographic (age difference, children,), physiological (weight difference), and relevant category (waiting time, ischemia).

C. Donor-recipient matching process for transplantation

The donor-recipient matching for transplantation is eight step hierarchy process and shown schematically in Figure 1.

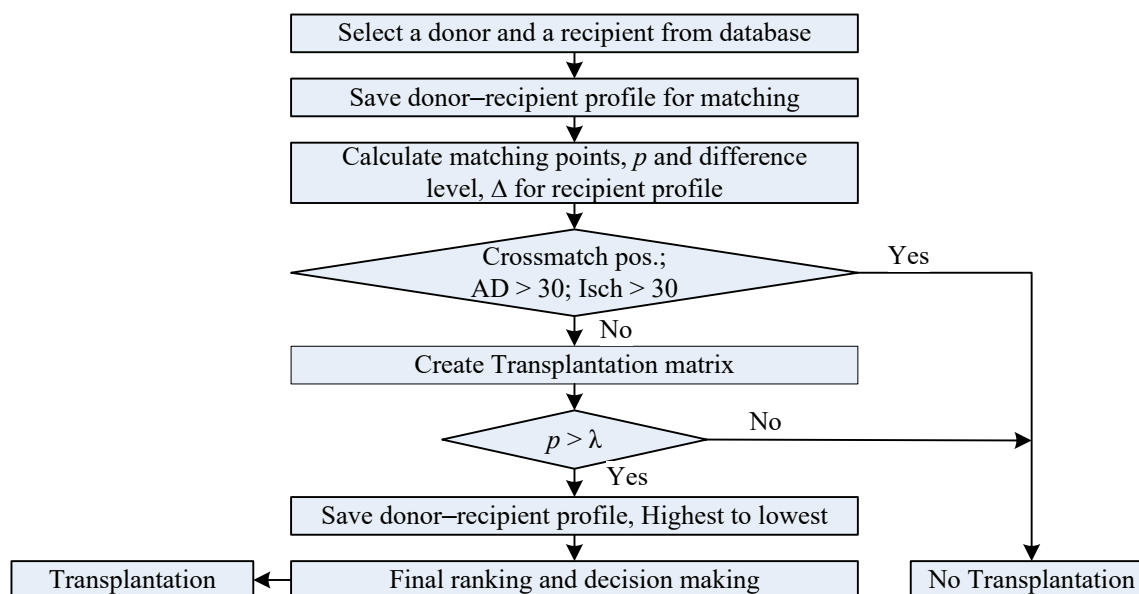


Figure 1: Donor-recipient matching process for transplantation or no transplantation.

The process of making a transplantation decision on donor-recipient match tasks can be performed by separating and structuring tasks into many simple tasks, displaying them in the form of hierarchy structure. The proposed algorithm works on the premise of this assumption.

D. Point calculation and image for donor-recipient match

Applying proposed decision algorithm, the transplantation team for decision-making can get and evaluate from the system's transplantation matrix donor-recipient matching results. For each donor-recipient pair accordingly to the point system and ranged highest to lowest the matching result has been presented.

Below, Table 2 represents two matched records, where abbreviation Donor_W_D2 means identification number (ID), where W means woman, M man, D donor, R recipient, the last numbers in ID means unique number. The first example shows the transplantation T1 matching results, where donor W_D1 who is woman best matches with woman recipient, ID number from recipient dataset W_R16. Another example on the same Table 2 represents another transplantation T2, where donor is man, ID M_1D, who best matches with recipient woman, ID W_R34.

Table 2: Transplantation matrix.

Transpl_T1	ABO	Crossm	HLA	Anti	Ch	AD	WD	WT	Isch	Pt.
Donor_W_D1	100	100	270	250		50	50	50		
Recipient_W_R16	100	100	125	200	cont.	50	50	25	tr.	650/74,7%
Transpl_T2	ABO	Crossm	HLA	Anti	Ch	AD	WD	WT	Isch	
Donor_M_D2	100	100	270	250		50	50	50		
Recipient_W_R34	100	100	155	100	cont.	20	25	50	tr.	550/63.2%

Together with the given matched points for the better interpretation the transplantation graphs for decision-making has been presented. The graph shows the two curves one for donor, another for recipient with the match scores.

For the transplantation T₁, see Figure 3, matches ABO Blood Type, crossmatch is positive, there is not the age difference and the weight difference. There is a difference of 145 points for HLA, 50 points for antibodies and 25 points of the waiting time match comparing with donor.

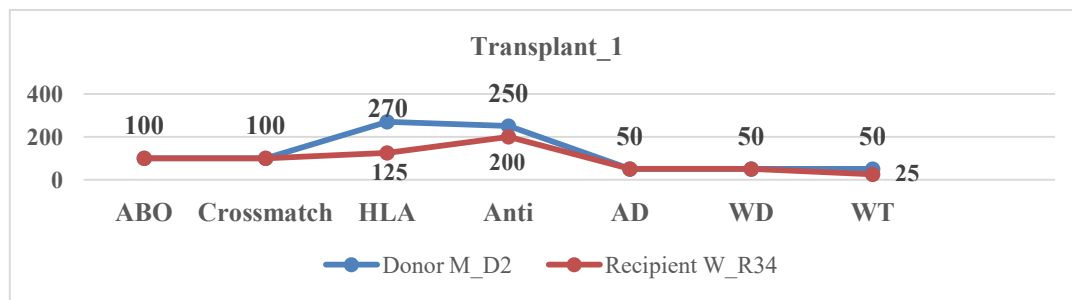


Figure 3: The transplantation T₁ donor-recipient match graph.

Second example transplantation T₂, see Figure 4, optimal match refer to ABO Blood Type, crossmatch is positive and waiting time. There is a difference of 115 points for HLA, 150 for the antibodies, 30 of the age difference and 25 of the weight difference comparing with donor.

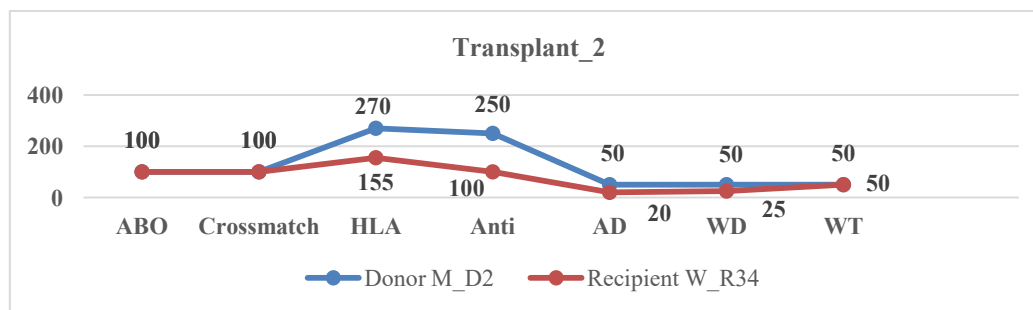


Figure 4: The transplantation T₂ donor-recipient match graph.

Experimental study proves that the proposed algorithm based on evaluation of criteria by points principle can selected donor-recipient pairs, evaluate donor-recipient pair match and rank them accordingly to allocated match points. Along with transplantation graphs proposed intelligent computing system can help transplantation team carry out comprehensive decision-making for the best renal allocation.

5 Conclusions and Future Work

This paper presents a multi-attribute decision algorithm using for donor-recipient match for LTC for the kidney transplantation based on national level medical experts' conclusions. This is the first step towards integration of ML techniques within precision medicine approach for clinical settings for LTC.

Proposed algorithm offers a practical way to make knowledgeable decisions by predicting likely outcomes from donor-recipient match for the kidney allocation. The strength of algorithm lies the identification of optimal or transplantation and even more important unsuitable donors or no transplantation for a specific respondent. It has been hypothesis that the proposed algorithm of matching may have potential to save more than 30% of grafts that fail within their first year.

On the basis of expert evaluation and case based reasoning and rule identification by transplant team expertise, 9 attributes within 4 categories have been identified, which effect the overall donor-recipient match. The hierarchy and patterns among attributes have been determined on the basis of comprehensive matching point system. A comprehensive decision has been assign the donor's kidney to the specific candidate on the waiting list. The new algorithm considers not only the best candidate on the waiting list, but also all the range of other candidates for receiving the kidney.

This new algorithm helps medical experts of LTC as well as other clinics to objectively decide which potential recipient should receive the kidney accordingly to offer of donor. Nevertheless, despite the proposed new decision algorithm, physicians for renal transplantation of LTC should make the final decision before the transplantation. The reason is to assign kidney to the recipient considered to have the most promising prognosis.

Ideally, kidney allocation should take into account not only donor-recipient matching, but also the potential outcome in terms of transplant success, post-transplant lifetime, potential remaining lifetime without a transplant, as well as kidney exchange program.

Finally, proposed algorithm shows strong potential to enhance the prediction of recipient survival and to identify important attributes that have an impact on individual. Future studies, should include more donor attributes, e.g. genomic, proteomic, to increase the better match. Kidney allocation should also follow the concept of survival and avoiding human-innate subjectivity. It is planned to investigate and to compare based on proposed decision algorithm various studies of neural networks, i.e., Kohonen net and genetic programming to predict transplant outcomes. It would be possible to consider their differences, highlight critical situations, and offer for LTC more in-depth and complete system where, so called “virtual medical expert” can be created, for which they are looking for.

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