The Spanish kidney exchange model: study of computation-based alternatives to the current procedure

Miquel Bofill[1], Marcos Calderón[3], Francesc Castro[1], Esteve Del Acebo[1], Pablo Delgado[2], Marc Garcia[1], Marta García[2], Marc Roig[1], María O. Valentín[2], and Mateu Villaret[1]

[1] Departament d'Informàtica, Matemàtica Aplicada i Estadística
Universitat de Girona, Girona (Spain)
[2] Organización Nacional de Trasplantes, Madrid (Spain)
[3] TAISA, Pozuelo de Alarcón (Spain)

Abstract. The problem of incompatible pairs in living-donor kidney transplant can be solved using paired kidney exchange, i.e., two incompatible patient-donor pairs interchange donors, creating a cycle, which can be extended to three or even more pairs. Finding a set of cycles that maximizes the number of successful transplants is a complex task.
The Organización Nacional de Trasplantes (ONT) is responsible for donation and transplantation processes in Spain. In this paper we compare the current ONT heuristic finding-cycles procedure with an integer programming approach by means of a true-data-based empirical simulation. The obtained results show that, although the two methods provide quite different solutions, they both exhibit weak and strong points.

1 Introduction and previous work

Living-donor kidney transplant is, nowadays, the treatment of choice for patients with end-stage renal disease. However, in over 30% of the cases, the living donor is incompatible with his/her intended recipient[1]. The nation-wide Kidney Paired Donation (KPD) programs allow incompatible pairs to be added to a pool in which patients can exchange their donors, resulting in transplant cycles. Solving this Kidney Exchange Problem (KEP), i.e., finding, from this pool, an optimal set of disjoint transplant cycles is a computationally hard task [2].

Two important problems arise in KPD programs: (i) Scheduled transplantation cycles do not proceed in all cases because of last-moment-detected compatibility problems, donor backing out, etc; (ii) it is not easy to find a compatible donor for high-sensitized patients, who tend to remain in the pool for a long period.

A collaboration has started between the Spanish Government-dependent *Organización Nacional de Trasplantes* (ONT) and Computer Science researchers from the University of Girona (UdG). From this collaboration, in this paper we compare two different procedures intended to obtain an appropriate set of transplant cycles from a pool of patient-donor pairs. The first procedure is the one currently used by the ONT, a greedy algorithm that prioritizes cycles of length 2 (2-cycles), since they have a lower probability of failure, and repairable cycles of length 3 (3-cycles), i.e. 3-cycles with some 2-cycle embedded. The second procedure is an Integer Programming (IP)-based one which guarantees the optimal solution in the number of proposed transplants, but may have scalability issues. We can find several IP-based approaches in the literature [3,4,5].

To support this comparison, we provide a long-run simulation of the activity of a living-donor transplant pool, taking into account cycle failures, cycle repairs in case of failures, entrances and releases of patients to/from the pool, etc. This pool is based on data provided by the ONT.

2 Problem definition and formulation

Traditionally, modeling of the KEP has departed from transplant graphs [2,3] defined by a set of vertices representing donor-recipient incompatible pairs and a set of weighted directed arcs representing compatibilities. The weight of each arc represents the utility of the transplant, defined by a team of medical specialists. A N-way kidney exchange corresponds, then, to a cycle of length N in the transplant graph. The Kidney Exchange Problem (KEP) can be defined as that of finding a maximum weight set of vertex-disjoint cycles having length at most k [3].

The KEP has been proved to be NP-Hard whenever cycles of length greater than two are allowed [2]. This makes it very reasonable to explore the utilization of both exact and heuristic methods to solve it, especially if the possibility of transplant failures need to be taken into account.

3 Description of both approaches

Our simulation compares two approaches to the KEP. The first one, based on Integer Programming, corresponds to the well-known cycle formulation [6], which was also used in [7] to solve the KEP in the UK. The second approach reproduces closely the heuristic method used by the ONT. It is a relatively simple three-step heuristic greedy algorithm which looks for good-enough solutions in an incremental way. Its main features are:

- It gives preference to 2-cycles over 3-cycles, when possible.
- It gives preference to cycles containing high weight transplants.
- It tries to include robust cycles in the solution. Robust cycles are those that have chances to be partially repaired with an embedded cycle if a failure arises during the solution's realization.

The heuristic method input is the set of vertices and the list C of all available cycles built by concatenating the list of all the 3-cycles at the end of the list of all the 2-cycles, both lists being ordered decreasingly by weight. It proceeds by selecting the cycle f in the first position of C, adding it to the solution S and removing from the list C all the cycles which are non-vertex-disjoint with f, repeating these operations until no cycles remain in C. This step of the algorithm gives preference to 2-cycles over 3-cycles (we incorporate them to the solution earlier) and to high-weighted cycles (they appear before in the list). The second step of the algorithm tries to convert 2-cycles to 3-cycles by selecting 2-cycles in the solution and looking for a non-assigned vertex able to be combined with the 2-cycle to form a 3-cycle. The third and last step looks for 3-cycles that can be decomposed into two 2-cycles by using an unassigned vertex.

When implementing the scheduled cycles, it is frequent that the *a priori* realizable transplants turn out to be unfeasible due to unforeseen causes. The ONT copes with the problem by preserving the cycles that do no present any failure and trying to find new cycles for the patients whose cycle is broken, which is done by running again the algorithm considering only the cycles where those patients appear. This reparation policy is also used, for the sake of fairness, in the IP-based approach. Notice that the ONT reparation procedure may take advantage of having chosen repairable 3-cycles (3-cycles containing embedded 2-cycles) in the second step of the heuristic algorithm (see 3),

4 Simulation description and results

We have aimed at comparing the ONT heuristic procedure and the IP-based approach. In this sense, We have simulated the evolution of a pool of patients where the best possible cycles are selected and implemented every three months, considering the reparation step described in the previous section. For the sake of realism (i) we allow a number of new patients to enter the pool between each cycle selection, (ii) we consider patient withdrawal (due to several reasons), and (iii) we take into account two failure probabilities:

1. Probability p_c of positive crossmatch, which depends (see [8]) on the patient's PRA and a probability variation δ_p which is specific for each of the scenarios described later.
2. Probability p_f of failure of patient/related donor.

We have considered the following 3 scenarios in our simulation: (1) $\delta_p = p_f = 0.0$; (2): $\delta_p = 0.1$ and $p_f = 0.05$; (3): $\delta_p = 0.2$ and $p_f = 0.1$. Such scenarios have been chosen according to the guidelines in the work of Bray et al. [8].

In the simulation procedure we have fixed a number of iterations (100 for the results presented below). For each iteration, a number of real-data-based pairs (50) are added to the pool, and next all the 2 and 3-cycles a priori feasible are generated. At this point, a set of cycles for transplantation is computed using each of the two approaches in 3. Then, transplants in the cycles are simulated and failed transplants are tried to be repaired. Finally, successfully transplanted patients are removed from the pool, and, before the new iteration, some of the remaining patients are also removed in order to simulate patient withdrawn (due to patient death or transplant obtained by another way). The experiment has been performed on 8GB Intel Xeon E3-1220v2 machines at 3.10 GHz. 10 independent runs have been performed for each approach and scenario, and their results have been averaged to reduce the randomness effect.

First of all we consider the number of cycles and successfully transplanted patients, as well as the size of such cycles. As we can see in Table 1, the number of performed cycles is slightly superior for the ONT method. This is mainly due to the fact that this approach schedules many more 2-cycles (and less 3-cycles) than the IP-based approach (see Table 1). This is a positive aspect for the ONT method in the sense that 2-cycles are less prone to fail.

Table 1. Theoretic number of cycles successfully performed and the resulting transplanted patients

Scenario	Total cycles		2-cycles		3-cycles		Transplants	
	IP	**ONT**	**IP**	**ONT**	**IP**	**ONT**	**IP**	**ONT**
1	360.3	370.1	84.7	158	275.6	212.1	996.2	952.3
2	343.9	356.7	83,1	159.4	260.8	197.3	948.6	910.7
3	324.9	336.5	76.3	152.1	248.6	184.4	898.4	857.4

In spite of that, we can also see that the number of transplanted patients in the IP-based approach is slightly superior in comparison with the ONT method. This is caused by the bigger amount of successful 3-cycles. This positive aspect for the IP-based approach is rather foreseeable, since it is just intended to maximize the number of proposed transplants.

We have also considered the stress put on the patients due to last-minute transplant failures. In Table 2 we show the evolution over the iterations of the number of times a patient has been selected for a transplant which at the end has not been performed. We can see in this table that this patient-demoralizing circumstance is noticeably more frequent in the IP-based approach than in the ONT approach, especially in the most pessimistic scenario.

Table 2. Evolution over the iterations of the number of times patients have been promised a finally undone transplant

Scenario	25 iterations		50 iterations		75 iterations		100 iterations	
	IP	**ONT**	**IP**	**ONT**	**IP**	**ONT**	**IP**	**ONT**
1	116.1	96.8	239	213.5	359.8	321.2	489.9	430.4
2	274.2	233.1	596.1	490.2	875.8	735.5	1170.2	1006.7
3	534.8	409.6	1194.4	959.6	1800.1	1482	2411.5	1981.5

With respect to the average waiting time in the pool, the experiments have shown very similar results for both approaches, with an slight edge in favor of the heuristic algorithm. It is worth to mention that both methods offer an acceptable computing time. In particular, a run involving 750 patients and about 100000 precomputed cycles takes less than one second for both algorithms. It will be interesting in the future to compare their scalability with respect to larger sets of patient/donor pairs and/or higher sized cycles.

5 Conclusions and future work

We provide an empirical comparison between the ONT algorithm for KEP solving and a classical IP approach. Results show that both of them have strong and weak points. On the one hand, the ONT algorithm performs better in avoiding patient stress due to last-minute failures of scheduled transplants, and in favouring 2-cycles in front of 3-cycles. On the other hand, the IP approach is slightly better regarding the actual number of transplants, while the average waiting time in the pool shows no significant differences between both approaches. The simulation computing time is similar for both methods; nevertheless, we left as future work the scalability comparison of the methods, an issue that could be interesting to study in face of a possible international kidney exchange network.

There are other possible lines of future research. On the one hand, the study of new algorithms that embrace the strong points of both approaches; in this sense, the method proposed in [4] for the UK KPD program could be a good starting point. On the other hand, we aim at extending this algorithm to consider together both cycles and altruistic-donor-based chains.

Acknowledgements

Work partially supported by grants TIN2015-66293-R (MINECO/FEDER, UE), TIN2016-75866-C3-3-R, TIN2013-48040-R and MPCUdG2016/055 (UdG).

References

1. Segev, D.L., Gentry, S.E., Warren, D.S., Reeb, B., Montgomery, R.A.: Kidney paired donation and optimizing the use of live donor organs. Jama **293**(15) (2005) 1883–1890
2. Abraham, D.J., Blum, A., Sandholm, T.: Clearing algorithms for barter exchange markets: Enabling nationwide kidney exchanges. In: Proceedings of the 8th ACM Conference on Electronic Commerce, New York, NY, USA, ACM (2007) 295–304
3. Constantino, M., Klimentova, X., Viana, A., Rais, A.: New insights on integer-programming models for the kidney exchange problem. European Journal of Operational Research **231**(1) (2013) 57 – 68
4. Manlove, D.F., O'malley, G.: Paired and altruistic kidney donation in the uk: Algorithms and experimentation. J. Exp. Algorithmics **19** (2015) 2.6:1–2.6:21
5. Klimentova, X., Pedrosa, J., Viana, A.: Maximising expectation of the number of transplants in kidney exchange programmes. Computers and Operations Research **73** (2016) 1–11
6. Roth, A.E., Sönmez, T., Ünver, M.U.: Efficient kidney exchange: Coincidence of wants in markets with compatibility-based preferences. The American Economic Review **97**(3) (2007) 828–851
7. Manlove, D.F., O'Malley, G.: Paired and Altruistic Kidney Donation in the UK: Algorithms and Experimentation. In: Experimental Algorithms: 11th International Symposium, SEA 2012, Bordeaux, France, June 7-9, 2012. Proceedings. Springer Berlin Heidelberg (2012) 271–282
8. Bray, M., Wang, W., Song, P.X.K., Leichtman, A.B., Rees, M.A., Ashby, V.B., Eikstadt, R., Goulding, A., Kalbfleisch, J.D.: Planning for uncertainty and fallbacks can increase the number of transplants in a kidney-paired donation program. American Journal of Transplantation **15**(10) (2015) 2636–2645