Increasing the Opportunity of Live Kidney Donation by Matching for Two and Three Way Exchanges

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Abstract:

Background: To expand the opportunity for paired live donor kidney transplantation, computerized matching algorithms have been designed to identify maximal sets of compatible donor/recipient pairs from a registry of incompatible pairs submitted as candidates for transplantation.

Methods: Demographic data of patients who had been evaluated for live donor kidney transplantation but found to be incompatible with their potential donor (because of ABO blood group or positive crossmatch) were submitted for computer analysis and matching. Data included ABO and HLA types of donor and recipient, %PRA and specificity of recipient alloantibody, donor/recipient relationship, and the reason the donor was incompatible. The data set used for the initial simulation included 29 patients with one donor each and 16 patients with multiple donors for a total of 45 patients and 68 donor/patient pairs. In addition, a simulation based on OPTN/SRTR data was used to further assess the practical importance of multiple exchange combinations.

Results: If only exchanges involving two patient-donor pairs were allowed, a maximum of 8 patient-donor pairs in the data set could exchange kidneys. If 3-way exchanges were also allowed, a maximum of 11 pairs could exchange kidneys. Simulations with OPTN/SRTR data demonstrate that the increase in the number of potential transplants if 3-way exchanges are allowed is robust, and does not depend on the particular patients in our sample.

Conclusions: A computerized matching protocol can be used to identify donor/recipient pairs from a registry of incompatible pairs who can potentially enter into donor exchanges that otherwise would not readily occur.

Introduction:

The live unrelated donor has become a major source of kidneys for transplantation. In 2003, more that 30% of live kidney donors in the United States were biologically unrelated to their recipient (1). The survival rate of a kidney transplant from an unrelated donor is now known to be excellent, with a 10 year survival equivalent to a kidney transplant from a sibling haploidentical to the recipient. (2).

Nevertheless, some potential kidney transplant recipients cannot identify a compatible donor within family or friendships because of an ABO blood type or crossmatch incompatibility. Although these immunologic obstacles have been overcome in some instances by desensitization protocols, these protocols have not been widely adopted because of the cost of their administration and the uncertain possibility of rejection (3, 4). Thus, some regions of the country have initiated ad hoc programs of paired live kidney donation between incompatible donor/recipient pairs so that transplantation could still be accomplished (5). These paired live donor transplants have been well received by the patients and centers, as they provide an opportunity for transplantation that otherwise would not be possible. However, paired donation is not being performed frequently because a systematic approach has not been developed to identify a sufficient number of incompatible pairs who can undergo simultaneous transplantation.

To expand the opportunity for paired donation, computerized matching algorithms were designed to identify maximal sets of compatible donor/recipient pairs from a registry of incompatible pairs submitted as candidates for live donor kidney transplantation (6, 7, 8). We report here on the effectiveness of the program by means of a simulation based on actual patient data. In addition, simulations based on Organ Procurement and Transplantation Network and Scientific Registry of Transplant Recipients (OPTN/SRTR) data have been used to further assess the practical importance of multiple exchange combinations. The subsequent simulations with OPTN/SRTR data demonstrate that the results are not dependent on special features of this patient population.

Methods:

I. Simulation with Local Patient Data

Demographic data of patients who had been evaluated for live donor kidney transplantation but found to be incompatible with their potential donor (because of ABO blood group or a

positive crossmatch) were submitted for computer analysis and matching. These entry data included the ABO blood type and HLA specificity of the donor and recipient, the %PRA (panel reactivity antibody) and specificity of recipient alloantibody (class I and II), the donor/recipient relationship (friend, spouse or other family member), and the reason the donor was previously determined to be incompatible. The HLA profile included the HLA-A, B, Bw4/6, DR, DQ and DR51/52/53 antigen types of both donors and recipients.

HLA antibodies

Recipient alloantibody specificities against antigens encoded at the same loci (A, B etc.) were determined. If antibody specificity could not be accurately determined due to a very high PRA, then "safe antigens" (i.e. those that were consistently negative in antibody screens) were included. Cw locus antigen types were not available for all potential recipients or incompatible donors; however, there was no patient with Cw locus specific reactivity.

Class II PRAs had not been determined for some patients prior to simulation. If the patient was otherwise unsensitized (n=10), the class II PRA was assumed to be 0%. If the patient had class I antibody and previous donor(s) HLA types were known (n=2), their previously mismatched class II antigens and any related split antigens were included as antibody specificities. If the patient had class I antibody and previous donor HLA types were not known (n=2), only self HLA class II antigens were considered to be safe.

HLA antigen assignments

There were 68 donor recipient pairs submitted for the simulation. In some instances there was more than one donor for a particular recipient (n=16). However, complete HLA entry data was not available on all of the submitted pairs (n= 35). Some donor workups were discontinued once an incompatibility was identified. In these cases, HLA-A, B and DR antigens were "assigned" to the incompatible donor, using HLA phenotypes from a list of deceased donors obtained from the United Network for Organ Sharing (UNOS). Since HLA-Bw4/6, DR51/52/53 and DQ antigens were not included in the UNOS donor list, these antigens were assigned based on the most common associations with the HLA-B and DR antigens of that donor. Assignments were made as follows:

Incompatible unrelated donors (spouse or friend) with incomplete HLA typing data (n=16) were assigned the same HLA phenotype as the first deceased donor in the UNOS donor list with the same ABO blood group (and race if known) as the incompatible unrelated donor.

Incompatible sibling donors with incomplete HLA typing data (n=9) were assigned HLA types from the deceased donor list based on the inheritance of HLA antigens. One quarter of the untyped sibling donors were assumed to be HLA identical and assigned the same HLA phenotype as their recipient. One half of the untyped sibling donors were assumed to share one haplotype with their recipient and were assigned the HLA phenotype of the first UNOS donor that shared one A, one B and one DR locus antigen with their recipient. One quarter of the untyped sibling donors were assumed to share no haplotypes with their recipient and were assigned the HLA type of the next deceased donor on the UNOS list with the same blood group.

Incompatible parent and child donors (n=8) were assumed to share one haplotype and were assigned HLA phenotypes as described for sibling donors assumed to share one haplotype. In one case, a deceased donor with an appropriate HLA type could not be found for a child donor whose mother was homozygous for a rare HLA-B antigen (B81). In that case, a donor who shared A and DR locus antigens was identified and one B locus antigen was changed to B81 so that they appeared to share a complete haplotype.

Other incompatible related donors (uncle, cousin; n=2) were assumed to share no haplotypes in both cases.

Matching algorithms

Accounting for ABO blood type and tissue-type incompatibilities, maximal sets of exchanges were identified, i.e. exchanges that included the maximum number of patients when:

- only 2-way exchanges are allowed,
- 2-way and 3-way exchanges are allowed,
- any size exchange is allowed.

The maximal two-way exchanges are found through different versions of the algorithm of J. Edmonds (9), as discussed in Roth et al. (7). Maximal 2-way, 3-way and maximal unrestricted exchanges are found through various formulations of the exchange problem as an integer programming problem. The integer programming formulation maximizes the number of transplants subject to the constraint that the cycle size not exceed the specified exchange size (2-

way, 3-way, or unrestricted). In the case of 3-way exchanges, we additionally constrain the solution to have the minimum number of 3-way exchanges (and hence the maximum number of 2-way exchanges) consistent with maximizing the number of transplants. The integer programs were solved with the commercial software CPLEX.

Assumptions made in simulation with local patient data

Donors were considered to be compatible if they did not have any of the antigens that the potential recipient had called antibodies against and none of the previously mismatched antigens. For class I and II high PRA patients where recipient antibody specificity could not be determined and only "safe antigens" were provided, donors were considered to be compatible if the donor's HLA type included only the potential recipient's own HLA antigens or "safe" antigens assigned for that patient. For potential recipients with high PRA in one class and low or medium PRA in the other class, donors were considered to be compatible if they had only the recipient's self or "safe" antigens in the high PRA class, and did not have any of the antigens that the recipient had antibodies against nor any of the previously mismatched antigens of the other class.

II. Simulation with OPTN/SRTR patient data

To determine if the results from this particular patient dataset can be generalized to a larger patient population, we conducted simulations based on data from the U.S. Organ Procurement and Transplant Network (OPTN) and the Scientific Registry of Transplant Recipients (SRTR) 2003 Annual Report, covering the period 1993-2002 (retrieved from http://www.optn.org on 11/22/2004). The purpose of these simulations is to verify that the difference between the 2-way and the 2- and 3-way exchanges that we see in the patient dataset is not an artifact of particular properties of that dataset. Distributions of (simulated) patient and donor blood types, gender and PRA distribution of the patients, and frequency of spousal donations, were generated using OPTN/SRTR data. Patient characteristics are from the new waiting list registrations data, living donor relational type distribution are from living donor transplants data. Numerical estimates are different than in the patient population considered above, but the simulations confirm how different exchange options and population sizes influence the frequency of additional live-donor transplants, across patient populations with different characteristics.

The probability of a positive crossmatch was based on patient PRA data. For simplicity in interpreting the results, patients were simulated in discrete PRA levels as follows:

- each low PRA patient (PRA <10%) has a positive crossmatch probability of 5% with a random donor,
- each medium PRA patient (10-80%) has a positive crossmatch probability of 45%,
- each high PRA patient (>80%) has a positive crossmatch probability of 90%.

The positive crossmatch probability between female patients and their husbands is approximately 33%, compared to approximately 11% between random pairs (10). We modeled the negative crossmatch probability between a female patient and her donor husband as 75% (i.e. (1-.33)/(1-.11)) of the negative crossmatch probability with a random donor:

$PRA^* = 100 - 0.75(100 - PRA)$

Patient-donor pairs were randomly generated using the population characteristics (assuming one donor per patient.) A pair was included in the sample population if they were incompatible by blood type or positive crossmatch. Incompatible pairs were generated until a sample size of n (n=25 or 100) incompatible pairs was reached. On average, 48 (198) unrelated patient-donor pairs were needed to produce 25 (100) incompatible pairs. Monte-Carlo simulation of 500 random populations was used for population sizes of 25 and 100. Once the incompatible pairs were generated, the same matching algorithm as described for the simulation with local patient data was used. The probability of a positive crossmatch was the same as that used to generate the incompatible pairs.

Two simulations were conducted. For simplicity only non-blood-related patient-donor pairs were considered in the first simulation. The influence of allowing 3-way exchanges in addition to 2-way exchanges can be most clearly assessed in a simple simulation, with fewer modeling assumptions than would be needed to try to simulate the general patient and donor population. However, in the second simulation a modified version was tested, with additional ad hoc assumptions regarding the number and relationship of potential donors that a patient may have available to them. These assumptions were similar to those used by Zenios et al (10) except for 3 assumptions chosen differently to make the simulation more suitable for our present purposes: (i) We assume that each patient can have 0,1 or 2 parents, 0 or 1 sibling, and 0 or 1

spouse (a total of 12 possibilities) as willing and medically fit donors and that each of these 12 scenarios occurs with equal probability. (ii) We use three levels of PRA sensitivity, low, medium and high, as we did in our original simulations above; and we statistically update the crossmatch probabilities of the patients with their "blood related" donors using a statistical model based on their PRA levels and relationship. (iii) We generate a single ABO genotype distribution that is the unconditional distribution for the US population obtained from the race conditional distributions reported in Zenios et al; we assume that each patient and donor belongs to this composite race.

Results:

I. Simulation using local patient data

Makeup of patient data set

The data set used for the initial simulation included 29 patients with one donor each and 16 patients with multiple donors for a total of 45 patients and 68 donor/patient pairs. The ABO types and the levels of antibody reactivity of these patients were evaluated. Twenty-three patients (51%) were ABO-0, 14 (31%) were ABO-A, 6 (13%) were ABO-B and 2 (4%) were ABO-AB. Twenty-one of the patients (47%) had PRA ≤15% with no defined HLA antibodies; 8 (18%) were moderately sensitized, with PRA between 16 and 79%; and 16 patients (36%) were highly sensitized with either class I or II PRA ≥80%. This reflects a more highly sensitized population than is present on the deceased donor waitlist in our area (77% with PRA ≤15%, 13% with PRA 16-79%; 10% with PRA ≥80%), which can be attributed to the increased likelihood that a highly sensitized patient would have a crossmatch incompatible donor.

Matching results

Of the 45 patients in the dataset, 14 were unmatchable because there was no donor compatible with the prospective recipient. Two more patients were then rendered unmatchable because they were not compatible with any of the remaining donors. Although 29 patients out of the original 45 (64%) had a compatible donor in the dataset, only 15 patient-donor pairs (33%) had a patient-donor pair that was mutually compatible with them (Table 1). Moreover, many pairs were mutually compatible with the same pair (e.g. pairs 12, 30 and 38 were mutually compatible only with pair 29), further limiting the number of possible exchanges.

Exchanges involving two patient-donor pairs (2-way exchanges)

If only exchanges involving two patient-donor pairs are allowed, a maximum of 8 patient-donor pairs in the data set could exchange kidneys, in four 2-way exchanges. If all matches were confirmed to be compatible, 8 of the 45 patients could receive transplants. One example of the possible paired exchanges is shown in Table 2A, involving three ABO-A, three ABO-B, and two ABO-O patients. Under these exchanges two moderately sensitized patients (R29 and R45) could receive transplants. There are a number of alternative ways in which these 4 exchanges can be organized (data not shown). Maximizing the number of exchanges has implications for which patient-donor pairs are matched. For example while pairs R1 and R29 are mutually compatible (Table 1), if they exchange kidneys then only 6 patients can receive transplants through pairwise exchanges, instead of 8.

Exchanges involving multiple patient-donor pairs

Exchanges involving up to three patient-donors pairs are logistically feasible by accomplishing these surgical procedures within one day. The advantage of such exchanges is readily demonstrated in the dataset: when 3-way exchanges are also allowed, a maximum of 11 patient-donor pairs could be identified who could exchange kidneys. The exchanges included one 2-way exchange (between two pairs) and three 3-way exchanges (i.e. three exchanges that each involves three patient-donor pairs). Four of the recipients are ABO-B, three are ABO-A, three are ABO-O and one is ABO-AB. Five sensitized patients, including one highly sensitized patient with a class I PRA of 93%, could potentially receive transplants. The details of these exchanges are shown in Table 2B.

The data also admit a possible 5-way exchange. If such an exchange is allowed with the test dataset, 12 patient-donor pairs could exchange kidneys. This would be accomplished with two 2-way exchanges, one 3-way exchange and one 5-way exchange. The details of the 5-way exchange are shown in Table 2C. Although not logistically feasible in most cases, it maximizes the number of patients who could receive transplants and demonstrates the power of the matching algorithm.

II. Simulation using OPTN/SRTR data

The distributions of patient and living donor data used in this simulation are shown in Table 3. For each population size, there was substantial gain from larger than 2-way exchanges, mostly from 3-way exchanges, which is similar to the result shown with our local patient data. As the population size increased the percentage of patients who could be helped by 2-way exchanges increased, and as a result the benefit from larger exchanges declined slightly. But 3-way exchange accounts for an even larger percentage of the benefit from larger exchanges (last row in Table 4 and Table 5). In the maximal 2-&3-way exchanges, when the population was n=25, 61% of the patients were in 3-way exchanges while 39% of the patients were in 2-way exchanges. When the population was n=100, 49% of the patients were in 3-way exchanges and 51% of the patients were in 2-way exchanges.

O donors account for only 23% of the incompatible patient-donor pairs, since O donors are mostly compatible with their intended recipients, while O patients are 59% of all patients in incompatible patient-donor pairs, since they can only receive O kidneys (Table 4). Similarly, high PRA patients are only 10% of all patients, but 18% in the population of incompatible patient-donor pairs (Table 5). However, exchanges provide some good news for highly sensitized patients, since selection also operates on the distribution of incompatible patient-donor types. High PRA patients are 35% of those with incompatible O-donors (Table 5), since, conditional on being incompatible with an O donor, a patient is more likely to have a high PRA.

Because O donors are potentially a match for any patient, high PRA patients with O donors have many opportunities for an exchange, and hence a high chance of success, even though they are incompatible with most donors. This is so even when the population of incompatible patient-donor pairs is only 25: Table 5 shows that in each such population there are on average just over two high PRA patients with O donors, and they have a 36% chance of being included in an exchange if only 2-way exchanges are possible, but a 51% chance if 3-way exchanges are also possible (and a 55% chance if exchanges of any size are possible). These patients do much better in a population of 100 incompatible patient-donor pairs: on average there will be just over 8 highly sensitized patients with O donors, and their chances of being included in a match are 69% when only 2-way exchange is possible, 91% when 3-way exchange is also possible, and 93% when exchanges can be of any size. Thus the disadvantage of being highly sensitized is ameliorated by having an easy-to-match O donor. In general, high PRA patients with any kind of

donor are helped by a larger population of incompatible patient-donor pairs, and when larger exchanges are possible.

A modified version of this initial model was also tested. As shown in Table 4B, this simulation generated similar findings to the original less complicated model, demonstrating that different modeling assumptions about the number and relationship of donors for each patient are not crucial assumptions. The predictions about the benefit of allowing both 2-way and 3-way exchanges are evident with both models, and both models confirm the advantage of 3-way exchanges as is shown with our local patient data.

Discussion:

Any adult can be a live kidney donor who is medically well, psychosocially suitable, and willing to donate. The issue for the potential transplant recipient is to find a donor compatible by blood type and crossmatch reactivity. For those who have a willing but incompatible donor, the concept of paired kidney donation was first proposed by Rapaport in 1986 (11). (See also Ross et al. (12)). However, this approach was not considered more extensively until ample data confirmed that the absence of an HLA match of the donor recipient pair would not be detrimental to outcome (2, 13). Today, centers around the world are developing policies for paired and three way donation (4, 14-18) when incompatible donor/recipient pairs are identified.

To further increase the number of transplants that can be done via optimal matching of donor exchanges, expansion of the donor/recipient pair pool is necessary. The development of multi-center or regional exchange programs would provide opportunities for such expansion, although there are potential obstacles that would need to be resolved. These include the need for donors to travel should centers be far apart, the logistics of crossmatching when multiple centers are involved, and issues related to data sharing and HIPAA requirements. In addition, all of the impediments that are known for any living donor will also be issues in donor exchanges.

It is now evident that there may be multiple ways to arrange exchanges (6, 7). Some of the issues involved in identifying sets of exchanges are related to those that arise in other kinds of matching problems, such as the matching of medical residents (19-21), and matching students to schools (22-24). In these cases too, there were substantial logistical difficulties associated with coordinating diverse centers with a tradition of operating independently. But there were

substantial gains to be made by making matches in a coordinated way, and the logistical difficulties in doing so were successfully overcome.

This report provides important evidence that a computerized matching protocol can be used to identify donor/recipient pairs from a registry of incompatible pairs who can potentially enter into donor exchanges. Actual patient data from a relatively small dataset of 45 patients and 68 incompatible donor/patient pairs were used to show that potentially compatible donors could be identified for 24% (n=11) of the patients using logistically feasible 2-way and 3-way exchanges.

The results of the computerized matching protocol demonstrate the utility of optimizing exchanges, i.e. matching pairs so that as many patients as possible can receive an exchange. Similar conclusions about the use of a computerized system have been recently reported by Segev et al (26). However, depending on the number of patients added to the registry on a regular basis, and the frequency that the match program is run, it is possible that there will be few opportunities to allow for optimal exchanges to be chosen unless patients are expected to wait for a defined period of time before matched exchanges are allowed to proceed. Balancing the wish to ensure the maximum number of patients receive transplants vs. the need for individual patients to receive transplants expeditiously may prove to be a challenge.

The ability to perform 3-way or more exchanges has been demonstrated to increase the number of possible exchanges that can be identified, both using the local patient data as well as the results based on the simulation involving larger populations of patient/donor pairs. It must be noted that there are many details that were not included in these simulations that might affect whether or not an exchange would proceed, including age, size, and preferences of the recipients, donors and physicians. But these factors are likely to be relatively consistent between the 2-way and 3-way exchange groups. Allowing 3-way exchanges does not prevent a 2-way exchange from being done should the circumstances require it. However, the use of multiple exchange combinations can greatly increase the logistical difficulties of such exchanges. Most donor exchange programs perform donor nephrectomies simultaneously to prevent the possibility of one donor withdrawing his or her commitment after the other donor has undergone nephrectomy. Multiple simultaneous surgeries can stretch the capabilities of many centers and require a great deal of careful coordination, but 3-way exchanges (which require six surgeries) have been demonstrated to be a viable option (16).

Theoretical results in a simple model in which there are no positive crossmatches between patients and other patients' donors suggest that the importance of three way exchanges in achieving maximal matchings arises primarily from the distribution of ABO blood types, and will not vanish even with very large populations (25). The additional transplants facilitated by three way exchanges comes both from high PRA patients (who may have idiosyncratic matching patterns), and from the way that O-donors (who are often the donors of high PRA pairs) help to fill the gap if there are different numbers of A-B and B-A pairs. For example, in a situation where there is an excess of B donor-A patient pairs, a (rare) O donor-B patient pair can form a 3-way exchange with a B donor-A patient pair together with a (very common) A donor-O patient pair. Therefore rare patient-donor pairs are benefiting from the 3-way exchange but are also benefiting the two other pairs involved in the exchange, thus increasing the number of patients benefiting from exchange.

The present analysis focuses only on direct exchanges between incompatible patient-donor pairs. The same techniques can be used to incorporate indirect exchange between patient-donor pairs and the deceased donor waitlist, and undirected donor kidneys, sometimes with a potential to facilitate exchanges involving additional incompatible patient-donor pairs. These indirect exchanges involve identifying not only the cycles of mutual compatibility that permit direct exchange, but also "chains" that begin with an undirected donor or end in a patient on the deceased donor waitlist. The possibility of such additional exchanges increases the total number of transplants that can be arranged (6). For example, an O blood type non directed (Good Samaritan) donor could be entered into the computer matching system and be identified as compatible with a sensitized recipient; thus, enabling the originally intended donor for the incompatible recipient to give to another recipient.

It is important to note that the computer program can identify only potentially compatible donor and recipient pairs. Crossmatches will be required to confirm compatibility. An incompatible crossmatch between a pair that the matching algorithm identifies as compatible will result in the transplants not being performed, and in cases of 3-way exchanges may prevent three transplants from being performed. A priority should be to minimize the number of potentially compatible donors who may be identified but later determined to be incompatible by crossmatch, and to thus limit the number of times a given donor must be crossmatched with a different recipient. Therefore, steps must be taken to ensure that compatibility can be predicted as

accurately as possible before the crossmatch is done. Extensive antibody screening using a sensitive and specific technique must be done, and complete antibody specificities (or safe antigens) must be identified for high PRA patients. Centers that utilize such techniques have reported success in predicting crossmatches (27, 28). Antibody screening methods and reagents are continuously being improved and expanded, which will further improve the ability to predict crossmatches.

Data management can be complicated in kidney exchange programs. In New England we have developed a web-based data entry form that will enable each center to enter their own patient and donor information. A designated coordinator is important to simplify communication and ensure complete and accurate data is entered. In addition, high-level algorithmic programs are available that can handle the exchanges for a large population of pairs.

Development of regional exchange programs, such as that under way in New England, are important for increasing the number of patients who can receive living donor kidney transplants, and will also help decrease the number of patients waiting for a kidney on the deceased donor wait list. Because the percentage of incompatible patient-donor pairs who can benefit from 2-way exchange increases as the population of pairs available for exchange grows, expanding local exchange programs to include regional and possibly a national exchange program should be advantageous. And since a substantial number of additional patients can receive transplants if 3-way exchanges are feasible, developing the ability to identify and perform 3-way exchanges will also be very worthwhile. Although the advantage of using 3-way exchanges cannot be confirmed without prospective studies, every successful match means that two or more recipients receive a transplant they otherwise would not have gotten, and every attempt to increase the number of transplants should be included in an exchange program.

Finally, a national system may be needed to secure a sufficient number of patient-donor incompatible pairs to make the opportunity of identifying compatible donors timely and realistic. However, the administration of such a system will need the cooperation of the entire transplant community to assure an ethical and medical oversight that is protective of the recipient and the donor.

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Table 1. Mutually compatible patients in local patient dataset.

	R1	R6	R12	R13	R24	R26	R28	R29	R30	R31	R38	R41	R42	R43	R45
R1				x	x	x		x					x	x	
R6															x
R12								x							
R13	x									x					
R24	x									x					
R26	x									x					
R28															x
R29	x		x						x		x				
R30								x							
R31				x	x	x							x	x	
R38								x							
R41															x
R42	x									x					
R43	x									x					
R45		x					x					x			

x indicates the row patient is compatible with at least one donor of the column patient and the column patient is compatible with at least one donor of the row patient.

Table 2A. Example of one possible combination of 2-way exchanges

Recipients and their incompatible donors prior to exchange #1										
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody spec**	**Prev. mm antigens**	**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA type**	**Reason incompat.**
R28	O	0%	0%			D28.2	Sib	B	A1,23; B8,70; Bw6; DR3; DQ2; DR52	ABO
R45	B	0%	41%	DR53	A32; B7,40; DR8,14,4, 53	D45	Child	O	A11; B62,75; Bw6; DR2,4; DQ1,3; DR53, 51	Pos XM
Exchange #1 –D28.2 gives to R45 and D45 gives to R28.										
Recipients and their incompatible donors prior to exchange #2										
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody specificity**		**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA type**	**Reason incompat.**
R29	A	26%	nd	A11, 3, 10, 25, 26, 32		D29	Child	O	A11,2; B27,55; Bw4,6; DR1,12; DQ1,7; DR52	Pos XM
R38	O	0%	0%			D38	Spouse	A	A23,74; B7; Bw6; DR1,9; DQ1,2; DR53	ABO
Exchange #2 – D29 gives to R38 and D38 gives to R29.										
Recipients and their incompatible donors prior to exchange #3										
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody spec.**	**Prev. mm antigens**	**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA type**	**Reason incompat.**
R1	B	13%	0%		None	D1	Spouse	A	A1,2; B8,63; Bw4,6; DR3,13; DQ1,2; DR52	ABO
R13	A	2%	0%			D13.2	Sib	B	A1,30; B8,41; Bw6; DR3,7; DQ2; DR52,53	ABO
Exchange #3 - D13.2 gives to R1 and D1 gives to R13										
Recipients and their incompatible donors prior to exchange #4										
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody spec.**	**Prev. mm antigens**	**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA type**	**Reason incompat.**
R31	B	0%	0%			D31	Spouse	A	A1,3; B14,57; Bw4,6; DR7; DQ2,3; DR53	ABO
R26	A	0%	0%			D26	Unrelated	B	A2,29; B7; Bw6; DR13; DQ1; DR52	ABO
Exchange #4 - D31 gives to R26 and D26 gives to R31										

Table 2B. Matching when 2-way and 3-way exchanges are possible.

Recipients and their incompatible donors prior to exchange #1									
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody specificity**	**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA type**	**Reason incompat.**
R29	A	26%	nd	A11, 3, 10, 25, 26, 32	D29	Child	O	A11,2; B27,55; Bw4,6; DR1,12; DQ1,7; DR52	Pos XM
R38	O	0%	0%		D38	Spouse	A	A23,74; B7; Bw6; DR1,9; DQ1,2; DR53	ABO
Exchange #2 – D29 gives to R38 and D38 gives to R29.									
Recipients and their incompatible donors prior to exchange #2 (3 way exchange)									
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody spec.**	**Prev. mm antigens**	**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA type**	**Reason incompat.**
R19	B	0%	50%	DR12; DQ2, 7		D19	Child	B	A24,32; B7,35; Bw6; DR2,3; DQ1,2; DR51,52	Pos XM
R43	A	0%	0%			D43	Spouse	B	A24; B7,39; DR2,8; DQ1,4; DR51	ABO
R31	B	0%	0%			D31	Spouse	A	A1,3; B14,57; Bw4,6; DR7; DQ2,3; DR53	ABO
Exchange #2 - D43 gives to R19, D31 gives to R43, and D19 gives to R31									
Recipients and their incompatible donors prior to exchange #3 (3-way exchange)									
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody spec.**	**Prev. mm antigens**	**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA type**	**Reason incompat.**
R45	B	0%	41%	DR53	A32; B7,40; DR8,14,4;53	D45	Child	O	A11; B62,75; Bw6; DR2,4; DQ1,3; DR51,53	Pos XM
R28	O	0%	0%			D28.2	Sib	B	A1,23; B8,70; Bw6; DR3; DQ2; DR52	ABO
				Safe ags	**Recip HLA**					
R41	O	93%	nd	A1,11,30; B13,18,37, 62,75	A33; B14; Bw6; DR1,11; DQ1,7; DR52	D41.1	Unrelated	O	A2,24; B50,52; Bw4,6; DR2,3; DQ1,2; DR51,52	Pos XM
Exchange #3 - D28.2 gives to R45, D41.1 gives to R28, and D45 gives to R41									
Recipients and their incompatible donors prior to exchange #4 (3-way exchange)									
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody spec.**	**Prev. mm antigens**	**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA Type**	**Reason Incompat.**
R24	AB	36%	42%	A23,24,9;		D42		B	A3; B44,62; DR1,4; DQ1,3;	ABO

				DR8,11			Spouse		DR53	
R42	A	0%	0%			D1	Spouse	A1	A1,2; B8,63; Bw4,6; DR3,13; DQ1,2; DR52	ABO
R1	B	13%	0%		none	D24	Cousin	B	A1,24; B35,46; Bw6; Cw1,4; DR2,12; DQ5; DR51,52	Called ab
Exchange #4: D42 gives to R24, D1 gives to R42, and D24 gives to R1										

Table 2C. Possible 5-way exchange

Recipients and their incompatible donors prior to exchange										
Recip ID	**Recip ABO**	**Cl I PRA**	**Cl II PRA**	**Antibody spec.**	**Prev. mm antigens**	**Donor ID**	**Relation**	**Donor ABO**	**Donor HLA type**	**Reason incompat.**
R45	B	0%	41%	DR53	A32; B7,40; DR8,14,4;53	D45	Child	O	A11; B62,75; Bw6; DR2,4; DQ1,3; DR51,53	Pos XM
R24	AB	36%	42%	A23,24,9; DR8,11		D24	Cousin	B	A1,24; B35,46; Bw6; Cw1,4; DR2,12; DQ5; DR51,52	Pos XM
R26	A	0%	0%			D26	Unrelated	B	A2,29; B7; Bw6; DR13; DQ1; DR52	ABO
R16	O	0%	0%			D16	Spouse	A	A2,34; B60; Bw6; DR2; DQ1; DR51	ABO
				Safe ags	**Recip HLA**					
R41	O	93%	nd	A1,11,30; B13,18,37, 62,75	A33; B14; Bw6; DR1,11; DQ1,7; DR52	D41.1	Unrelated	O	A2,24; B50,52; Bw4,6; DR2,3; DQ1,2; DR51,52	Pos XM
5-way exchange - D24 gives to R45, D26 gives to R24, D16 gives to R26, D41.1 gives to R16, D45 gives to R41										

PRA, panel reactive antibody; Prev mm antigens, mismatched HLA recipient was exposed to during previous transplant(s); Ab spec, HLA antibody specificity in recipient serum; Relation, relation of donor to recipient; Reason incompat, reason donor was incompatible to recipient (ABO mismatch or positive crossmatch); Safe ags, HLA antigens patients serum does not react with; Recip HLA, Recipient HLA type.