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Transplant queueing

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1 Introduction The problem of optimal dynamic allocation of randomly arriving live organs (e.g., kidneys) to 'candidates' queueing for transplant is more severe than ever. There is a growing gap between demand and 'supply' (from deceased 'donors'). In the USA, only a quarter of wait listed patients receive a deceased donor's kidney transplant within 5 years [1]. Various procedures are used, based mainly on candidates' queueing time seniority, when determining 'who will get the cadaver,' but allocation according to the best-fit human leukocyte antigen (HLA) criterion is rarely implemented. Since a newly arriving live organ cannot be stored, it should be assigned upon arrival to one of the waiting candidates, or otherwise lost. The 'donor-priority rule' increases the supply, but compromises the average quality, leading to a decreased social welfare [2]. The aim of this note is to encourage the use of a multi-objective policy, based simultaneously on HLA best-fit considerations, and on candidates' waiting time seniority fairness, when determining the allocations of the stochastically arriving scarce resource, live organs.

2 Problem statement A human being possesses two series of antigens, Series-1 and Series-2, from which, upon birth, two antigens from each Series are randomly 'selected'. Consequently, there are 5 possible levels of HLA-matching between a randomly arriving graft and a random candidate. Let H denote the number of gene mismatches between a live organ and a random candidate. H can assume the following values: (i) $H = 0$, i.e., all 4 antigens match (A-match); (ii) $H = 1$, a single mismatch (B-match); (iii) $H = 2$, two mismatches (C-match); (iv) $H = 3$, three mismatches (D-match); and (v) $H = 4$, no matches at all (E-match). Let $f_i = P(H = i), i = 0, 1, 2, 3, 4$, and let $F_i = P(H \leq i)$, $F_4 = 1$. Different mismatches yield different corresponding 'rewards'. For example, a reward can be calculated as the probability that the graft survives at least one year. According to a set of data on a population of age 55-64 and its corresponding gene frequencies [3], and assuming that a recipient's antigens are #1 and #2 from Series-1, and #7 and #12 from Series-2, the probabilities are $f_0 = 0.0094$, $f_1 = 0.0941$, $f_2 = 0.3134$, $f_3 = 0.4073$, and $f_4 = 0.1758$. The corresponding rewards are $x_0 = 0.70, x_1 = 0.62, x_2 = 0.49, x_3 = 0.47$, and $x_4 = 0.44$, where x_i is the reward when $H = i$. It should be emphasized that any other appropriate values can be considered.

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Let T denote a candidate's lifetime (e.g., on dialysis). Let $G(t) = P(T \leq t)$ with density $g(t)$ and hazard function $r(t) = g(t)/[1 - G(t)]$. Let $0 \leq \beta(t) \leq 1$ be a continuous non-increasing discount function with $\beta(0) = 1$. Let X denote the random 'reward' from a random HLA-type match, with distribution $P(X \leq x)$. Suppose there is only a single candidate waiting for transplant. Then, the following holds [3]:

Theorem *Let the arrival process of kidneys follow a non-homogeneous Poisson process with rate $\mu(t)$. If G is increasing failure rate, that is, $r(t)$ is non-decreasing, then there exists an optimal policy characterized by a continuous non-increasing function $\lambda(t)$ on $(0, \infty)$, such that an 'offer' of a kidney with a reward value $X = x$ at time t is accepted iff $\beta(t)x \geq \lambda(t)$. $\lambda(t)$ is the solution of the differential equation:*

$$\lambda'(t) = r(t) \cdot \lambda(t) - \beta(t) \cdot \mu(t) - \int_{\lambda(t)/\beta(t)}^{\infty} (1 - P(X \leq x))dx$$

If $r(t)$ is increasing and $\mu(t)$ is non-increasing, a simple upper bound on $\lambda(t)$, decreasing in t, is: $0 \leq \lambda(t) \leq [\beta(t)\mu(t)/r(t)]E[X]$. T can be approximated [3] by a Gamma distribution with density $g(t) = \theta^2 t e^{-\theta t}$, scale parameter $\theta = 0.4$, and mean $E[T] = 5$. For example, given the above population's gene frequencies and letting $\beta(t) = 1$, the optimal policy for the single candidate is of a threshold type as follows: from 0 to 1.83 years of 'dialysis age'—wait for at least B-match; from 1.83 to 8.05 years—wait for at least C-match; beyond 8.05 years—wait for at least D-match; never accept an E-match. [why? because the E-match reward, x_4, is below the asymptote of $\lambda(t)$]. Note that, in this example, a transplant is not conditioned on receiving an A-match. Consider now the actual case when n candidates are queueing for transplants and a random live organ arrives. This event generates a set of n different levels of HLA compatibility, resulting in n corresponding i.i.d. random rewards $X_1, X_2, \ldots, X_n$, where X_j denotes the reward of the j-th candidate in line (according to a first come first served (FCFS) discipline). Allocating by the FCFS, the mean attained reward is $E[X] = \sum_0^4 f_i x_i$. However, let $X^*_{(n)} = max(X_1, X_2, \ldots, X_n)$. Then, we argue that the newly arriving kidney should be allocated according to the **HLA best-fit** policy, namely assigned to the candidate having the value $X^*_{(n)}$ provided that $X^*_{(n)} \geq \lambda(t)$ for that candidate. This policy creates a new measure of effectiveness [4], called **Expected Value of Transplantation (EVT)**, which takes into account the quality of each possible transplant in terms of its corresponding HLA quality. Thus, with $\bar{F}_i = 1 - F_i$, the mean value of such allocation policy is $E[X^*_{(n)}] = (1 - \bar{F}^n_0)x_0 + \sum_1^4((1 - \bar{F}^n_i) - (1 - \bar{F}^n_{i-1}))x_i$. For a given queue, with an arbitrary influx process of candidates and an arbitrary inter arrival process of live organs ('service' time), let L denote the number of waiting candidates. Set $P_n = P(L = n)$. Then, the HLA best-fit policy yields the following EVT value: $EVT = \sum_0^\infty P_n E[X^*_{(n)}]$, where $E[X^*_0] = 0$, and $E[X^*_{(1)}] = E[X] = \sum_{n=0}^4 f_i x_i$. Clearly, $EVT \geq E[X]$ [4]. Moreover, one can envision [5] future technologies by which it will be possible to store arriving live organs (at cost) so that a double-ended queue will form: waiting candidates on the one hand, and stored organs on the other hand. Under the HLA best-fit matching, 3 measures of effectiveness are investigated in [5]: (i) Expected Reward per Transplantation; (ii) Rate of Reward from Transplantation; and (iii) Gained Rate of Reward per one dollar of expenditure. Numerical examples show the advantage of the HLA best-fit allocation.

3 Discussion The question now is 'what about **fairness**'? Should candidates possessing low-frequency antigens be discriminated when using the HLA best-fit criterion? For the majority of people, the word 'queue' means a FCFS discipline. However, the FCFS order does not necessarily imply **quality efficiency** (think, for example, on Shortest Processing Time First policy, or on Processing Sharing service mechanism). Using the HLA best-fit procedure in live organ allocation is closely related to a Random Order of Service policy. The issue of quantifying 'fairness in queues' has been investigated in the queueing literature (e.g., [6–8] and references there). In [6], the issue of unfairness in an M/G/1 queue is discussed, while in [7, 8] a measure of fairness, or discrimination, called Resource Allocation Queueing Fairness Measure (RAQFM) is proposed. The RAQFM deals with both relative job seniority and relative job's service time, and it accounts for individual job discrimination, as well as for system unfairness. Consider a single-server queue where $L(t)$ denotes the number of customers present in the system at time t. The fundamental principle underlying RAQFM is that at every instant t, all customers present in the system deserve an **equal share** of the server's capacity. Suppose customer j arrives at time a_j and departs at time d_j while requiring a total service time s_j. The overall discrimination of this customer, D_j, is the difference between the customer's service requirement and the total attained service during the customer's sojourn time in the system: $D_j = s_j - \int_{a_j}^{d_j} [1/L(t)]dt$, where D_j might be positive or negative. An important property of this measure is that for a non-idling service-conserving system, the sum of the individual discriminations equals 0 at any instant t. Various service disciplines are discussed in [8]. The subject area of research proposed in this letter is a **combined** queueing-type analysis regarding the multi-objective dichotomy of (i) **quality efficiency** based on HLA best-fit criterion, and (ii) **fairness** associated with lengths of time candidates wait for transplant—on the other hand.

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