Organ Transplantation Regions: The Need for Optimization

Nan Kong, Steven Shechter, Andrew J. Schaefer
Department of Industrial Engineering
University of Pittsburgh
Pittsburgh, PA 15261

James E. Stahl
The Decision Analysis and Technology Assessment Group
Massachusetts General Hospital
Boston, MA 02114

Abstract

Since the National Organ Transplant Act of 1984, the number of people receiving organs each year has increased [1]. Unfortunately, the number of donations has not kept up with the number of patients needing them, resulting in a severe shortage of organs [1]. This requires that we allocate organs as efficiently as possible. Currently in the U.S., organs are allocated at a local, regional, and national level in that order depending on patient-organ matches. In this paper, we consider the effect of region design on total intra-regional liver transplants and formulate it as a set-partitioning problem.

Keywords
Integer programming, Set partitioning problems, Organ allocation

1. Introduction
The tenth leading cause of death among adults in the United States is end-stage liver disease (e.g., chronic liver disease and cirrhosis) [2]. Over 25,000 people died from this in 1998. Presently, the only recourse for such patients is to receive a liver transplant. Fortunately, patients at almost any stage of their disease can receive a liver transplant and expect an 80% – 90% chance of a five-year survival [3,4]. Unfortunately, liver transplantation is costly and is limited by the supply of viable donor organs [5]. In 1999, approximately 4,700 people received a liver transplant [6], but the number of patients who have died each year while waiting for a transplant has increased from 196 in 1988 to 1,317 in 1999. Though the pool of available organs has more than doubled in the last 10 years from 1,800 in 1988 to 4,900 in 1998 it still has not been able to keep pace with demand. The number of patients registered with the United Network for Organ Sharing (UNOS) for liver transplant has increased from 616 in 1988 to over 16,000 in 1999.

Due to the severe shortage of organs available for transplantation, organ allocation is a critical component of the transplantation process and is central to the current policy debate on this topic. Livers are allocated hierarchically at a local, regional, and national level (see Figure 1).

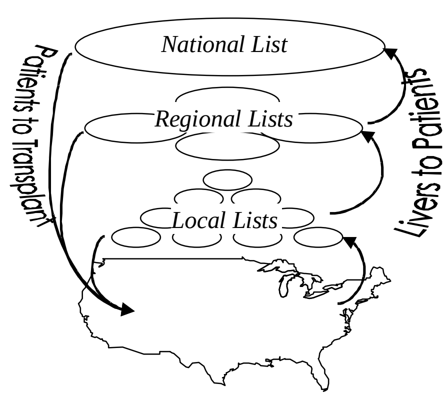

Figure 1. Current Allocation Scheme

There are 62 local areas, each represented by one organ procurement organization (OPO) (see Figure 2).

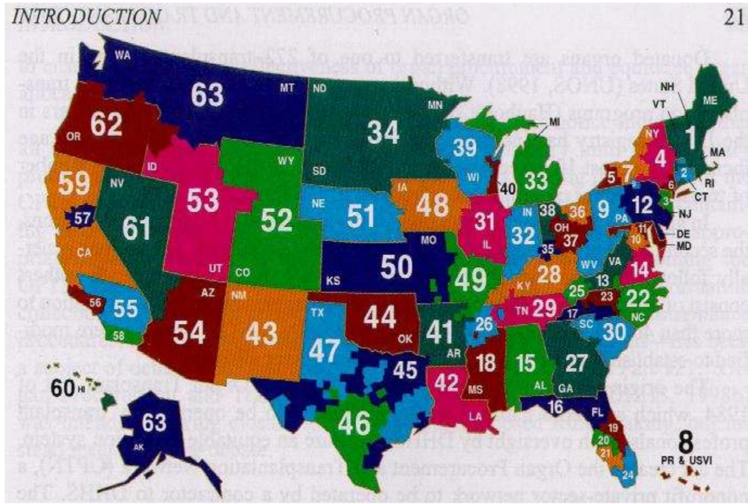

Figure 2. Current OPO Map [1]

The country is also divided into 11 regional areas (see Figure 3).

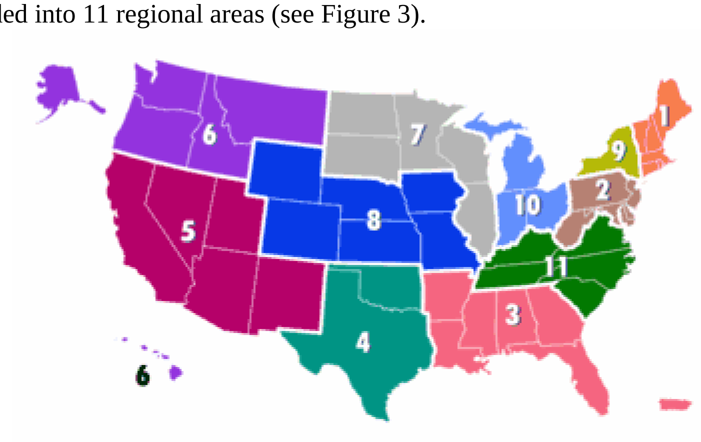

Figure 3. Current Region Map [6]

Presently, when a donated liver becomes available in an area, the OPO covering that area is responsible for obtaining the liver and preserving it for transplantation. The OPO then contacts UNOS to check the patient waiting list in the OPO area to determine if there is an appropriate match. If no match is found, UNOS then considers the regional level. Finally, if no match is found at the regional level, the organ is offered to any U.S. patient who is a good match for the organ.

In addition to increasing the number of successful transplants, another goal of UNOS is to have an equitable allocation scheme [6]. The notion of fairness, though, is open to debate. Some feel it means equalizing the wait times among patients with similar medical conditions, regardless of geographic location. However, when considering the travel time and medically acceptable cold ischemia time (time from when blood stops flowing to the donor organ until the time when the recipient's blood starts flowing to it), this may not be a good idea. Another fairness consideration is increasing transplant access for minorities and the poor [1].

2. Problem Solutions

There are many approaches to extending the lives of patients waiting for a liver transplant. Living donor transplantation is a growing practice whereby a living relative or friend offers a patient a portion of his or her liver. Other areas of research may include xeno-tranplantation (animal to human organ transfer) or development of machines to assist in organ and patient survival (as in the case of dialysis machines for kidney patients). As industrial engineers and operations researchers, we focus on improving the allocation process. This too can be done in different ways. For example, we could research the algorithm for matching patients and livers and determine the best way to evaluate potential matches. Also, we could reconsider the hierarchical method of searching locally, then regionally, then nationally. Perhaps an organ should just go to the most urgent patient in the country (while considering travel time in the decision), regardless of what OPO obtained the organ.

In our research, we try to improve the allocation process at the regional level. Specifically, we want to develop a set of regions that maximizes the total expected intra-regional transplants. We considered two strategies in our analysis. First, we employed a strategy where the number of transplant regions was constrained to 11 as with the current system. This was to examine the hypothesis that the current system is optimal when the number of regions is designated as 11. Second, we examined a strategy where the number of regions is unrestricted in order to find the overall optimal solution. In addition to performing this analysis for the general problem, we considered the notion of fairness and then reformulated the problem.

2.1 General Problem

For the purposes of this analysis we modeled the country as a network. In this model, OPOs represented the nodes of the network and an arc joined two contiguous OPOs. Several assumptions were made. First, a region was defined as a set of no more than 9 contiguous OPOs. Second, as in the current system, an OPO was only allowed to supply one region. We also assumed that the number of intra-OPO transplants was independent of the region. This allowed us to focus our analysis on the number of organs flowing from an OPO to the other OPOs in its region. Our current research does not consider organs reaching the national level and thus we assumed that any organ that did not match at the local level would match at the regional level. Furthermore, we assumed that the probability a liver is sent to another OPO in the region is independent of travel time and depends only on the ratio of the OPO population to the region population. This is the crux of the problem--we want to balance region size with cold ischemia time by considering the likelihood a liver is functional once it reaches the various OPOs in the region. We model this with a decay function based on distance.

Our first step was to identify all possible region configurations. We used a depth-first search algorithm, resulting in over 450,000 possible regions. For each region the expected number of intra-regional liver transplants was evaluated by considering OPO populations, OPO donation probabilities, and the decay of the liver as a function of distance between OPOs. A binary integer program was solved over these regions to maximize the total number of intra-regional liver transplants. Because we assumed each OPO must be part of exactly one region, our problem was a set-partitioning problem.

2.2 Fairness

After obtaining results for the problem of strictly maximizing total intra-regional transplantations, we incorporated a measure of fairness into our analysis. We chose to measure fairness from the perspective of an OPO, and defined it as the expected number of organs flowing into the OPO. We added another decision variable, α, to the problem with objective coefficient ρ and added constraints ensuring that each OPO had a fairness measure of at least α. The value of ρ determines how much of the solution is weighted towards fairness versus maximizing total intra-regional transplantations.

3. Problem Formulation

3.1 General Problem Formulation

Let m be the number of OPOs in the U.S. and n be the number of hypothetical regions containing up to 9 OPOs. To formulate this problem, we introduce binary decision variables x_r where $x_r = 1$ if region r is chosen, and $x_r = 0$ otherwise. Every constraint matrix coefficient a_{ir} (i=1,2,…m and r=1,2,…,n) also takes on values of 0 or 1, where $a_{ir} = 1$ if region r contains OPO i, and $a_{ir} = 0$ otherwise. Each objective function coefficient, c_r, measures the expected number of intra-regional, inter-OPO liver transplants.
Hence, the formulation is as follows:

$$\max \sum_{r=1}^{n} c_r x_r \quad (1)$$

$$\text{subject to} \sum_{r=1}^{n} a_{ir} x_r = 1 \qquad i=1,2,\ldots,m \quad (2)$$

$$x_r \in \{0,1\} \quad (3)$$

The above formulation is a typical set-partitioning formulation. As mentioned above, in the current UNOS system the number of regions is designated as 11. Hence, we also add the following constraint to restrict the number of regions to 11.

$$\sum_{r=1}^{n} x_r = 11 \quad (4)$$

3.2 Fairness Measure Formulation

Using the notation we defined in the previous section, the formulation considering fairness is as follows:

$$\max \sum_{r=1}^{n} c_r x_r + \rho\alpha \quad (5)$$

$$\text{subject to} \sum_{r=1}^{n} a_{ir} x_r = 1 \qquad i=1,2,\ldots,m \quad (6)$$

$$\sum_{r=1}^{n} f_{ir} x_r - \alpha \geq 0 \qquad i=1,2,\ldots,m \quad (7)$$

$$x_r \in \{0,1\} \quad (8)$$

where f_{ir} is the measure of fairness. Specifically, f_{ir} is the expected number of livers flowing to OPO i from other OPOs within region r. When the number of regions is restricted to 11, we also include Equation (4) in our constraints.

4. Future Considerations

One of the assumptions we made in our model was that a region must consist of no more than 9 contiguous OPOs. If we allowed a region to contain up to 10 contiguous OPOs, the number of possible regions increased from around 450,000 to about 1.4 million. Current computing limitations prohibit the exact solution of this problem. We hope to come up with a good heuristic to allow for a region to have more than 9 OPOs grouped together. By expanding the set of possible regions, we are likely to improve our solution.

We also plan on considering the transplantations at the national level. Once an organ does not match at the OPO level, we ideally want to set up the regions to maximize the total intra-regional *plus national* transplantations. This will lead us to figure out the probability an organ does not match at the regional level and then to determine the likelihood of it going to various areas of the country outside the region. While considering national transplantations is not possible within the current set partitioning model, we plan to investigate approximations that would allow us to retain the set partitioning structure.

We also want to devote more research to developing an accurate decay function based on cold ischemia time. We performed sensitivity analysis based upon different functional relationships between distance and liver survival. With more data, we should be able to choose an accurate function relating these two measures. We are currently performing a meta-analysis to determine this relationship [7].

In the future, we will also consider other measures of fairness such as transplant access for people of various races and socioeconomic status. Since some OPOs cover large areas, we may also consider fairness from the perspective of different locales within the OPO. Then we can evaluate disparities in waiting time for people with similar medical conditions living in different parts of the country.

Researchers at the University of Pittsburgh are currently developing a simulation of the current liver allocation process [8]. Once the development is complete and the simulation model is validated, we will use it to test some of the proposed region designs. Note that we have assumed certain terms in our formulation to be deterministic (e.g., the objective coefficients and the decay function). A sophisticated simulation model will allow us to see if this approximation is sufficient.

References

1. Penhoet, E. D. et al., *Organ Procurement and Transplantation*, Washington, D.C., National Academy Press, 1999.
2. Health Care Financing Administration, O.o.t.A., National Health Statistics Group., *Table 9: Personal Health Care Expenditures, by Type of Expenditure and Source of Funds: Calendar Years 1992-99*, 2001.
3. Owings, M. and L. Kozak, *Ambulatory and inpatient procedures in the United States, 1996 National Center for Health Statistics.* Vital and Health Statistics, 1998. stat(13)(139).
4. Essex-Lopresti, M., *Operating theatre design.* Lancet, 1962. **353**(9157): p. 1007-10.
5. Essex-Lopresti, M., *The anesthetist and theatre planning.* British Journal of Anesthesia, 1963. **35**: p. 649-653.
6. The UNOS webpage. Available at www.unos.org
7. D.B. Petitti, *Meta-Analysis, Decision Analysis, and Cost-Effectiveness Analysis*, Oxford, Oxford University Press, 2000.
8. Roberts, M.S., D.C. Angus, C.L. Bryce, L. Weissfeld, J. Stahl, and A.J. Schaefer, “The Optimal Timing of Liver Transplantation Simulation Model: Background, Rationale and Structure”, working paper, Center for Research on Health Care, University of Pittsburgh, Pittsburgh, PA, 2002.