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A new organ transplantation location–allocation policy: a case study of Italy

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Abstract In this paper, we propose a location model for the optimal organization of transplant system. Instead of simulation approach, which is typical when facing many health care applications, our approach is distinctively based on a mathematical programming formulation of the relevant problem. In particular, we focus on the critical role of time in transplantation process as well as on a spatial distribution of transplant centers. The allocation of transplantable organs across regions with the objective of attaining regional equity in health care, is the aim of this paper. Our model differs from previous modeling approaches in that it considers the nationwide reorganization of the transplant system, identifying system barriers that may impair equity and efficiency. The demolition of these barriers may leads on a reduction of waiting lists and of wasted organs. We provide the basic structure and the properties of the model, and validate it on a real case study. The experimental validation of the model demonstrates the effectiveness and robustness of our proposal.

Keywords Organ transplantation · Facilities location · Optimal allocation · Prioritization rule · Mathematical programming

1. Introduction

The allocation of scarce donated organs is both an increasingly complex clinical and social problem, as well as a challenging example of mathematical programming problem formulation. The processes leading to donor identification, consent, organ procurement and allocation continue to dominate debates and efforts in the field of transplantation. A huge shortage of donors remains while the number of patients needing organ transplantation increases. For instance, in Italy, at the end of 2003, the number of donors was only 21 per million of population. Nevertheless, the data show a slow increase of donors over the years. The 2003 Italian data (Italian Ministry of Health, National Transplant System) show that the number of patients waiting for a kidney was 6554, for lung was 1461 and for heart 636. The mean waiting time ranges from a rate of about 1.5 years for a lung to 3.3 for a kidney. The mortality rate of patients waiting for an organ is between 1.29% for a kidney and 12.32% for a lung. This despite Italy is one of the countries with the lowest patient mortality rate. The problem of long waiting times for transplant candidates and the continual growth in waiting list size underscores a simple reality: supply of organs does not meet the need. This evidence has produced substantial debate about the mechanisms for allocating organs to potential recipients, with issues of fairness, efficiency and regional versus national interests ([1, 2]).

When summarizing the transplantation process, many issues arise that involve the transplantation context. The following discussion focuses on the key issues that are most relevant for the purposes of our study:

- the factors considered in the development of an organ allocation policy;
- the design of a equitable transplant system.

Organ allocation procedures must make some difficult choices. In order to optimize transplant outcomes, the allocation policy must maximize the number of clinical matches between the tissue type of the donor

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and the tissue type of the recipient. However, assigning priority based only on clinical information is deemed inequitable, because it restricts access to transplantation to the candidates with the most common tissue types. To alleviate this concern, the allocation system also assigns additional priority points based on each candidate's waiting time. The ultimate allocation decision depends on the total priority points. Some others criteria could be present in this process. To be more specific, generally two elements determine the allocation of organs for transplantation. The first is the prioritization, currently comprised of two factors: the mean waiting time and the severity of illness. The prioritization determines to which patient, within a waiting list of patients, the organ will be allocated. The second element affects the distribution of organs among different areas of the country. This part of the system determines to which waiting list the organ will be offered first. Because these elements are so closely linked, the distribution scheme may act as defacto prioritization scheme leading to inefficiencies and distortions.

As far as the design of the transplant system is concerned, we have to take into account the spatial distribution of some organizations (referred as OPO—Organ Procurement Organization in the USA), that play a crucial role in the design of a fair end equitable transplant system. These organizations, operating in distinct geographic regions, are responsible for procuring all the organs donated in their region and allocating them to the candidates registered on their transplant waiting list. They offer services in organ donor referral, evaluation and surgical recovery, and coordinate the organ procurement transplantation process in designated service area.

It is worth to note that also other countries (for instance Italy) have similar organizations with the same functions and characteristics. In the rest of the paper, we shall refer to these organizations as OPO, but it is clear that the applicability of the proposed model is quite general. Once the candidates are prioritized, the OPO offers the organ to the top priority candidate. If the candidate is readily available, the transplantation is performed, otherwise the organ is offered to the next candidate and the procedure is repeated until an available candidate is found. Under this allocation scheme, organs are transplanted locally, i.e., into candidates that are registered on the waiting list of the OPO that procured the organ.

As evident, the actual allocation scheme is affected by issues of geographic proximity and spatial distribution, although in the principles of policy-makers, health administrators and many analysts, the importance of equity is beyond discussion (see [3] for a conceptual discussion). Despite this general agreement, however,there is not a generally accepted definition of equity and consequently is not clear how equity should be measured. Following the notation of [29] we define equity as the absence of differential effects within a population caused by an action. In a facility location context the action is the siting of facilities and the effect is the impact of this distributional decision.

In operational terms, and for the purposes of this study, the action is the location of the transplant facilities in a region, while the effect is the patients likelihood of receiving an organ. The principle of equity should be present in all the phases of the transplantation process. Before transplantation, equity can be achieved by equalizing the transplant eligibility among patients with the same needs but belonging to different areas. Here for eligibility we mean the priority of the candidate in the waiting list. The transplant candidate with higher priority leaves the waiting list to obtain a transplant. The transplantation is performed on condition that the recipient reach the transplant hospital in a reasonable time. Therefore, once the organ is allocated, the access of the transplant service can be measured in terms of distance to the nearest hospital or time taken to travel to the health facility. That is, in our case, two individuals with the same severity of illness, but perhaps from different groups, are being treated equitably when they have the same likelihood of access to the organ. The probability of receiving an organ clearly depends on the size of the waiting list in which the patient is registered. This size is influenced by the location of the OPOs within the national area.

It is now well recognized that there exists an important trade-off between the two criteria of efficiency and equity used in the allocation policy. This trade-off has been studied in [4], where it was demonstrated that because of the continued shortage of organs, priority points assigned on waiting time dominate any points accrued as clinical compatibility. Hence, the allocation policy becomes essentially a first come first transplanted policy.

This directly refers to the distribution and design of health care resources and policies and, in particular, the spatial distribution of OPOs, the definition of the related organ donor referral area and the location of transplant-performing hospitals play a crucial role in the design of a fair end equitable transplant system.

Our contribution is placed in this respect. In particular, we propose a mixed integer linear programming model to face the problem of transplant system organization. The proposed model can be used to analyze simultaneously:

- the location problem of OPOs and referring donor hospital and transplant centers (the more hospitals an OPO has referral agreements with, the greater its scope and the more donors it is likely to procure),
- the districting problem,
- the waiting lists balancing problem.

These issues have a crucial role for the fairness and the equity of the transplant system, because they affect the distribution of organs among different areas of the country.

Only a few countries have adopted legislation of presumed consent for organ donation. This strategy, aimed to increase cadaveric organ donation, is in fact the policy of many European nations [5]. Our model has a very wide application and can be used in a context of presumed consent or not. The only difference is that in countries with presumed consent, the organs are explanted after the death, unless an individual specifically requests to not donate while still living.

The rest of the paper is organized as follows. In Section 2, we provide a description of the current transplant systems organization and we review the literature in this field. In Section 3, we give a detailed description of the mathematical formulation of the proposed model. Section 4 presents a case study for which computational results are reported. Finally, conclusions and suggestion for future work are given in Section 5.

2. The transplant system

The goal of an efficient and fair transplant system is to allocate organs in a equitable and timely fashion. A fair and efficient transplant system should guarantee the greatest survival rate, for patients and for organs used, equality, across OPOs and nationally, and limited costs. The logistics of coordination and organ retrieval could vary from one country to another, but the principles remain the same.

When donor organs become available after an individual dies, an organ procurement organization (OPO) takes the organs into custody. The OPO then matches the donor organs with the appropriate transplant patients, by gathering information about the donor organs. Generally, a ranked list of transplant patients, who can receive the donor organs, includes, typically, the following information:

- organ type, blood type and organ size;
- level of medical urgency;
- distance from the donor organ to the patient;
- time on the waiting list.

The last two information are affected by the spatial distribution of the transplant centers with respect to the position of the waiting patients. That is, the distribution system causes a distortion in the prioritization system. Moreover, for historical reasons, the distribution system offers the organ first to patients in the local area, then to the regional area, and finally to the nation at large. The concept of the local use of the organs has been called "local primacy." The policy of local primacy has the side effect of affecting prioritization scheme in an implicit and explicit way. The hide effect is the de-facto rule of assignment of the harvested organ to the first arrived patient. The apparent effect of local primacy is the presence of distance consideration in current allocation policy. In fact, the system advantages potential recipients who are registered at or near a donor hospital, over those who may live at a greater distance from the donor facility. In addition, the area that an OPO covers is based on historical boundaries and can vary in size, from part of a city to a whole state. OPO borders are drawn at the county level and may cross-state lines. Furthermore, the OPOs may administer non-contiguous areas.

The reasons that the current system operates this way is historical. In USA, for instance, prior to the formation of the national system in 1987, many OPOs existed and each served its own area. When the national system was introduced, the OPOs boundaries were maintained. The same situation occurred in Italy, where the Inter-Regional Centers (CIR) continue to be part of the national transplant system.

Once the appropriate candidate is located, the organ procurement organization takes the organ and delivers it to the transplant center where the transplant will be performed. This entire process must occur very quickly, as organs are only transplantable for a short time period after they have been removed. The elapsed time between removal and implantation is critical for the organ because organ quality deteriorates as the elapsed time increases. Organs cannot be used if they have been waiting more than an upper bound time known to clinician as "cold-ischemia time." Therefore, the organ decay rate and the distance the organ travels determine the optimal size and distribution of regions. In fact, the transplant failure mostly depends on the quality of the harvested organ.

The time spent in the transplant process has two components. For the organ, the first segment of travel time is between the explantation and the arrival to the transplant center. The second segment of waiting refers to the time spent by the potential host traveling to the transplant center. To increase the likelihood the organ will find a recipient within the cold-ischemia time, the organ retrieval team should explant the organ and then travel to the transplant hospital in the faster possible way. On the other hand, the patient has to travel several kilometers to the transplant center to receive the organ. Because each OPO has a single list of patients who are awaiting transplantation, the current system appears to create a context of inequality between patients in different regions, measured in terms of mean waiting time. The number of people waiting for a transplant varies greatly between regions, as does the time they must wait for an available organ. Typically these disparities are measured by mean of waiting time, the generally accepted measure for regional equity.

The model proposed in this paper seeks the optimal location of transplant centers, donor centers and OPOs, in order to reduce the total transplant system time, to improve efficiency and to equalize waiting time across the entire country.

Most of the literature concerning the transplantation problem focuses on policy for allocating donated organs to waiting patients. A simulation model that allows a comparison of different policies for allocating donor hearts on pre-transplant outcome is given in [6]. Similarly a punctual evaluation and comparison of different allocation methods for renal transplant has been carried out in [7].

The technical efficiency of OPOs has been analyzed using DEA in [8]. A discrete event simulation model of the USA liver allocation system is proposed in [9]; the model has been validated with data from patients of the University of Pittsburgh Medical Center; different selection and organ allocation rules are compared in terms of life expectancy, size of waiting list, and other relevant outcomes characteristics of the transplantation process.

The problem of allocating kidneys to autonomous transplant candidates, who may refuse a kidney in anticipation of a superior future kidney, is described in [10]. The authors represent the kidney allocation problem using a sequential stochastic assignment model. The reward from allocating a kidney to a particular candidate depends on both their types. The objective is to determine an organ allocation policy that maximizes total expected reward. Deciding eligibility for kidney transplantation is the goal of [11]. A decision model calculates the minimum predicted one-year graft survival rate maximizing quality-adjusted life expectancy. The survival rate depends on the patient's health and demographic characteristic. Selecting the best time for kidney transplantation is the problem treated in [12]. A theorem that helps solve the dilemma of early kidney transplantation is proposed and related formula is given.

It is worth mentioning that most of the previous works are simulation models, aiming at examining how different allocations policies can affect the national transplant system performance, in terms of patient outcomes, waiting times, and equity across different patient groups. The role of operations research in a complex and critical public policy problem, as the organ transplantation problem, does not have to confine itself to descriptive model. The design of a fair and efficient transplant system has received very little attention. Our work moves toward this direction.

To the best of our knowledge the only work in this perspective is [13]. The purpose of that paper is to determine the optimal configuration of transplant regions in which the USA is currently divided, in order to maximize total intra-regional transplant. The allocation criteria underlying this model is local primacy. Because of the concept of local primacy, the current system ties the OPOs as units for organ procurement with the units for organ distribution. The factors that determine the best geographical boundaries for organ procurement may not be expected to be the same factors that determine the best unit of organ distribution.

Our model relaxes the concept of local primacy disconnecting the procurement role from the distribution role of OPOs. The demolition of these system barriers would result in greater equity, fairness and efficiency, in terms of reduction of waiting lists and wasted organs. A simulation model that reproduces the actual transplant experience has been proposed in [14]. Using this model to test alternative allocation policies, the authors showed that proposed changes to remove regional preference would have a profound impact on liver transplant survival, with a decrease in the number of candidates who die while waiting.

3. Model description

In this section, we design and formulate our Transplant Location Allocation model (TRALOC model for short). TRALOC is clearly not able to fully capture the complexity of the transplant system. Nevertheless, the assumptions we made are quite general and allow an elegant and easy formulation. We make clear that the objective of our study is to make the appropriate simplifications that lead to a tractable model, whose solution achieves three important goals:

- determine the districting problem that concerns the best partitioning of a region into OPOs;

- assign the explantation-performing hospitals and the transplant perfoming hospitals to the referring OPO;
- balance the mean waiting time of patients on the transplant waiting lists among different areas.

First of all, we discuss the key issues and the basic assumptions that are most relevant for the purposes of our study.

In general, each OPO may serve none, one, or more than one transplant center. We consider each OPO having a single main transplant center. Organs that match patients are transplanted here. This leads to an equivalence between the location of OPOs and the location of the Transplant Centers. The organs are harvested in the explantation-performing hospitals. We assume that each patient chooses the closest OPO and can be registered only in the related waiting list. This assumption increases the equality of the system. In fact, within the typical organization of a transplant system, patients with sufficient resources may be listed as potential organ recipients at two or more transplant centers. This, however, shifts the responsibility of choice to patients who are sufficiently knowledgeable to seek the best deal and affluent enough to pay for the additional travel, doctor visits, etc.

Let $I = \{i : i = 1, 2, ..., M\}$ represent the set of explantation centers and $J = \{j : j = 1, 2, ..., N\}$ be the set of potential transplant centers. Each explantation center $i \in I$ will belongs to one OPO $j \in J$ and will refer to one transplant center. We fix the number p of OPOs to be opened following the general framework of the p-median problem [15, 16]. The number of OPOs to be opened depends on the extension of the region, on the national guidelines, and least but not last, on the subjective choice of the policy makers. We assume that the allocation policy is given. As we mentioned before, patients on a candidate list are prioritized in accordance with point-ranking schemes of the adopted policy. It is worth to recall that non-clinical criteria could be present. In fact, in the current allocation policies practice, points may be assigned based on waiting time, on distance from the near OPO, from transplant centers and donor hospitals. The presence of this spatial allocation criterion may advantage potential recipients who are registered near a donor hospital/transplant center, over those who may live at a greater distance from the donor/transplant facility. The location of such facilities, so as to minimize the weighted average distance of the system, introduces a fairness criterion new in this context.

As before specified, the separation among the two role of the OPOs, procurement and distribution, allows radical changes in the transplant system. In fact, the assignment of explantation centers to one OPO will be determined separately from the decision of where to allocate the unit organ procurement. From a formal point of view this leads to a separation between the set of donor hospitals and the set of transplant hospitals belonging to an OPO.

The model we propose can be viewed as a location–allocation problem. This is because with $p \geq 2$ the location of the new facilities will determine the allocation of their service in order to best satisfy the nodal demands. The p-median problem has been extensively used as a basis to build problems related to public sector facility location–allocation modeling and is one of the most popular models for public facility location problems [15, 17].

Since its formulation in the late sixties, early seventies, the p-median problem has been modified to be adapted to specific location problems or to allow a better "real world" implementation in the public sector. Services such as public schools, pharmacies, primary health care centers have benefited from this model. Considering maximum distance or time constraints in formulating a location problem leads to the notion of coverage (see [18] for a comprehensive discussion). This formulation has been used in a developed country for locating kidney dialysis machines, a form of treatment for which the patient must make frequent, repeated journeys [19]. Here we use the notion of coverage in order to enforce the technical and surgical possibility of a successful transplant. For a comprehensive review of location allocation model in health service development we refer to [20].

We assume potential recipients of explanted organs (demand points) aggregated to P locations; let $L = \{l : l = 1, 2, ..., P\}$ be the set of potential recipients with the associated annual demand h_l with $l \in L$. Once an organ is available and a clinical allocation policy assigns the organ to the first ranked waiting host, this has to travel to the transplant center. The distance the patient travel to reach the transplant facility is crucial. The organ quality and the likelihood of a successful transplant decrease as the elapsed time from organ retrieval to organ transplantation increases. A measure of travel time between the patient $l \in L$ and the transplant facility $j \in J$ is measured by means of terrestrial distance d_{lj}. We assume travel distances related to the travel time, given an average speed for terrestrial trips. The distance traveled by the organ from the donor hospital $i \in I$ to the transplant center $j \in J$ is the aerial distance a_{ij}. This is motivated by the fact that transportation of explanted organ is usually performed with the hospital emergency helicopter. This assumption broadens the organ harvesting area of each OPO.

It is now possible to give a mathematical programming formulation for our location model (TRALOC: Tansplant Location Allocation Model).

$$\min \sum_{i=1}^{M} \sum_{j=1}^{N} a_{ij}\, x_{ij} + \sum_{l=1}^{P} \sum_{j \in T_l}^{J} h_l\, d_{lj}\, y_{lj} + E \tag{1}$$

$$\sum_{j=1}^{N} x_{ij} = 1, \quad i = 1, \dots M; \tag{2}$$

$$\sum_{j \in T_l} y_{lj} = 1, \quad l = 1, \dots P; \tag{3}$$

$$y_{lj} \le z_j, \quad i = 1, \dots M, \quad l = 1, \dots P; \tag{4}$$

$$x_{ij} \le z_j, \quad i = 1, \dots M, \quad j = 1, \dots N; \tag{5}$$

$$\sum_{j=1}^{N} z_j = p, \tag{6}$$

$$E \ge \sum_{l=1}^{P} h_l y_{lj}, \quad j = 1, \dots N; \tag{7}$$

$$x_{ij} \in \{0, 1\}, \quad i = 1, \dots M, \quad j = 1, \dots N; \tag{8}$$

$$y_{lj} \in \{0, 1\}, \quad l = 1, \dots P, \quad j = 1, \dots N; \tag{9}$$

$$z_j \in \{0, 1\}, \quad j = 1, \dots N. \tag{10}$$

Here $T_l = \{j \in J \mid d_{lj} \le r\}$, where r is a coverage distance related to the cold-ischemia time t. Note that T_l is the set of all those candidates that are within an acceptable distance of the transplant center j. The maximum value preset for the travel time is the cold-ischemia time. After that time, for clinical reasons, the transplantation could not be performed. We assume the transplantation is equally good if performed in transplant centers at different distances/time, as long as these distances are smaller than the maximum value. That is, we do not take into account the decay factor of the harvested organs. This assumption, made purely for purposes of tractability, has to be relaxed in future research. Because the cold-ischemia time is different for different organs, this data cannot be aggregated. This implies that we have to solve different problems depending on the organ we are considering.

The binary decision variables are x_{ij}, y_{lj}, z_j. If the donor center i belongs to the OPO j this implies $x_{ij} = 1$. We recall that, from previous assumption, each OPO has a main transplant center servicing all demand area assigned to it. In particular $y_{lj} = 1$ if the demand point l belongs to the OPO/transplant center j. The number of OPO to be located ($z_j = 1$ if OPO j is activated) is fixed to p (see constraint (6)). As we mention before, solving the problem parametrically in p may provide valuable insight at the system design stage. Constraint sets (2)and (3) are classical p-median constraints and require that each demand node, as well as each donor center, has to be assigned to exactly one OPO. Constraint sets (4) and (5) restrict these assignments only to open OPOs.

The most important issue raised in the process of solving location problems is the selection of a suitable criterion or objective function. The formulation of an objective function depends greatly on the ownership of the organization, both whether public or private and the nature of the facilities, as has been mentioned earlier. The goals and objectives of public facility location are in general difficult to capture [21, 22]. An objective value which reflects the total travel distance but ignores equity in access to transplantation should not be acceptable in public facility location. Our problem formulation enforces equity by restricting the difference in transplant waiting list size between subgroups of candidates. The objective function, to be minimized, is composed by three terms. This objective reflects the perspective of a central decision maker who makes organ allocation decisions based on a combination of efficiency and equity criteria. The first term $\sum_{i=1}^{M} \sum_{j=1}^{N} a_{ij}\, x_{ij}$ minimizes the total distance between explantation-performing centers and transplant centers. This term reflects the first component of the waiting time as before mentioned. The second term $\sum_{l=1}^{P} \sum_{j \in T_l}^{J} h_l\, d_{lj}\, y_{lj}$ minimizes the demand weighted total distance traveled by the patients to the transplant center in order to receive an explanted organ. Toregas and ReVelle [23] showed that this formulation also minimizes the average travel distance between the sited facilities and the demand. We should raise a criticism about the sum of these two components. In fact, the two time components could partly coincide. However it should be pointed out that the time spent by the organ to the transplant center is, in most of the cases, a little fraction of the time spent by the potential host travelling to the transplant center. Furthermore, the second term is weighted by the level of demand of organs reflecting the greater importance of this term on the first one. In order to achieve also a balanced spatial distribution of services, the third part of the objective minimizes the maximum size of waiting list given that a patient belonging to the OPO j is also part of the OPO's waiting list. In fact the decision variable E is the maximum over j of the sum of requests arising from OPO j (see constraint (7)). Since the maximum waiting list size across OPOs is to be minimized, we want to find a set of locations that will give the smallest maximum waiting list size possible when evaluated for all OPOs.

The three terms in the objective function can be viewed as conflicting components to be optimized. The first component is the minimization of the total time in the transplant process, while the second component encourages the equity criterion discussed above. As in traditional multiobjective optimization we simply aggregate together all the various objectives to form a single scalar objective function. Since the different objectives have different units attached to them, the weights are not meant to imply any relative value between objectives. In other words, higher weights are associated with the objective component which more emphasis is placed on. The greatest potential use of this methodology is in the design phase of a transplant system. In the preliminary design phase, politicians, and other appropriate parties could use the model to scope out a range of alternative locations. The selection of a preferred locational decision will most likely be a compromise between objectives. The problem of how to prioritise and weight the contributions of the various objectives is not further discussed in this paper. The choice is subjective and depends on the relative importance the policy makers give to equity.

4. A case study: the Italian transplant system

4.1. Introduction

We chose as case study the Italian context. This choice has been motivated from the peculiar structure of the Italian transplant system and its consequence. The national organ sharing system is managed by the Ministry of the Health. The main organ of reference is the National Transplant Center (CNT). The CNT ensures the coordination of the regional and inter-regional Centers, controls all the structures in which the organs are explanted and transplanted. From CNT directly depend three Inter-Regional Centers (CIR): the North Italy Transplantation (NITp), the Inter-Regional Association of Transplantation (AIRT) and the Center-South Organization of Transplantation (OCST). The Figure 1 shows the territorial distribution of the three CIR in Italy.

As far as the organ donation is concerned, we remind that in Italy this is regulated only by the public system, on the basis of presumed consent by the donor. There is not private sector for organ donation.

Fig. 1 Territorial distribution of CIR in Italy

The Italian Transplant System is substantially based on the same management rules and adopts the same allocation policy of the USA system. From a conceptual and functional point of view, the Italian CIRs are analogous to OPOs. The area that a CIR covers is based on historical boundaries. Each CIR may serve, differently from OPO, not-contiguous regions. This fragmentary distribution of CIRs within the national area evidently leads to organ allocation distortions.

To make it clear, we describe an example of inefficient organ allocation. We recall that when an organ becomes available within a region, this will be offered first to regional waiting list, then to the CIR waiting lists, and finally the the nation at large. The organ allocation for transplantation is based on prioritization scheme. Different criteria can be adopted, as we mention before. The basic criterion used in Italy ranks all patients, waiting for the organ, on the basis of the degree of histological compatibility. An organ is a "local resource" because is considered as "produced" in the region in which is available. In this framework the concept of local primacy, like in OPOs, is respected. Coming back to our example, if an organ becomes available in Puglia (region belonging to the AIRT) is to be offered to the patient who had the most priority on the local waiting list. We suppose the eligible patient living in Piemonte. Having a single list within the AIRT forces to offer first the organ in Piemonte that belongs to the same CIR, bearing a higher traveling cost and, above all, taking higher risks. A patient with higher priority, but listed for examples in the OCST, does not have access to that organ. Evidently in the same clinical condition, the likelihood of a successful transplant strongly depends on the organ cold-ischemia time. A patient

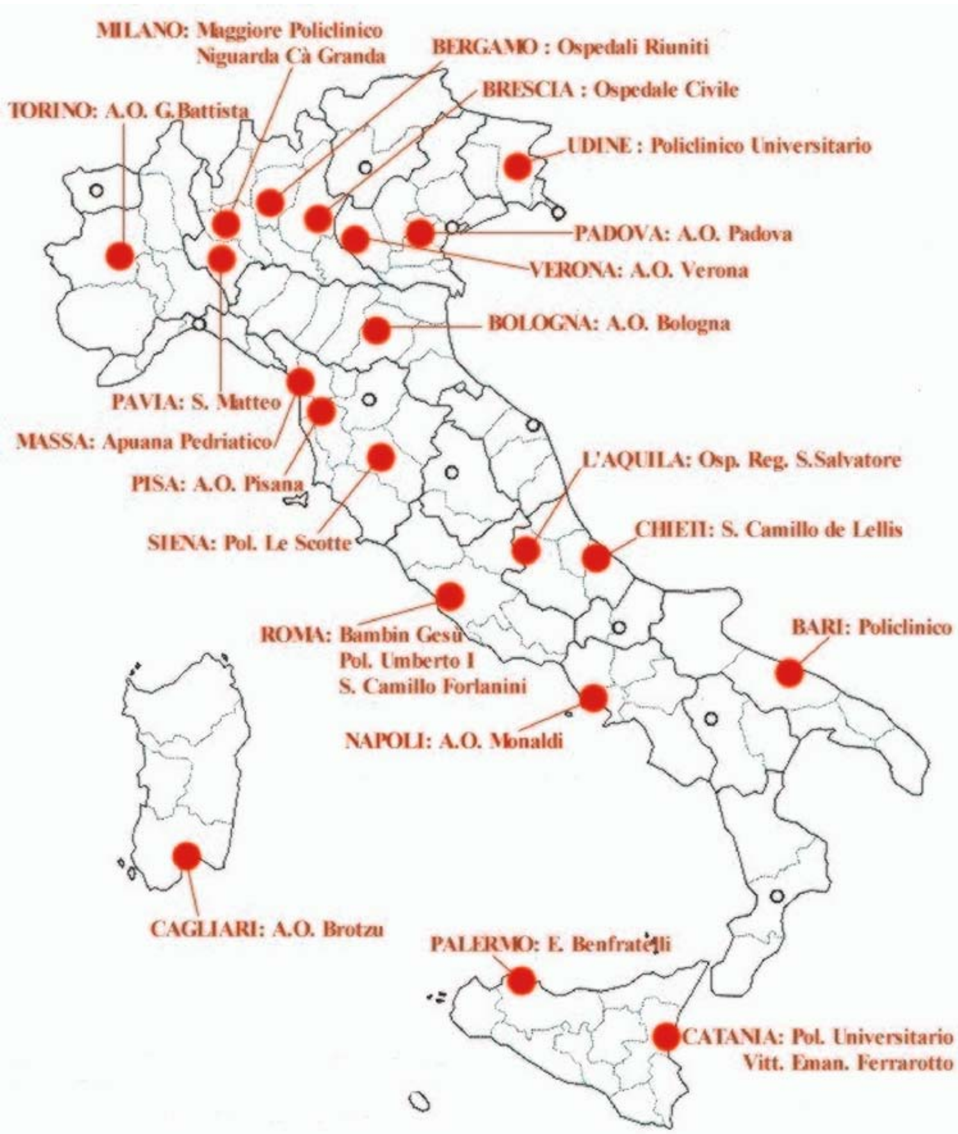


Fig. 2 Distribution of the 20 tranplant centers for the heart

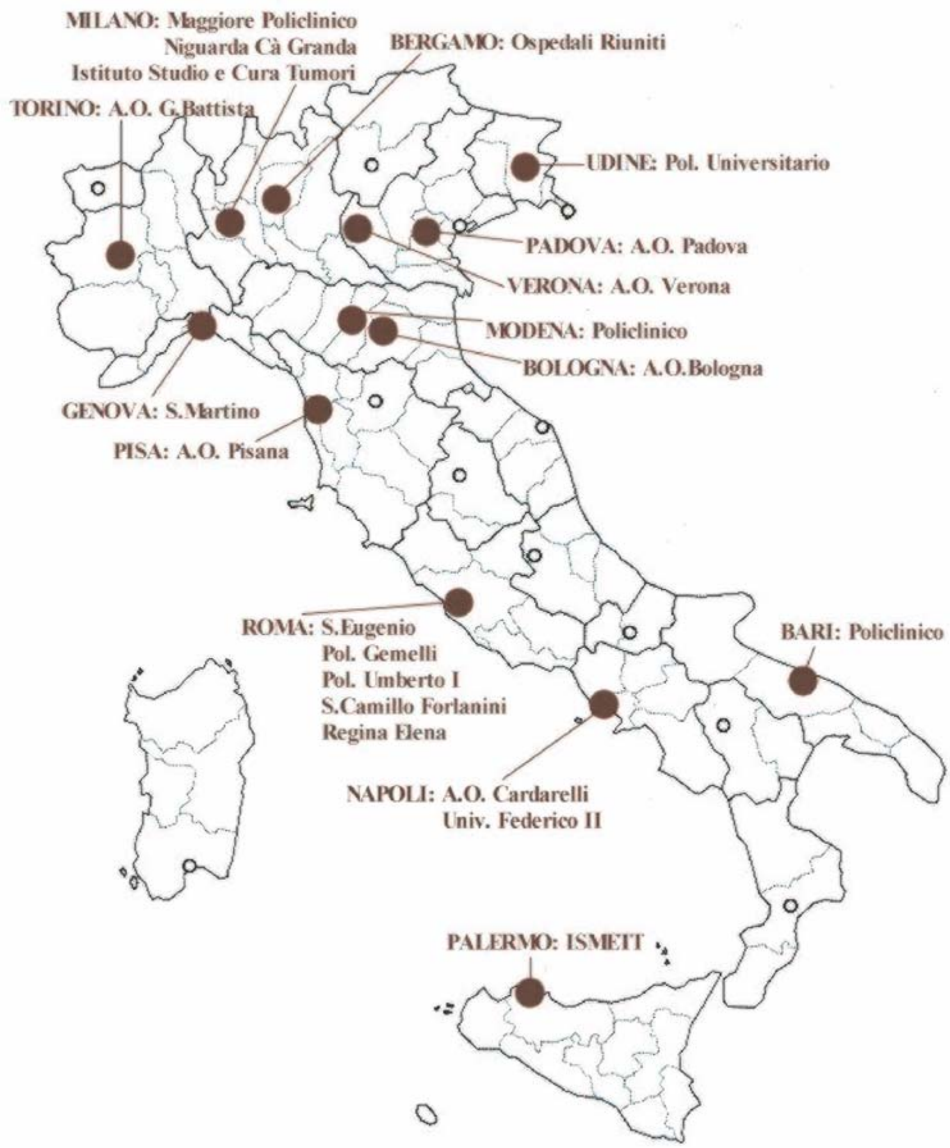


Fig. 3 Distribution of the 14 tranplant centers for the liver

waiting in Calabria (OCST) would have taken greater advantage of the transplant, simply for the better condition of the harvested organ.

The Figures 2, 3 and 4 show the number and distribution of transplant center, respectively, for the heart, liver and kidney (these organs will be considered for the application of TRALOC model).

In conclusion the actual CIR distribution affects the organs allocation policy and produces unexpected and unwanted consequence as the precedence of the distribution scheme over the priority scheme. Moreover, analyzing the Transplant Centers localization within the national area, differences and iniquities in access become evident. Last, but not least from an organizational point of view, the actual Transplant Center location implies a high resource duplication in the well-served areas and a resource absence in the disadvantaged ones.

4.2. Application of TRALOC

With the aim to asses and validate our model, we applied it to the Italy transplant network. Geographic data, demand data and potential locations for siting OPOs, were obtained through publicly available data from the official site of the Italian Ministry of Health [24]. The national area is divided into 20 regions and 105 provinces. In particular each province represents a demand node and, therefore, our problem is a 105-node network. Each node is at the same time a demand point, with an associated value of demand for each organ, and a location of an explantation-perform-

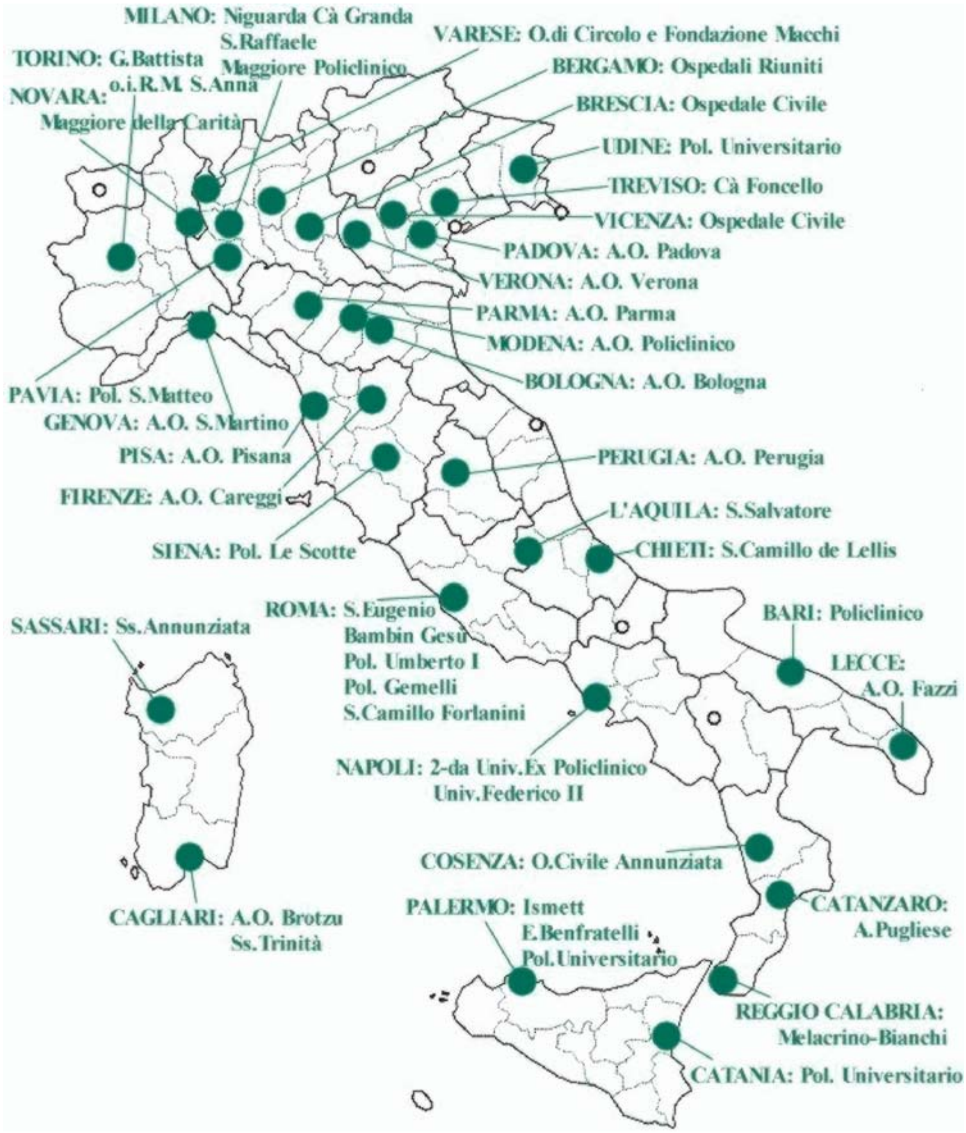


Fig. 4 Distribution of the 33 tranplant centers for the kidney

ing hospital. We have also defined the set of potential transplant centers, selecting 52 potential locations in such a way to have a balanced geographical distribution. Hence $I = \{i : i = 1, 2, ...M\}$ is the set of explantation-performing hospitals, $J = \{j : j = 1, 2, ...N\}$ is the set of potential transplant centers, $L = \{l : l = 1, 2, ...P\}$ is the set of potential recipients, with, respectively, $M = 105$, $N = 52$ and $P = 105$. Then we have worked out the aerial a_{ij} and terrestrial d_{lj} distances to complete the graph's definition. The organs demand h_l at each demand node has been calculated using the regional values of the waiting lists at December 31, 2003.

We have assumed that each OPO has a circular coverage area. For each organ, we have defined the covering radius r, using values proportional to the cold-ischemia time t. In particular we have worked up the coverage radius by the formula $r(t) = t * average\ speed$, considering an average speed of $90 km/h$. We have considered three different values of the critical time t for the coverage radius: t, $t/2$ and $t/3$. We tested these three values in order to evaluate the sensitivity of the solution to different safety levels; in fact higher is this value, farther is the potential host. Because in our model the number of OPOs to be opened p is

Table 1 The cold-ischemia time (in hours) for different organs

	Heart	Liver	Kidney
t = *cold ischemia time*	5	12	18

Table 2 Values of p chosen

Values of p	Heart	Liver	Kidney
$p{*}_{r(t)}$	4	1	1
$p{*}_{r(t\backslash 2)}$	9	3	2
$p{*}_{r(t\backslash 3)}$	18	5	3
p_{act}	24	21	44
p'	15	10	20
p''	30	16	30

fixed, there is no correlation between this value and the critical values of t chosen. Nonetheless, the link between the minimum number of OPOs required to cover the system area $p{*}$ and the values of t has been investigated. As we expected raising the safety level of the system implies higher costs in terms of minimum number of OPOs needed. More generally, the choice of these values is up to the system planner who might also impose different restrictions for different organs.

The Table 1 shows the values of t for different organs.

We have tested different values of p (number of OPOs to be opened), on the basis of the knowledge of the minimum required number $p{*}$: the actual number p_{act} of transplant centers located in Italy and other two arbitrarily chosen values p' and p''. In fact, despite the number of OPOs to be opened is fixed in the model, it would be interesting for the policy makers to evaluate alternative choices in preliminary design phases or to assess the performance of the actual system in subsequent phases of the system design. In particular, the choice of p_{act} allow us to compare the actual configu-

Fig. 5 Optimal distribution of the heart transplant centers with service areas

ration with the optimal configuration leading from the experimental results. The minimum number $p*$ has been determined by the solution of a problem derived from TRALOC with an added penalty term in the objective function and without restriction on the number of OPOs to be opened. This added term has to penalize the number of OPO to open. Obviously we have different values of $p*$ for different values of covering parameter r. The values of $p*$ are useful to choose correctly the values of parameter p used in the different instances of the model. If the minimum number of transplant center to be located exceeds the value of p' or p'', we do not solve the corresponding problem. Table 2 summarizes the values of p chosen.

In this way, we have obtained 44 different instances referred by using the notation $organ - r(t) - p$. Finally, in order to evaluate the influence of the parameter E in the objective function, each problem instance has been solved again but without this term.

4.3. Results

The computational experiments have been carried out on a Pentium 3 processor. The numerical results have been collected using the state-of-the-art software Lingo 6 Extended [25].

A first set of experiments was carried out with the aim to investigate, for each organ, the minimum value $p*$ of p. The values $p*$ obtained for each organ can be extracted from Table 2. In order to show the poor efficiency level of the actual Italian Transplant System, we compare the real situation with that obtained from

Fig. 6 Optimal distribution of the liver transplant centers with service areas

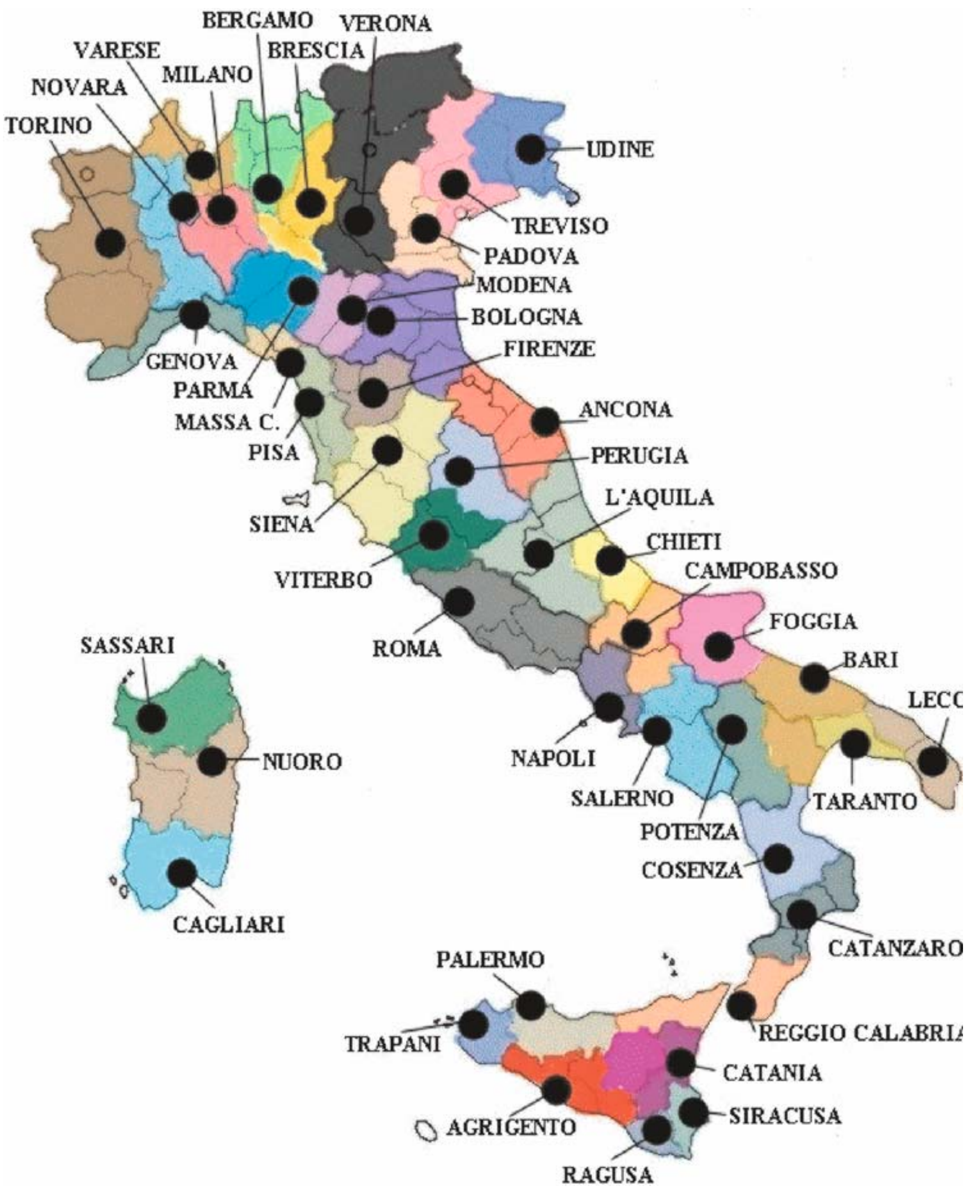


Fig. 7 Optimal distribution of the kidney transplant centers with service areas

the TRALOC model. In particular, the validity of our model becomes evident when we compare the computed optimal solution with the actual configuration of transplant centers for each organ.

Figures 5, 6 and 7 show, respectively, the optimal transplant centers location with the relevant optimal service areas for the problem instances He_r(t\2)_p_{act}, Li_r(t\2)_p_{act} and Ki_r(t\2)_p_{act}. For the same problem instances, Figures 8, 9 and 10 report the optimal acquisition areas configuration for the transplant centers located by the model. By comparing the actual distribution of the transplant centers, the TRALOC model determines in all the cases a better and more equitable transplant centers location, because of a better balanced spatial distribution of the transplant centers over the national territory. It is important to note that analogous behaviors have been observed for all the other problem instances.

We recall here that, differently from the actual limiting situation, our model admit a separation between organs "acquisition areas" and "service areas." More specifically, we have a set of demand points served by an OPO and a set of donor hospitals offering the organs. These two sets may not coincide due to the differences between the aerial and demand weighted terrestrial distances. As mentioned before this assumption destroys the *de facto* local primacy criterion.

It worth to mention here that treating separately each organ gives the best allocation of OPO within the area of interest. Nevertheless the decision maker can

Fig. 8 Optimal distribution of the heart transplant centers with acquisition areas

decide to enclose transplant centers for different organs in the same OPO.

Other experiments have been carried out to show the trade-off between the number of OPOs and the total waiting list in the system. Rather than analyzing the effect of the variation in the number of OPOs on the total waiting list, we have considered the length variation in the waiting list of the most congested OPO. With this aim we analyzed the variation of the E value in the objective function as a result of the decrease of the number of OPOs in the system.

As we expected, lower the values of p leads to higher value of E. This evidence confirms the classical trade-off between equity objectives to be pursued and level of resources to be utilized. In particular Figures 11, 12 and 13 give evidence of this fact for each organ and for each r.

This behavior can be explained observing that a low number of center to be opened imposes a high value of E, that is a higher length of waiting list for that organ. We observe a substantial reduction in the waiting list even for little improvements in the number of transplant center to be activated.

Another set of experiments has been carried out to investigate the influence of the additional term E in the objective function, with respect to the behavior of the model without this term. In fact, the effect of this term can be appreciated in the problem instances $\mathtt{He\_r(t\backslash 2)\_p}*_{(\mathtt{r(t\backslash 2)})}$, in which we observe a reduction of 7.62% in the waiting list simply by adding the term E in the objective function. Higher reduction (42.35%) can be observed for the problem instances $\mathtt{He\_r\ (t\backslash 3)\_p}_{act}$. For this last test problem, thank to the presence of this term, the highest waiting list, that would

Fig. 9 Optimal distribution of the liver transplant centers with acquisition areas

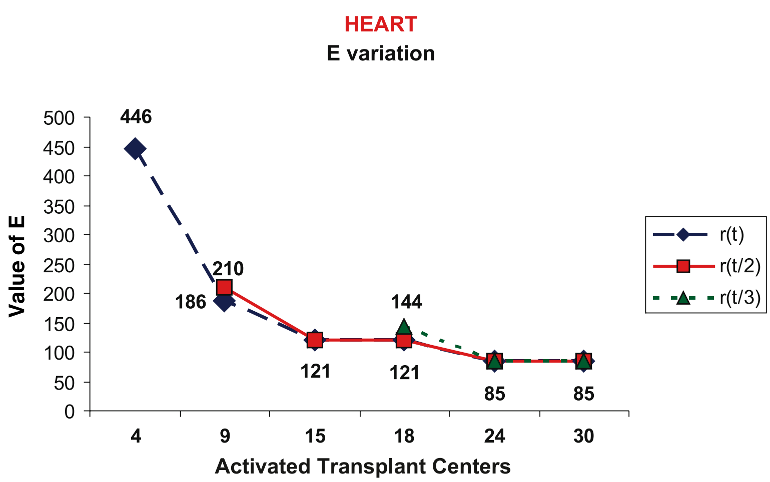
be obtained from the model solution in case we had skipped the term E in the objective function, has a reduction of 3.1%.

5. Conclusions

The contribution proposed in this paper was basically motivated by the observation that the current system of organ allocation (not only in Italy, but in most of the developed countries) is hampered primarily by geographic inequalities in waiting times among various areas of the country. Equalizing waiting time should be the goal of a socially optimal transplant system. Disconnection of the OPO as the unit procurement from the unit of distribution will be necessary. In the present work has been proposed a new model to be used as a logical framework for the decision making process. The model addresses the equity problem considering on the same time the specificity of the health sector considered. The inclusion of clinical parameter as the cold-ischemia time and the related decay factor, is a first attempt to provide an holistic view of this complex problem involving different challenging aspect. Previous models for the design of national transplant systems have not accounted for equity and have focused on single aspects of the transplant process. Although the novelty of the model, we mention here several weakness to overcome. The first aspect relates to the unrealistic assumption about the patients' choice of the OPO in which to be registered. Often distance considerations are not the only criteria considered by

Fig. 10 Optimal distribution of the kidney transplant centers with acquisition areas

Fig. 11 Heart: E variation in function of the activated transplant centers for different values of r



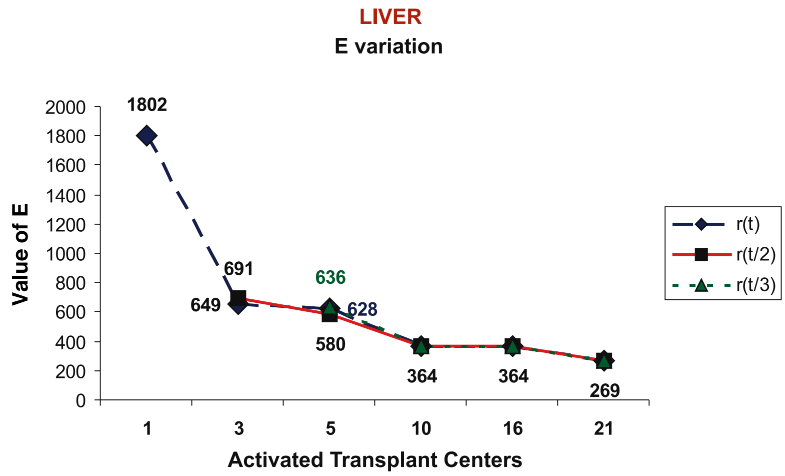


Fig. 12 Liver: E variation in function of the activated transplant centers for different values of r

the patients. Furthermore the willingness of the living potential donors to donate can be affected by the OPO size or the perception of OPO's fairness. In our model this issue was ignored. We identify the demand areas as usual in the p-median problems. That is, in order to implement the discrete problem in a real world setting, we performed a spatial aggregation of the demand. This can leads to distortion in the solution of the problem depending on the granularity level chosen. We believe that our choice is a good compromise between the clarity of the results and the real world situation. In this paper we addressed the accessibility topic ignoring the needs of the system to evolve in response to changing conditions, as well as short-term fluctuations in the availability of service providers as a result of their being busy serving other patients [30]. In particular, demand, cost and travel distance or travel time data are assumed to be fixed and not random in our model. Although in our view, there is no reason to consider the short-term availability of the hospital facilities, being the transplantation process a rare event, we may consider the randomness of the demand to extend our model in a probabilistic way. Long-term uncertainty about the conditions under which a system will operate could be taken into account in order to make location decisions robust with respect to uncertain future conditions. We believe that adaptability, robustness and reliability will become increasingly important in future applications in health care. An other natural extension of the TRALOC model could be the relocation of the existing OPOs, considering the past locational decisions and predicting the patients' flow.

There are studies which have explicitly addressed the efficiency of earlier locational decisions. Among these are those by [26, 27]. In both these studies, the problem of locating optimal sites was considered as a p-median problem. Mehrez et al. [28] conducted a study to locate a new hospital in Israel using location–allocation models in conjunction with the Analytic Hierarchy Process (AHP) approach. First the problem was analyzed using the p-median method.

Finally, the model has not yet been fully validated with real-life data. We hope that a validation with real

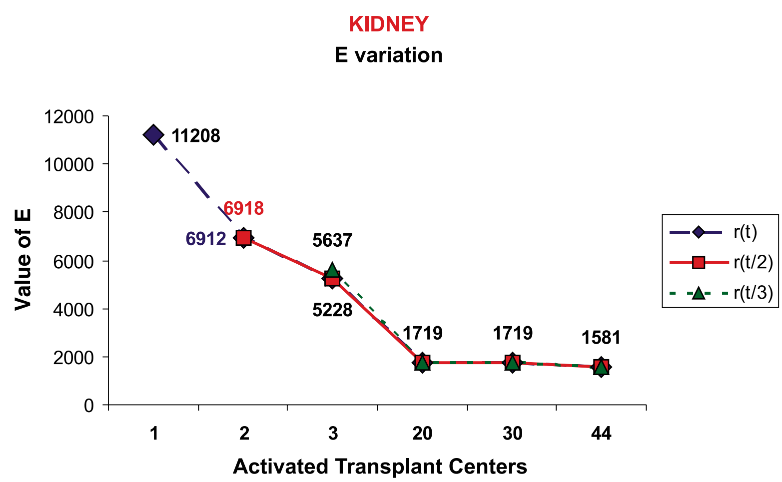


Fig. 13 Kidney: E variation in function of the activated transplant centers for different values of r

world data will show the ability of our mathematical modelling effort to effectively suggest viable solutions to the transplant system design problem.

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