AN INTELLIGENT AGENT SOLUTION

FOR THE KIDNEY DISTRIBUTION

AN INTELLIGENT AGENT SOLUTION FOR IMPROVING THE EFFICIENCY OF THE KIDNEY DISTRIBUTION PROCESS

By

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Abstract

Kidney transplantation is an effective treatment for renal disease that was previously fatal. However, the demand for donor kidneys far exceeds the supply. Due to the scarcity of volunteer donors, the cadaver organs that are retrieved must be optimally utilized. By expanding organ retrieval and sharing pools and improving donor-patient matching algorithms, the utilization of donated organs is enhanced and encouraging medical results are obtained. However, the benefits of enlarged donor and recipient pools may be offset by increasing complexity and decreasing efficiency in the organ distribution process thus increasing cold ischemia time. It is critical to improve distribution process efficiency in order to minimize the time taken to complete the entire process, and thus further enhance patient and graft survival. I attempt to apply supply chain management concepts, agent technologies, mobile communication technologies and decision-making theory to improve the efficiency of the cadaver kidney distribution process. In this thesis I analyze what are the bottlenecks in current cadaver kidney distribution and investigate how agent technology can be applied to improve this process. I propose a distributed multiagent system operating in a mobile and wireless communication environment to assist transplant coordinators in coordinating with multi-parties in this time-critical distribution process. A prototype system has been developed to help transplanting coordinators in allocating the kidney recipient.

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Chapter 1

Introduction

In this thesis, I attempt to apply supply chain management concept, agent technology and decision making theory to improve the efficiency of the cadaver kidney distribution process.

Renal transplantation has been accepted as a form of therapy for in chronic renal failure patients. During the last few years, there have been significant improvements in the area of kidney transplant. This operation is easier than other major organ transplants. Patients can be treated with dialysis (to filter the blood and remove fluid and waste products) until a suitable kidney donor can be found.

A healthy kidney can be obtained from a living donor (maybe a blood relative or an unrelated donor, such as a spouse) or from a donor that has recently died, but has not suffered kidney injury.

Transportation of the healthy kidney is done in a cooled saline solution that preserves the organ up to 48 hours, permitting the necessary analyses to determine blood and tissue donor-recipient matching (this matching is done before the operation). (*Medical Encyclopedia*)

Although the renal transplantation, in comparison to dialysis, is lifesaving and makes patients live longer, the success of transplantation as a form of treatment for end-stage renal disease leads to increasing numbers of patients on the waiting list. Unfortunately, this increase over the years has been aggravated by a fall in the number of available cadaveric kidneys. Only a few patients with end-stage renal

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failure are lucky enough to obtain a kidney promptly (Toledo 1986). A majority of such patients in the world wait long before a suitable cadaver kidney is available. For example, in Ontario, Canada, during the past 2 years, the number of cadaveric donors recorded by the Ontario Trillium Gift of Life Network (TGLN) has decreased by 23%. In Canada, fewer fatalities, better health care and new surgical techniques may contribute to fewer donors. Consequently, Canadians needing a kidney often face lengthy waits for transplants- up to six years in Toronto, which has some of the longest queues in the country (2000-2001 annual report http://givelife.ca/).

Since there are difficulties involved in procurement, a shortage of cadaver kidneys prevails. At present, it is unlikely to increase the donation rate dramatically to solve the donor organ shortage issue in kidney transplantation. Considering the marginal donated kidneys, the cadaver organs that are retrieved must be optimally utilized. Researchers have made efforts to maximize the use of donated kidneys, optimize organ graft outcomes and enhance the fairness of accessing organ transplants.

To optimize organ graft outcomes, one current method is to expand organ retrieval and sharing networks. With the further expansion of organ retrieval and sharing network to enhance matching and equitableness, more participants and larger geographical areas are involved in sharing data for decision-making. The complexity of this process increases as the number of kidneys and potential recipients increase. As the process becomes more complex, the benefits of enlarged donor and recipient pools (to maximize matching and enhance fairness) may be offset by decreasing efficiency and thereby increasing cold ischemic time. Although optimized renal

allograft allocation algorithms can generate a list of optimal potential recipients, the final recipient can't be identified and confirmed just through allocation algorithms. The procedures of identifying the best available recipients for a particular kidney, transporting it to the transplant center where the recipient is and arranging the transplant operation are complex and inevitable in the kidney distribution process. The complexity of the process includes time constraints, combinations of heterogeneous information, real-time multi-point updating, real-time cooperation in operation and decision-making across different tasks, functional areas, and organizational boundaries in order to deal with problems and uncertainties.

So an efficient and effective kidney distribution management system is critical to effectively support the use of cadaver kidneys. Efficient distribution systems in cadaver renal transplantation should be evaluated from logistical efficiency, the balance of cost against rates of graft survival, and satisfying allocation criteria. With current manual processing, the kidney distribution is very inefficient and with unnecessary delays.

Although many researchers have made their efforts in the field for optimal use of donor kidneys that come available and maximizing transplant results through tissue typing/ matching within the last decades, the research on how to improve efficiency of the cadaver kidney distribution process has been largely ignored in the past and has caught attention only recently. My study just focuses on this area. My research questions include: 1) What is the relationship between inefficiency and renal graft outcome? 2) What are the tasks and bottlenecks in the current kidney distribution process? 3) How can agents be deployed to solve these bottlenecks? I

present an agent-based solution for improving the efficiency of kidney distribution processes by integrating mobile and wireless technologies into its design and implementation. In this thesis, based on my prescriptive statistics and summaries of case studies, I will give a conceptual analysis on current kidney distribution process. The conceptual analysis provides what I need for the design stage. Based on my analysis and literature reviews, I identify the bottlenecks in this process, propose an agent-based solution to overcome those bottlenecks, develop a multi-agent prototype system architecture design and implement the prototype system for future testing. The implementation is documented and attached as an appendix. These appendices include descriptions of agent interactions, agent definitions, agent programs and MIDP applications. The rest of the thesis is organized as follows. Section 2 gives a description of the traditional kidney distribution process and reports on an analysis of current inefficiency in this manual processing; Section 3 discusses why and how agent technology could solve these problems and support efficient kidney distribution management. Section 4 proposes an agent-based prototype model for intelligent collaboration, information retrieval, and problem solving under this specific medical environment. Section 5 describes the implemented prototype as part of the proposed multi-agent system and gives a detailed scenario of organizational decision-making in kidney distribution to illustrate the interactions among software agents. Section 6 presents concluding remarks.

Chapter 2

Analysis of the problem domain of the donated kidney distribution process

In this chapter, I will present the factors that influence kidney transplant outcomes, discuss the factors that affect the efficiency of donated kidney distribution, analyze the working method and logistical management in the current kidney distribution process, and then identify the features and bottlenecks of this process.

2.1 Factors that influence kidney transplant outcomes

Studies based on the analysis of national kidney allocation data in the UK have shown that a number of factors significantly influence renal graft survival. They include: 1) year of graft, 2) donor age, 3) recipient age, 4) whether the recipient had diabetes, 5) cause of donor's death, 6) cold ischemic time, 7) matching for HLA, 8) kidney exchange (Fuggle et al. 2002). On the kidney distribution issue, I should devote my attention to two of these factors, HLA matching and cold ischemic time (CIT). As noted, all of the significant factors that influence renal allograft outcome, except for HLA matching and CIT, could be identified in advance for the kidney allocation algorithm. That is to say only these two factors may change during the kidney distribution process but may others not. I wonder whether these two factors affect each other. Studies report that the best outcome was achieved with kidneys that had no mismatches at the HLA-A, HLA-B, and HLA-DR loci (000 mismatches).

mismatch at HLA-A and/or HLA-B (denoted 100, 010, 110, a favorable matchgrade) also showed improved transplant survival over transplants of all other matchgrades (Morris et al. 1999). While HLA matching as a main factor for transplant survival is confirmed by studies in Europe and the USA (Bresnahan et al. 2002), some retrospective analyses also showed that lengthy cold storage is harmful to the kidney, and in some instances the benefits from increased levels of HLA matching with kidneys that are transported may be outweighed by the harmful effects associated with increased ischemic times (Morris et al. 1999). So, in order to ensure the benefits from increases in cold ischemia time should be reduced. In the following section, I will attempt to provide further insight on the issue of balance of HLA-matching and cold ischemic time. Elements that would necessarily lead to delay of the kidney distribution will be considered.

2.2 Factors that affect the efficiency and effectiveness of donated kidney distribution

Organ transplant involves many steps and many people to ensure a good result. The primary goal of cadaver kidney distribution is the optimal use of organs procured from all cadaveric donors for achieving a good graft outcome. Efficient distribution systems in cadaver renal transplantation have several components, which include logistical efficiency, cost, and satisfying allocation criteria. Logistic efficiency in transplantation is important because of the critical impact of cold ischemia time on allograft survival. Up to now, cost has not been an important factor but will eventually have to be considered. The organ shortage has increased the complexity of renal transplantation. Many variables have to be considered when matching cadaver organ donors with recipients, especially if the best survival outcome is to be achieved. Optimal graft survival is critical for minimizing the return of recipients with failed allografts to the waiting pool (thereby minimizing another stress on this scarce resource). At the same time, this "medical" or "utility" goal has to be balanced against the need to ensure that cadaver organs are distributed fairly (with "equity"). This equity principle is of major importance in almost all jurisdictions, as cadaver donor allografts are generally regarded as a public resource (Yuan et al. 2001b).

Concerning cadaver kidney distribution, in addition to the balancing of HLA matching and equity of access to transplantation, the widespread kidney sharing network will add to the challenge of balancing the degree of medical matching and cold ischemia time. There are time restrictions on how long a donated organ can remain viable for transplantation. Presently, the time available for kidney preservation (from the time a kidney is "harvested" until the time it is transplanted with blood flow in the recipient) is 48 hours. Ideally the kidney should be transplanted under 24 hours. To avoid the marginal kidney being discarded, it is necessary to find the recipient satisfying the allocation criteria and transplant the kidney for the recipient as soon as possible. So it is critical that the distribution process itself is efficient in order to minimize the time taken to complete the overall process.

2.3 The current kidney distribution process

Because of the organ shortage, the process of managing and distributing kidneys that are available is complex and time-consuming and often surrounded by controversy. The kidney distribution process refers to procedures performed during the period starting with the event that a kidney is donated and ending at the event that the transplantation takes place. The following provides an overview of the way kidneys are currently allocated, with an emphasis on the procedures in the national and regional distribution of cadaver kidneys.

In the UK, United States and Canada, the kidney allocation systems follow a similar 3-tier national allocation scheme (see Figure 1). Within the tiers, kidneys are offered in a priority order where pediatric patients have priority over adults and local patients over national patients. At any point in the allocation scheme where more than one patient is equally eligible, a point score is used to differentiate between the patients. These points have been required as a tiebreaker for most of the kidneys allocated. The factors included in the point system of kidney allocation are shown in Table 1. In other countries, the geographic sequence and point score system of cadaver kidney allocations are similar to those shown in Figure 1 and Table 1.

Tier 1 – 000 mismatched patients priority order Local pediatric HSP* National pediatric HSP (Local pediatric HLA-DR homozygous) (National pediatric HLA-DR homozygous) Local pediatric not-HSP National pediatric not-HSP Adults in same priority order Tier 2 - Favorably matched patients (100, 010, 110 mismatched) priority order (Local pediatric HLA-DR homozygous) (National pediatric HLA-DR homozygous) Local pediatric National pediatric 1 Adults in same priority order Tier 3 – Non-favorably matched patients Kidneys retained for local center/transplant alliance use according to local policy *HSP = highly sensitized patient

Figure 1 3-tier national allocation scheme (Fuggle et al. 2002)

Table 1Factors included in the Points Score (Fuggle et al. 2002)

Factors included in the Points Score										
Recipient age	Favors younger recipients									
Donor/recipient age difference	Avoids large age differences									
Matchability	Favors rare HLA types & sensitized patients									
Transplant unit import and export balance	Favors high center balance									
Waiting time	Favors longest waiting									
Sensitization status	Avoids positive crossmatches									
	1									

In the following discussion, I will use the situation in the United States as an example of national kidney sharing, use the situation in Ontario, Canada as an example of regional distribution of donated kidneys and use the situation in Hamilton's local St. Joseph's hospital to illustrate coordination work in local transplant centers. However, the problems in the kidney distribution process are universal.

2.3.1 National kidney sharing (UNOS)

In October 1987, the United Network for Organ Sharing (UNOS) established a national kidney-sharing program to increase the number of HLA-matched transplantations, decrease organ wastage, supervise equitable distribution of organs, lower transportation costs and provide data on organ sharing. UNOS is responsible for promoting, facilitating and scientifically advancing organ procurement and transplantation throughout the United States while administering the national organ allocation system based on scientific and medical factors and practices. Approximately 1000 kidneys are transplanted into HLA-matched patients every year. Even with the change in matching criteria implemented in 1995, only 13 percent of the pairs of HLA-matched kidney donors and recipients were from the same geographic region. If the national program of organ sharing were abolished, only 2 percent of patients (about 150 per year) would receive full HLA-matched kidneys. As a result of the cooperation of all U.S. transplantation centers, HLA-matched transplants included in the national program of organ sharing are rejected less often and have a higher rate of survival than HLA-mismatched transplants (Takemoto et al. 2000).

For the purpose of managing organ allocation, staffed 24 hours a day, 365 days a year, UNOS oversees approximately 64 organ procurement organizations (OPOs) that service one or more of the 279 transplant centers. Transplant centers, tissue typing laboratories, and organ procurement organizations (OPO) are all

involved in the organ sharing process. All patients accepted into a transplant hospital's waiting list are registered with the UNOS Organ Center, where a centralized computer network links all organ procurement organizations and transplant centers. This computer network is accessible 24 hours per day, seven days per week. A formula for matching based upon objective medical criteria for kidney ensures equitable allocation of donated kidneys among patients medically qualified for a transplant.

When kidneys are donated, a complex process begins. The OPO that recovered the kidney accesses the UNOS computer, enters information about the donor organs into the UNOS computer and runs the match program. Factors affecting ranking include blood type and size of the kidney, tissue match, length of time on the waiting list as well as medical urgency of the patient and immune status. Therefore, each donor will generate a different list of potential recipients ranked according to the UNOS policies on kidney allocation. Distance between donor and recipient is a factor in allocating the kidney, as transit time limits practical shipping distances. So the list is accessed first for potential recipients at centers within the local area of the donor hospital. If no matches are found, the search is broadened to a larger region of the country and then nationwide if necessary.

After receiving a printout of the list of potential recipients, the transplant coordinator contacts the transplant team of surgeons and the transplant physicians caring for the top-ranked patient to offer the organ. Sometimes the top patient will not get the organ for one of several reasons. For example, when a patient is selected, he or she must be available, healthy enough to undergo major surgery, and willing to

be transplanted immediately. Also, laboratory tests designed to measure the compatibility between the donor organ and recipient are necessary for some transplants. A surgeon will not accept the organ if these tests show that the patient's immune system will reject it. If the organ is turned down, the next center on the potential recipient list is contacted, and so on until the organ is placed.

Once the organ is accepted for a patient, transportation arrangements are made, all testing is complete, surgery is scheduled and transplantation takes place.

The following is a flowchart of the kidney distribution. See Figure 2



Figure 2 Flowchart of the kidney distribution process

From the above description of the national kidney distribution process, I note that the organization of this process is critical and complex. This process includes not only the donor/recipient operation itself and the evaluation of donors and potential recipients but also information exchange, decision-making and collaboration between multiple parties (including hospitals, physicians, patients, ambulance service and so on).

2.3.2 Regional kidney sharing (TGLN)

To further learn the details of the traditional kidney distribution process, an investigation on the Trillium Gift of Life Network (TGLN) has been made. The trillium Gift of Life Network was created in December 2000 by the Ontario Government and recently assumed the role of Ontario's central organ and tissue donation agency. A selection of TGLN's donor files that contain the level of detail about the process and timing of kidney distribution were reviewed. Parts of data of donor files were gathered and the conversations with the organ procurement and distribution coordinators made us further understand the current organ procurement and distribution process. Although the files they currently have jurisdiction over pertain to cases facilitated within the central and northern Ontario region rather than the entire Ontario province, they have been enough to give a sense of the issues and processes in one region that may be generalizable to other regions.

Hospitals within the Ontario region report all potential donors to their local organ procurement organization (like TGLN) in a timely manner. The organization then evaluates the patient's potential for organ donation, assists in the administrative details necessary for the declaration of death, and acts as intermediary between the donor hospital (including the nurses and physicians) and transplant center.

Once brain death has been declared and the decision has been made to proceed with organ donation, management of the donor is redirected toward optimizing potentially salvageable organs.

After a potential donor has been identified, the donor coordinator from the organization obtains a detailed medical and social history. Potential organ recipients are categorized according to a kidney allocation algorithm.

Serologic analysis must be done for human immunodeficiency virus HIV (1 and 2), cytomegalovirus CMV, hepatitis B surface antigen HBsAg, hepatitis B core antibody HBcAb, hepatitis C virus HCV and human T cell lymphotropic virus type (HTLV I/ II).

After the potential organ donor has been studied and stabilized, the donor coordinator contacts local and regional transplant programs about their needs for renal and extrarenal organs.

For kidneys, when there is a six-antigen match (i.e. a perfect histocompatibility match between a donor and a recipient on all six HLA-A, HLA-b, and HLA-DR antigens) or when there is at least phenotypic identity between a donor and a prospective recipient (i.e., no HLA mismatch), the kidney must be offered to the matched recipient regardless of geographic location.

Donors are initially evaluated by physicians on the basis of verbal reports of laboratory results and recent donor medical histories; however, the decision whether to use an organ ultimately depends on an experienced transplant surgeon's evaluation of the organ during the procurement procedure. If the organ is usable, this evaluation information will be provided to the transplant center that will make the clinical

decision whether to accept or reject the organ based on the available data or the need for additional information as well as the potential recipient's medical status.

After the transplant center informs the donor hospital that they would accept the kidney, the logistics of organ retrieval and transplantation must be arranged. Phone calls are made to the Intensive Care Unit (ICU), Admitting Department, and other members of the retrieval team. The provincial Air Ambulance System or ambulance is requested to arrange transportation to that transplant center. Multipleorgan harvests require considerable coordination between different institutions, surgeons, and coordinators. In the meantime, it is important that the donor be kept stable. The interval between the pronouncement of death and the donor procedure should be kept as short as possible.

The selected recipient is located and told to come to the hospital's Admitting Department as soon as possible. After informing various hospital departments (Operating Room, Anesthesia, Blood Bank and Biochemistry) about the impending transplant, all necessary equipment is assembled for the operation.

The potential recipient is sent from the Admitting Department to the Transplant Unit where the patient has a physical examination, blood tests, and other tests.

Before the retrieval team (usually a coordinator and surgeon) leaves for the donor hospital, the coordinator phones to confirm that ground or air transportation has been arranged, the donor's condition is still stable, and the operating start time.

Before the donor is brought to the Operation Room (OR), the retrieval teams should review the donor's chart in the ICU. Both the declaration of brain death and

the consent for organ donation should have been signed and included in the chart. In addition, blood type, serologies, and laboratory test results should be confirmed.

The kidney is flushed with a preservation solution before removal. The donor organ is removed and packed in ice for the return trip. The coordinator phones the transplant center to inform the surgeon who will operate on the recipient that the kidney is suitable. The recipient will go to the operating room shortly.

After the retrieved kidney arrives in the transplant hospital, T cell Xmatch could be done. Then the recipient will be anaesthetized and surgery will begin. The donor kidney is removed from cold storage, placed in the recipient's abdomen and the surgery continues. After the surgery is completed, the recipient is transferred to the Intensive Care Unit.

2.3.3 Local kidney sharing

Since the management of local renal allograft is not as complex as the shipped allograft, I won't pay much attention to local kidney distribution issue. However, local transplant center as a critical part of the enlarged kidney sharing network still needs my further investigation. An effective and efficient coordination within or between transplant centers, specially the smaller transplant centers, may improve the overall kidney distribution process. Large, geographically compact population centers may be able to sustain efficient independent organ donation systems capable of offering their recipients the benefits of a large pool size, while smaller centers need to interact with others in order to realize maximum matching and enhance fairness (Yuan et al. 2001b). For example, when a kidney is available,

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there is only one coordinator in charge of the arrangement of organ retrieval and transplant in some small transplant centers in Canada. This coordinator should be in contact with donor coordinators, physicians, members of the transplant team, potential recipients and various hospital departments to schedule the surgery. If no suitable recipient is found locally the coordinator has to find other transplant centers where there is a matched recipient who could accept it.

2.4 Methodologies applied in supply chain management

The complexity of the cadaver allograft retrieval/allocation process is not unique to transplantation, which shares many characteristics exhibited by commercial "supply chains." A supply chain consists of suppliers, factories, warehouse, distribution centers and retailers, working together to convert raw materials to products and delivered to customers (Bowersox and Closs, 1996). There is no single authority over all the chain members. Cooperation is through negotiation rather than central management and control. The interdependence of multistage processes also requires real-time cooperation in operation and decision-making across different tasks, functional areas, and organizational boundaries in order to deal with problems and uncertainties.

The logistical management in the integrated "supply chain" process has received great attention and has been studied thoroughly for decades. Logistics is the process of planning, implementing and controlling the efficient, effective flow and storage of goods, services and related information from the point of origin to the point of consumption for the purpose of conforming to customer requirements

(Council of Logistics Management, 1991). In a strategic sense, logistical management leads a boundary-spanning initiative to facilitate effective supply chain relationships. A well-designed logistical effort must have high customer response capability while controlling operational variance and minimizing inventory commitment. A well-designed and operated logistical system can help firms achieve competitive advantage.

Logistical management is not specific to supply chains and it also exists in the cadaver kidney distribution process. Within this medical environment, the logistics include procuring kidneys from donors, allocating resources for kidney distribution, distributing a particular kidney to the most suitable recipient, preparing kidney retrieval and transplant operations, etc. Due to the above-mentioned similar features between kidney distribution and supply chain management, it is feasible to apply the methodologies used in a supply chain to analyze the distribution process of renal allograft and measure its logistical efficiency.

2.4.1 A Gantt Chart of cadaveric kidney distribution

To analyze the current management of the cadaveric donor kidney procurement and distribution process, I need to address the following relevant questions:

- 1. What activities are required for completing this process?
- 2. In what sequence should these activities be performed?
- 3. When could each activity begin and end?

4. Which activities are critical to completing the process in time? (Bowersox and Closs, 1996)

To study the relationships between activities of multiple parties and time in the kidney procurement and distribution process, a Gantt chart schedule of activities of multiple parties is given to describe the process moment by moment. A Gantt chart is a graphical representation of the duration of tasks against the progression of time. The basic purpose of a Gantt chart is to break a large project into a series of smaller tasks in an organized way. A Gantt chart could allow me to access how long the process will take, learn the order in which tasks need to be carried out and analyze dependencies between tasks. In the chart, the left-most column lists each of the tasks in chronological order according to their start time. The remaining columns show the timeline. The timeline represents the activity duration. And the point in time represents events of the process.

Figure 3 below is a Gantt chart of the cadaveric kidney procurement and distribution process. This figure is based on my own analysis of the collected records from TGLN and St. Joseph's hospital. I summarized all the activities mentioned in those kidney distribution records, their durations, and their perform sequence.

Note:

 The assumption is that the regional kidney procurement and distribution process has no serious delays, it is under general situation and the duration of CIT is about 16 hours (the average CIT of regional distribution is about 16 hours).

- The statistics starts from the time when the procurement coordinator was aware of the potential donor to end of donated kidney storage time.
- The durations of activities are provided based on data from the case study of actual donor records. Since there is no complete and clear record without missing information on the duration of all the activities included in this process, some durations take the average values.
- One event could trigger other events. The occurrence of a certain event could have several prerequisites that some predecessor events should have occurred. The relationship of activities is represented by vertical dashed line.

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Parties Time (Hour)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
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Transplant team											6															

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Figure 3 Gantt chart of the cadaveric kidney procurement & distribution process

Events in Figure 3:

- 1. Received call for a potential donor
- 2. Death declaration
- 3. Blood sample obtained
- 4. ABO result obtained
- 5. Offer kidney
- 6. Coordinator contacted with physicians and gave donor information
- 7. Bed in ICU checked
- 8. Arrange transport
- 9. Accepted kidney
- 10. Retrieval team departed
- 11. Donor operation started
- 12. HLA typing and Xmatch (B cell) result obtained
- 13. Renal allocation recommendation
- 14. Coordinator contacted with potential recipient
- 15. Organize transplant team
- 16. Arrange transport to return
- 17. Patient arrived at hospital
- 18. Retrieval team with kidney departed to come back
- 19. Donor operation ended
- 20. Kidney arrived transplant hospital
- 21. Begin to do Xmatch (T cell cross-match)(4hr or 6hr-8hr) or do biopsy (4hr-6hr)
- 22. Xmatch or biopsy result obtained
- 23. Transplant OR timing
- 24. Confirmed OR time
- 25. Transplant OR started

Although I have given a Gantt chart mentioned above to describe the timing of individual activities in the process, the actual process could not progress against the schedule completely, and furthermore, it may vary greatly. The variances result from particular characteristics of the process, emergency and uncertainties. Those uncertainties (the start time of activities, the availability of potential transplant candidates, bed issue, etc.) and their sequential delays make the management of this process complex and difficult.

2.4.2 Critical path analysis

The critical path is a chain of activities from the start to the end of the process. Critical path networks highlight which tasks are critical for a process to stay on schedule. Those activities on the critical path should be performed in a specified sequence. A delay in the starting time of any critical path activity results in a delay in the process completion time. To analyze the critical path in the donated kidney procurement and distribution process, a visual presentation of the sequence of activities is given by network-based method as follows.

Figure 4 shows an activity network for kidney procurement and distribution process. Uncertain factors haven't been considered into building the critical path of the network.

Donor hospital and organ procurement organization



Figure 4 Network for cadaveric kidney procurement and distribution

Activities	Duration
Blood sample obtained	< 1 hour
ABO test HLA typing (biopsy)	1 hour 10-12 hours 4-6 hours
Generate renal allocation recommendation	10 mins
Arrange organ offer and give organ info	30 mins ~ 18 hour
Discuss with organize retrieval team	1 hour ~ 2hours
Contact with (booking->departure) air ambulance or ground transport	15 mins \sim 7 hours
Confirm donor surgical operation time	15 mins ~ 30 mins
Retrieval team on the way	20 mins ~ 3 hours
Donor operation	Multiple organ 6 ~ 8 hours Kidney 2 hours
Kidney on the way	20 mins \sim 3 hours
Kidney Arrived and Physician reviewed charts	10 mins ~ 30 mins
Crossmatch	6 - 8 hours
Physician made decision	5 mins ~ 20 mins
Confirm transplant operation time	1 hours ~ 3 hours
Transplant operation	3 hours ~ 5 hours

Table 2Critical Path Activities

From Table 2, I noticed that there are great variations on the duration times of the posted activities. The reason is that there are many uncertainties involved in the kidney distribution process, the time delay is due to responding and handling unexpected events such as traffic problems, kidney refusal from potential recipients, absence of transplant surgeons, etc. Although renal allograft allocation algorithms can generate a list of optimal potential recipients, due to a variety of uncertainties (patient's present health status, patient opinion, bed issue, weather, etc.), the final recipient cannot be identified and confirmed just through allocation algorithms. The processes of identifying the best available recipients for the donor kidneys and arranging kidney transportation and kidney transplant are time-consuming. Cadaver kidney distribution that is only based on an allocation algorithm is not enough to be efficient. I will devote more attention to the logistical efficiency as well as the cost issue in measuring the efficiency of this process.

2.4.3 Statistics of data from UNOS, TGLN and local transplant centers

In order to figure out the problems and bottlenecks in the current cadaver kidney distribution process, in particular, the practical work of the transplant coordinator, I collected statistical data about kidney transplant from UNOS and I also gathered data and detailed records about the practical steps of kidney distribution and their execution time in different cases from TGLN and St. Joseph's hospital. A total of 45 donor files were reviewed and 40 donor records were retrieved from the TGLN center and a total of 31 donor files were reviewed from the transplant center at St. Joseph's hospital. Some records were excluded from statistical analysis because of missing important information (time information like CIT and HLA tying start time, detail operation records and reasons of delays). The known characteristics of the excluded records were not significantly different from those of records included in these analyses.

The statistics of collected data are as follows:
Kidney transplant performed by CIT-by distance between donor hospital and transplant center supplied by UNOS



Figure 5 Kidney transplant performed by CIT - by distance

between donor hospital and transplant center

Based on UNOS and OPTN data as of June 28, 2002

Sample kidney transplant data regarding CIT and distance supplied by TGLN

Table 3a Sample data of local kidney distribution provided by TGLN as of December 2002

No.	Distance	From donor hospital to Transplant	CIT
1	Local	(HSC -> HSC)	24hr 25min (age 4)
2	Local	(HSC -> HSC)	28hr 13min (age 4)
		3 hrs flight(HSC -> Halifax)	N/A
3	Local	(SMH ->TGH)Toronto	10hr 39min
		(SMH ->TGH)	13hr 58min
4	Local	(SBK ->TGH)Toronto	20hr 26min
		(SBK ->TGH)Toronto	22hr 36min
5	Local	(Scarborough Hospital, Grace Division	12hr 17min
5		->TGH)Toronto	
6	Local	(SMH -> TGH)Toronto	7hr 20min
7	Local	(SBK -> TGH)Toronto	19hr 21min
		(SBK -> KGH)Kingston	N/A
8	Local	(SMH -> TGH)Toronto	5hr 35min
9	Local	(SMH -> TGH)	21hr 20min
		(SMH -> TGH)	23hr 53min
10	Local	(SMH -> TGH)	4hr 11min
		(SMH -> TGH)	15hr 42min
11	Local	(SMH ->TGH)	11hr 11min
		(SMH ->TGH)	13hr 51min
12	Local	(SMH ->SMH)	15hr 35min
		(SMH ->TTH)	12hr 24min
13	Local	(SBK ->TGH)	6hr 20min
14	Local	(MSH ->TGH)	11hr 55min
15	Local	(SMH ->TGH)	12hr 29min
16	Local	(SBK ->TGH)	16hr 09min
Local	Average		14hr 23min

No.	Distance	From donor hospital to Transplant hospital	СІТ
Regional 1	1857km	(Halifax ->Toronto)	23hr 52min
Regional 2	1373km	SMH (Thunder bay -> Toronto)TSH	14hr 17min
	1373km	(Thunder bay -> Toronto)SMH	9hr 30min
Regional 3	446km	(Ottawa ->Toronto)TGH	15hr 57min
Regional 4	446km	(Ottawa ->Toronto)TGH	25hr 42min
Regional 5	254km	(Kingston ->Toronto)TGH	14hr 22min
	185km	(London ->Toronto)HSC	27hr 40min (age 8)
Regional 6	103km	(Barrie ->Toronto)SMH	12hr 45min
	103km	(Barrie ->Toronto)TTH	20hr 30min
Regional 7	68km	(Hamilton ->Toronto)TGH	6hr 54min
Regional 8	68km	(Hamilton ->Toronto)HSC	11hr 28min
Regional 9	68km	(Hamilton ->Toronto)HSC	18hr 13min
Regional 10	55km	(Oshawa ->Toronto)TGH	24hr 32min
Regional	Average	i# - > i Girl iToronto	16hr 59min

Table 3b Sample data of regional kidney distribution provided by TGLN as of December 2002





Figure 6 Kidney transplant performed locally by CIT

Based on TGLN data as of December 2002

CIT by distance for regional kidney allocation-supplied by TGLN





Based on TGLN data as of December 2002

Sample kidney transplant data supplied by St Joseph's hospital in Hamilton

Table 4a 2001-2002 sample data of local kidney distribution provided by St.		
Joesph's transplant center		

No.	Distance	Donor hospital or Transplant hospital	CIT
1	Local	Mac medical center	30 hr 25 min
2	Local	HGH	21 hr 31 min
3	Local	HGH	18 hr 28 min
4	Local	HGH	15 hr 44 min
5	Local	HGH	15 hr 51 min
6	Local	HGH	15 hr 59 min
7	Local	HGH	15 hr 09 min
8	Local	HGH	14 hr 21 min
9	Local	HGH	14 hr 11 min
10	Local	St. Joseph	13 hr 13 min
11	Local	HGH	13 hr
12	Local	HGH	12 hr 17 min
13	Local	HGH TO	12 hr 11 min
14	Local	HGH	10 hr 27 min
15	Local	HGH	9 hr 7 min
16	Local	HGH	8 hr 55 min
Local	Average	end of horizontal states on of the	15 hr 3 min

No.	Distance	Donor hospital or Transplant hospital	СІТ
Regional 1	65km	Kitchener	15 hr 38 min
Regional 2	65km	Kitchener	11 hr 45 min
Regional 3	68km	Toronto	27 hr 22 min (3 hr delay for
	Street 1		police)
Regional 4	68km	Toronto	27 hr 8 min
Regional 5	68km	Toronto	26 hr
Regional 6	68km	Toronto	17 hr 23 min
Regional 7	125km	London	26 hr 31 min
Regional 8	125km	London	25 hr 47 min
Regional 9	125km	London	24 hr 30 min
Regional 10	125km	London	23 hr 4 min
Regional 11	125km	London	23 hr 7 min
Regional 12	125km	London	21 hr 7 min
Regional 13	125km	London	19 hr 54 min
Regional 14	304km	Windsor	27 hr 58 min
Regional 15	441km	Sudbury	19 hr 27 min
Regional	Average	defit pearlied brack in the	24 hr 11 min

Table 4b 2001-2002 sample data of regional kidney distribution provided by St. Joesph's transplant center

Kidney transplant performed locally by CIT-supplied by St. Joseph's hospital



Figure 8 Kidney transplant performed locally by CIT





CIT by distance for regional kidney allocation-supplied by St. Joseph's hospital

Figure 9 CIT by distance for regional kidney allocation

Based on St. Joseph's hospital data as of 2001-2002

These statistics data and detailed records relating to kidney distribution management conducted by coordinators were analyzed according to the duration of cold ischemia before transplantation, distance between donor and recipient and transplant cost variance with the expansion of kidney sharing network. In the rest of this section, I will give the analysis on two issues, including the relationship between CIT and Distance and the relationship between cost and HLA-matching as well as CIT.

1) The relationship between CIT and the distance between donor hospital and transplant hospital

I have stated in previous sections that with the widespread kidney sharing, the deleterious effect of a longer CIT owing to an increased organ exchange and

shipping would diminish the benefit of a better HLA match. But the kidney sharing within the USA doesn't seem to affect CIT greatly.

To further understand the relationship of between CIT and deliver distance in kidney distribution, I will overview the sample transplant data provided by TGLN. See Table 3. The table also shows that compared with the CIT of local distribution, the CIT of regional distribution within the Ontario region doesn't increase very much (about 2hr 30 minutes (16hr59mins – 14hr23mins)). Based on the data from the Scotland-Northern Ireland Kidney Allocation Alliance and on the United Network for Organ Sharing (UNOS), the studies to assess the effects of the extended period of ischemia associated with shipping HLA-matched kidney suggest that the introduction of a regional kidney allocation alliance has improved the degree of HLA matching and increased the exchange of organs, without a significant increase in the CIT and any detrimental effect on graft survival (Oniscu et al. 2002) and a superior graft outcome with little increase in the duration of cold ischemia justifies national sharing of HLA-matched kidney transplants (Takemoto et al. 2000).

But according to the UNOS Scientific Renal Transplant Registry, more than 83 percent (6387 of 7614) of the HLA-matched kidneys and 23 percent (18,469 of 81,364) of HLA-mismatched kidneys were shipped by the organ-procurement organization for transplantation at distant transplantation centers through September 1999. (The mean \pm SD) duration of cold ischemia was 23 \pm 8 hours for the patients who received HLA-matched kidneys, as compared with 22 \pm 10 hours for the patients who received HLA-mismatched kidneys (P<0.001)). After HLA mismatching was taken into account, studies demonstrate that the shipment of renal allograft is

associated with an increased rate of organ failure in the first year after transplantation, but not subsequently (Mange et al 2001). The organ failure refers to delayed allograft function (defined by the use of dialysis within the first week) and acute rejection within the first year. The prolonged CIT is associated with organ failure (Cecka et al. 2001).

Studying sample data gathered from St. Joseph's hospital, I noted that the CIT of example Local 1 in Table 4a has the longest CIT among all collected cases there. The difference of the example from other examples is the donated kidney from a 9-year-old child. Many potential recipients turned it down for this reason. The actual kidney allocation was delayed. Usually, if the donor has 'marginal' characteristics, the time of kidney distribution will be prolonged markedly.

Considering the regional kidney allocation cases, I found that the average duration of CIT in St. Joseph's is about 7 hours longer than that in TGLN. What causes the big time difference? If the kidney transport time between donor and recipient could not be shortened further, the increased complexity of co-ordination and co-operation in this process may also account for the increase of CIT. After investigating the work of donor coordinators and transplant coordinators, I found that centers, especially the smaller transplant centers like St. Joseph's, have problems with the efficiency of coordination and contact management in the current manual processing of matches. To improve the degree of HLA matching, smaller centers may need to contact with other transplant centers to ensure the benefits.

Currently, the donor coordinator and recipient coordinator take important roles during the entire distribution process. They have to perform the following

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tasks: 1) facilitate the referral consultation process; 2) oversee the evaluation; 3) collect information (donor information, lab reports, test results, physicians' opinion, recipient information etc.); 4) deliver it to others by those communication facilities (the telephone, cell phone, pager and fax as the main communication facilities); 5) present findings of the evaluation to the retrieval team/transplant team; 6) follow through with the team's recommendations, 7) identify the recipient; 8) reserve the operation room and bed, ensuring all necessary equipment is available; 9) create a transplant schedule in coordination with organ procurement organization, ambulance system as well as hospital departments; 10) inform various medical staff, patient and surgeons about the upcoming transplant; and 11) finally file all the records related to the kidney.

I know that CIT includes transportation time and management time. Through the realistic kidney distribution case study, I notice that the regional distribution usually will take a longer CIT than local distribution and the CIT difference between local and regional distribution is not equal to but greater than their transportation time difference. So only the reason of longer transportation time in regional distribution can not explain the prolonged CIT in regional allocation. Except for longer distance or longer time for transportation, I want to know what else could contribute to the increased CIT in regional distribution cases? At the end, I found that most of the time is taken for contacting the local and regional transplant center, inquiring the opinion of the physician and the potential recipient and waiting for the reply of transplant center or individual (patient, physician etc.). Each transplant center will be in contact with 1-10 potential recipients (most of them are considered as backup recipients). It usually takes an average of 2 hours to finish multiple pretransplant questionnaires in order to find the final recipient.

Consequently, in the enlarged kidney sharing network, the longer distance between donor and recipient and the increased complexity of kidney distribution could result in longer CIT. And I found that the logistical efficiency in those abovementioned centers is a critical factor to influence CIT and finally the benefit resulting from a better HLA matching. Coordination and collaboration are the key success factors for effective and efficient cadaveric kidney distribution in a widespread kidney sharing.

2) The relationship between cost and HLA-matching as well as CIT

HLA-matching and the duration of cold ischemia are both important factors associated with survival of renal allograft, but they offset each other. How do they affect each other? I will discuss it in this section.

Rejection is the most expensive event that can occur after a transplant procedure since additional medications, dialysis, and extended hospitalization becomes necessary (Takemoto et al. 2001). Much like the effect of HLA mismatching on graft survival, the effect of HLA mismatching on costs is not constant over the range from zero to six mismatches. The benefit of reduced HLA mismatching, in terms of graft survival, is most pronounced when there are no HLAantigen mismatches; however, the effect of mismatching on costs is most pronounced when there are six mismatches. According to a generalization of the Kaplan-Meier method for continuous data, a recent cost estimate found that to compare with HLA mismatches, zero HLA mismatches reduced the three-year cost

of renal transplant by 20,000 USD. When the number of HLA mismatches increases, the medicare payment increases (Schnitzler et al. 1999). Although there is a clear potential to save money through better HLA matching, higher costs are also associated with increasing cold-ischemia time. Prolonged CIT is associated with delayed graft function (DGF). Recipients with DGF have a 20% lower graft survival rate (Cecka et al. 2001). The hospital stay of recipients with DGF is prolonged, partly because of the need for dialysis, thus costs increase markedly. In addition, due to the increase of the incidence of rejection in patients with DGF, evaluation and treatment of rejection episodes are associated with additional costs (Matas and Delmonico, 2001). Based on the analysis of data on payments made by Medicare from 1991 through 1997 for the care of renal transplant recipients, the duration of cold ischemia has a linear relation to average medicare payment (Schnitzler et al. 1999). Approximately 8000 transplantations of cadaveric kidneys are performed each year in the United States; the annual saving to medicare from every hour by which the average cold-ischemia time is reduced is therefore approximately USD 2.3 million. Gjertson et al (1991) assumed that organizational and shipping costs in the national system of allocation would average approximately USD 1,000 per transplant. The inclusion of estimated shipping costs would have further reduced the relative economic benefit of national allocation (Schnitzler et al. 1999). Bear in mind that the least expensive transportation does not result in the lowest total cost of organ distribution process. Additionally, because it is expensive for hospital to maintain donors, reducing the donor waiting time for "harvest" could bring on additional cost savings.

In conclusion, because of the deleterious effects of the longer cold ischemia time owing to an increased organ exchange and shipping, economic benefits resulting from improvement of quality of HLA-matching will be more readily available with a shorter CIT.

2.5 The bottlenecks of the current process

Based on the analysis of the current donated kidney distribution process, I identify practical limits to efficiency in distribution of allografts.

In current manual processing, the problems I found are as follows:

1) Delay caused by the sequential confirmation procedure

In the United States, all patients who require cadaveric transplantation are placed on a national transplant waiting list. This potential recipient list is maintained by the United Network for Organ Sharing (UNOS). When a kidney is available, the donor blood type and tissue type are entered into the UNOS computer. Although it is quick to identify the best possible match potential recipient by this sharing network, the sequential nature of calling Organ Procurement Organizations (OPO) and recipients with each kidney offer can result in delays, particularly with older donors; nonheartbeating donors or donors with other 'marginal' characteristics. In such situations, many OPOs, centers or individual recipients refuse the offered kidney (Matas and Delmonico, 2001). After generating the list of potential recipients, the transplant coordinator contacts the transplant surgeon caring for the top-ranked patient to offer the organ. Laboratory tests designed to measure the compatibility between the donor organ and recipient are necessary for some transplants. A surgeon Master Thesis - Jiangxu Zhao

will not accept the organ if these tests show that the patient's immune system will reject it. If the organ is turned down, the next center on the potential recipient list is contacted, and so on until the organ is placed. The transplant coordinator of the donor hospital won't inform the next OPO until the previous OPO turns down the kidney. A positive cross-match at the receiving center remains a significant cause for organ reallocation (Oniscu et al. 2002) If numerous OPOs, centers and individuals turn down a kidney, the actual allocation is delayed, further prolonging CIT. Due to more use of kidneys from older cadaver donors ("unideal" donors), this kind of delay increases in current kidney distribution.

It is important to rule out an unsuitable patient early in the process, before proceeding with full evaluation. If HLA typing and confirming the potential recipient could be completed before the donor operation, the length of CIT might be shortened greatly.

2) Time-consuming contact process

The transplant donor coordinators are responsible for contacting the physicians and donor's relatives, informing potential recipient's hospital about the donated kidney, report the donor's basic information and inquiring if the recipient transplant centers are willing to accept the kidney. After the kidney is accepted, they still keep in touch with the transplant coordinators of the recipient's hospital to schedule the "harvest" and arrange the transportation. The transplant coordinators in recipient hospital are responsible for assisting transplant centers in collecting information of donor and recipients, contacting the potential recipients and their

surgeons, informing various hospital departments about the impending transplant, and scheduling the surgery. The coordinators should monitor the whole distribution process and respond to the unexpected emergency. To share information about the process of the kidney distribution, many calls are made among the related transplant people. Sometimes it takes more waiting time to reach the person the coordinator cannot contact immediately and the same information will be repeated several times to different people.

Currently, I noted that information exchange is mainly through telephone. The coordinator will call or page someone to let him/her be aware of the new situation or consult him/her about next step, and then wait for the answer or confirm (call back to acknowledge). If the physician or other coordinator has some questions, requirement or decision, the coordinator might have to contact other people to inform or consult. When waiting for an important reply or result, the coordinator will make a call again every other 10-30 minutes to check whether the information is available now and learn the current progress. Sometime the coordinator will call twice for a double check.

If we could ascertain as many uncertain factors as possible in the early process or before the X-clamp time of kidney, we may improve the efficiency in the contact process and reduce unnecessary delay on CIT.

3) The complexity of coordination and cooperation

When the kidney sharing occurs in a widespread area, the cooperation in kidney distribution and decision-making is across different tasks, functional areas

and organizational boundaries. The donated kidney is not only shared locally but also shared regionally, nationally and internationally. Under time pressure from CIT, the coordination as part of logistics management of organ retrieval and transplantation is critical to ensure best use of the donated kidney to save lives. Figure 10 shows the cooperation in the kidney distribution.



Figure 10 Cooperation in the donated kidney distribution

Moreover, due to uncertainty factors, it is difficult to estimate the start time and duration of activities that are involved in the distribution process. Effective cooperation is needed to support the handling of unexpected workflow, especially the delay in the starting time of the critical path activities that will result in a delay on finish time of the overall process. Considering the cross-functional coordination among so many people, departments and organizations and the time restrictions (CIT) of the donated kidney, the cooperation of the donated kidney distribution is complex and important. As shown in Figure 10, the task of the coordinator as the hub of the process network is vital for the process management. Improvements in getting coordinators to work efficiently could get a better kidney procurement and distribution management.

4) Inadequate and poor information sharing

Poor information and knowledge sharing lead to poor coordination. As we know, time delays, errors and incomplete information will result in process delays, incorrect decision-making or unexpected complications. Worst of all, the most valuable resource, the kidney, may be wasted. Current information sharing in kidney distribution process is at a low level. With current manual processing, information sharing is untimely and the coordinators become the bottleneck of the information exchange. Phone calls, faxes, face-to-face reports and paper document delivery are the main methods for exchanging information between different parties and this kind of information sharing method is error-prone and inefficient. The applications of information technology in the process are also at a low level. The coordinators have lots of things to do and they probably make mistake under time pressure. Sometimes they may even forget to inform physicians of important information. If those things happen, the process might be delayed, and worse, physicians could make an error in decision-making. Error may also result from outdated data about patients. Due to the infrequent checking on the health status of patients, data about patients kept in

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hospitals usually are not up-to-date. The donors' medical histories and behavioral risk data provided by their families are inaccurate and incomplete. The transplant coordinators cannot monitor kidney distribution performance on a real-time basis. Without such necessary information, physicians or other parties of the process cannot make effective decisions efficiently. If they could easily access the information they needed earlier, the decisions could be made sooner and actions could be taken more quickly.

The efficient and effective data sharing and integration of information is critical to support clinical decision-making, strategic planning and program development. Therefore, a real-time multi-point updating and information management system is needed. A tremendous amount of information must be collected, reviewed, analyzed, and synthesized in a cost-effective manner.

In summary, considering the effect of the logistical efficiency on length of CIT and the effect of CIT on allograft survival and cost, the efficiency of donated kidney distribution in enlarged donor and recipient pools in order to maximize matching and enhance fairness could be improved by minimizing any detrimental effect of prolonged cold ischemia time on graft function and survival. Based on the analysis in my thesis, cold ischemia time could be shortened by improving the efficiency of cooperation and coordination management during the kidney distribution process. So problems in coordination and contact management, particularly the delay problem, are the key challenges that I attempt to overcome.

How to enhance the logistical efficiency and resolve the limits mentioned above are what I would discuss in the following chapters.

Chapter 3

The rationale of adopting agent technology in the kidney distribution process

In this chapter, I will explore the characteristics of kidney distribution process and the justification of using agent technology combined with mobile and wireless technologies in support of cadaver kidney distribution.

3.1 The requirements of efficient donated kidney distribution

Having identified the inefficiencies in cadaver kidney distribution and demonstrated that cooperative and coordinative behavior is a key success factor to improve the overall distribution process, the next question becomes whether information technology has a place in this environment for further improvement.

Based on the analysis of current kidney distribution process in which coordination work is predominantly done manually through human interaction, I believe that effective and efficient kidney distribution management should have the following characteristics:

- A sound coordinating mechanism or organization structure;
- An effective communication network suitable for mobility and distributed feature in collaboration work;
- Real-time multi-point data updating, information exchange and information sharing;

- Timely allocation of resources;
- An efficient process for identifying and tracing dynamic the availability of people or other resources;
- Effective decision making under time constraints;
- Constant monitoring and timely reminders; and,
- Dynamical and flexible task assignment in response to unexpected events.

Choosing the right technology and implementation strategy for such an application is important.

3.2 Enabling technology for the improvement of efficiency of kidney distribution

Today information technology can significantly enhance healthcare in general (Bergeron, B.P. and Bailin, M.T. 1999). Since we know that kidney distribution shares many characteristics exhibited by commercial "supply chains" and I have analyzed the distribution process using methodologies applied in supply chain management, I might try to solve those problems in kidney distribution by the information technologies already applied in supply chain management. Fortunately, many information systems have been developed to deal with those processes in supply chain management. One such system are "agents", a technology that is capable of enabling flexible and dynamic coordination of spatially distributed entities in supply chains (Yuan et al. 2001b). Mobile technology has been applied in supply chains to complete distribution, manufacturing and quality transaction from

1999)(Paggy 2002). Agent technology combined with mobile and wireless technologies brings a potential solution to help improve the efficiency of donated kidney distribution. It becomes very important to explore the potential of agent technology and mobile technology in this environment.

3.2.1 Agent technology

The notion of agents and multi-agent systems is the core idea in distributed artificial intelligence (DAI), a branch of artificial intelligence (AI). Agents are automated software entities operating through autonomous actions on behalf of the user – machine and humans. Agents usually have the following properties (Wooldridge and Ciancarini 2001):

- *Autonomy*: agents encapsulate some state and make decisions about what to do based on this state, without the direct intervention of humans or others;
- *Reactivity*: agents are situated in an environment, are able to perceive this environment, and are able to respond in a timely fashion to changes that occur in it;
- *Pro-activeness*: agents do not simply act in response to their environment, they are able to exhibit goal-directed behavior by taking initiatives;
- Social ability: agents interact with other agents (or humans) via some kind of agent-communication language (KQML or FIPA ACL, etc.) and typically have the ability to engage in social activities in order to achieve their goals.

Agents can exhibit some degree of artificial intelligence. They can autonomously perform tasks in an open environment. Intelligence is the amount of learned behavior and reasoning capacity that an agent may possess. At the most basic level, the agent may follow a set of rules that are predefined by a user. The agent can then apply these rules to respond to the environment. More intelligent agents will be able to learn, and will be able to adapt to their environment, in terms of user requests and the resources available to the agent (Papazoglou 2001).

It should be pointed out that a software component possessing only some of these capabilities can hardly be considered an intelligent agent. For example, an expert system is typically able to exploit knowledge, use symbols and abstractions and is capable of goal-oriented behavior. However, expert systems generally can't execute autonomously, learn, or communicate and cooperate with other systems. Thus, in most cases, I do not consider them intelligent agents.

A multi-agent system consists of a group of agents that can take specific roles within an organizational structure. Different types of agents may represent different objects, with different authority and capability, and perform different functions or tasks. They are capable of acting autonomously, cooperatively, and collaboratively to achieve a collective goal. A multi-agent system can be defined as a loosely coupled network of agents that work together to solve problems that are beyond the individual capabilities or knowledge of each agent (Durfee et al. 1989). Multi-agent systems have the traditional advantages of distributed and concurrent problem solving, but have the additional advantage of sophisticated patterns of interactions. The step from an isolated single-agent scenario to open multi-agent systems offers

the new quality of emergent behavior: the group of agents is more than the sum of the capabilities of its members (Fischer et al. 1996)

The agent metaphor is believed to have great potential in addressing distributed, large-scale, and dynamic applications. Intelligent agents represent a higher level of abstraction in designing and implementing applications. They can facilitate the incorporation of reasoning capabilities within the application logic (for instance, the encapsulation of kidney allocation rules within agents). They permit the inclusion of learning and self-improvement capabilities at both infrastructure (adaptive routing) and application (adaptive user interface levels). Agents can participate in high level (task-oriented) dialogues through the use of the interaction protocols in conjunction with built-in organizational knowledge. This makes agents hold a great potential in reducing the complexity of transactions and improving the effectiveness of interactions. Particularly, agents can be perceived as a promising technology when combined with mobile devices to improve the effectiveness and efficiency of interactions involved in distributed collaboration. Human users can delegate agents to conduct multiple conversations simultaneously. Additionally, agent technology can help address some technological challenges such as concerns about effective searching, security and privacy, etc (Papazoglou 2001).

In the literature, I can find that agents were successfully adopted in various domains such as process control, supply chain management, and even financial risks monitoring (Nissen 2000; Wang et al. 2002; Chen et al. 2000). Basically, several important domain characteristics are often cited as a rationale for adopting agent technology (Bond and Gasser 1988; Nwana and Ndumu 1999):

- Data, control, expertise, or resources are inherently distributed;
- The system is naturally regarded as society of autonomous cooperating components; and
- The system contains legacy components, which must be made to interact with others.

I can see the enormous opportunities for using intelligent agents in facilitating the coordination in the donated kidney distribution process. In this process, the entities, information and control are distributed. Many people and organizations are involved in it. All participants have their own resources and decision making tasks. They coordinate and cooperate each other to combine their resources to create capabilities needed to achieve a better outcome of kidney distribution. The coordination is cross-functional. The geographical scope of cooperation in this process is through negotiation rather than central management and control. To realize the integrated overall performance in kidney distribution, all the resources should be organized appropriately. Frequent information exchange is needed for decision-making across different tasks. Therefore it seems apparent to adopt a distributed architecture consisting of many software agents specialized for different tasks. This architecture supports share of agent capabilities and retrieved information. The agents can coordinate flexibly on demand, depending on the information requirements of a particular decision making task.

As a matter of fact, European researchers have already provided wide discussions on the feasibility and utility of deploying software agents and multiagent systems in today's medical environment (Nealon et al. 2002)(Cortés et al.

2000)(Moreno et al. 2001c). Several architectures of multi-agent systems have been proposed and parts of those designs have been developed. For example, multi-criteria decision aid agent is proposed by Valls et al. (2002b) to support the selection of the best organ receiver. They claim to use a multi-agent system to find the most appropriate receiver for an organ. But their research is different from mine and they focus only on transplant candidate ranking. The agents explained in their system intend to support the human decision-maker with multi-criteria decision aid techniques and the suggestion of the suitable candidates. Moreno, A., et al. (2001a) discuss the application in finding efficient organ transport routes using multi-agent systems. Agent technology is used in assisting the process of finding the most efficient way of transporting an organ, suitable to be transplanted, to the hospital where it must be implanted. They have designed and implemented a multi-agent system that provide a fast mechanism for finding the best transportation route, thereby avoiding potentially fatal delays due to mistakes in the coordination of different means of transport. Moreno et al. (2001b) discuss hospital arrangements for a transplant operation using agents. They focus on the management of a team that is going to make the surgical operation to implant an organ to a patient. They propose to use a multi-agent system to solve this scheduling task in a short period of time. Their system described in that paper has been implemented using FIPA.

3.2.2 Mobile and wireless technology

Since the cadaveric kidney could be donated anytime and anywhere, under critical time constraints the kidney distribution process is usually in a state of emergency and it is important to locate related people, report the new available kidney to them and get their response as soon as possible. However, when it happens, the contacts are in their normal lives and they could be any place, so in the wired network people might not be able to be reached immediately, and worse, unreachable potential recipient will lose a great chance to save his/her life. To overcome the time and location constraints in the emergency communication, mobile and wireless technology could be deployed to makes information and people accessible anywhere and anytime (Perry et al. 2001). For kidney distribution, mobile communication networks enable ubiquitous contact among coordinators, members of retrieval team, physicians and patients.

Mobile applications rely on the use of handheld devices. These devices range from pagers, cell phones, and palmtops, to pocket PCs. Using mobile devices could facilitate the work of mobile personnel and avoid occupying too much time and attention, which may disturb their current work at the moment. Mobile devices such as cell phones and PDAs (Personal Digital Assistant) have tiny screens, some of which display only three lines of text at once (Lucas 2001). Mobile interactions usually are facilitated through two technologies: WAP and SMS. WAP is a derivative of the request-response protocol HTTP (Hyper Text Transport Protocol), which requires constant connection. This makes it incapable of meeting mobile users' demand for more effective and real-time interactive applications (Feng and Zhu 2001). SMS (Short Message Systems/Services) is a derivative of the old

numeric paging network, with additional functionality for two-way communication and support for text and attachments (Leung and Antypas 2001). We should not expect kidney distribution personnel to use their handhelds to input rich information with awkward interfaces of those handhelds.

Wireless technology has been adopted in healthcare services (Moore and Wesson, 2003). In Europe, research has been ongoing in the area of application of agent technology in the mobile and wireless communication environment. For example, in FACTS project FIPA (The Foundation for Intelligent Physical Agents) agents are designed and implemented for a personal travel application. Their agent-based system can be accessed from the wireless environment using Wireless Access Protocol (WAP). Their current work has been the development of a Mini Personal Travel Assistant (MPTA), an agent available on a mobile device, such as a phone or a Personal Digital Assistant (PDA), which will be with the user at all times including on-trip (Núñez-Suárez et al. 2000).

If mobile individuals involved in the kidney distribution process carry about wireless handhelds (such as cellular phones) as part of their normal duties, mobile and wireless technology could help address the aforementioned barriers to distributed collaboration through automatic notification, reminder, information storage, and remote two-way communication in emergency situation. Based on my analysis, I know that a kidney can be available anywhere and at any time and mobile people such as physicians and patients are usually can not be reached by their home or office telephones. So with the help of mobile and wireless techniques, those related people, unreachable before, can be reached immediately now. Thus most of delays caused by the complexity of contact tasks will be reduced.

3.3 A discussion of how agent technology can support improvements in the

kidney distribution process

Generally, agent technology, combined with mobile and wireless technology solutions, concentrates on providing support for the planning and control of distribution processes using multi-agent systems. Agents would make many improvements in supporting the cooperation and coordination in this process. The advantages of using agent technology are illustrated in Table 5:

Features of technologies	Activities	Bottlenecks
Autonomy	Parallel working mode	Delay caused by the sequential
	Decision making	confirmation process
Anytime anywhere	Multiparty contact	Time-consuming contact
Autonomy	Massive real-time	process
Pro-activeness	interaction	-
	Dispatch messages	
Collaborative behavior	Simplify the coordination	The complexity of coordination
and communication	Monitor	and cooperation
ability		
Autonomy		
Reactivity		
Pro-activeness		
Pro-activeness	Collect, analyze and	Inadequate and poor
Autonomy	disseminate information	information sharing
Reactivity	quickly, pro-actively and	
	autonomously	

Table 5 Credits of agents in overcoming bottlenecks in the kidney distribution process

Finally, the increase in the speed of arriving at solutions to the problems in the activities using agent technology will improve the efficiency of overall cadaver kidney distribution process.

Chapter 4

A multi-agent architecture for donated kidney distribution process

The literature review and process analysis provided earlier gives a picture of how potential agent technology combined with mobile technology in improving the efficiency of cadaver kidney distribution. In order to further clarify what specific roles agents could play in kidney distribution, the activities during the kidney distribution process are studied and classified into five major tasks. To support these tasks, the agents' roles are further examined and identified. Based on these understandings, a multi-agent architecture for coordination during donated kidney distribution is proposed.

4.1 Requirements analysis

4.1.1 Identification of the key tasks of cadaver kidney distribution

Five major tasks in cadaver kidney distribution are identified here, illustrated in Figure 11. These tasks are presented in a natural order but they are not necessarily sequential and can be parallel or iterative.



Figure 11 Five tasks of cadaver kidney distribution

4.1.1.1 Registration

If a new cadaveric kidney becomes available, the donor record should be created and the donor information for kidney offer (such as donor name, age, sex, race, blood type, HLA typing, pertinent past medical or social history, etc.) should be registered to the organ sharing network. This registration task usually is carried out by the organ procurement organizations. Quick collection and verification of donor information is important for kidney distribution.

4.1.1.2 Matching

Based on the collected donor data and patient data in the database, the matching between the donor and patients should be done to find transplant candidates for a particular kidney. There are many patients distributed around the country waiting for kidney transplants. It is important to take into consideration factors such as age of the donor and patients, ABO blood type, HLA matching, PRA, waiting time, medical urgency with which the potential recipient requires the kidney, the distance to the kidney's donor (which influence cold ischemia and economic cost of the transport of the kidney). Within the defined allocation region (local or remote patients), a list of the potential recipients who are matched is generated by a kidney allocation algorithm.

4.1.1.3 Allocation

The algorithmic matching between donor and recipient does not necessarily determine the actual recipient who will receive the donated kidney. Since the final decision whether to use the kidney will remain the prerogative of the patient and the transplant surgeon and/or physician responsible for the care of that patient (the physicians and surgeons exercise judgment about the suitability of the organ being offered for the specific patient), in fact the kidney may not be distributed to the toprank transplant candidate listed in priority for allocation. Thus after ranking the transplant candidates for a particular kidney, the next step is to allocate the kidney to an available patient and identify other available resources. To do so, patients, related individuals (physicians, etc), departments or organizations will be chosen for further contact. The information about them should be collected. Real time interactions are performed. Due to time pressures in kidney distribution, efficient communication and information sharing among participants is needed. The progress of contact procedure should be monitored constantly. Response information should be collected and analyzed. Once the final recipient is determined, various associated resources such as transplant hospital, retrieval team, surgeon, transportation, operation room, bed, necessary equipment and so forth should be allocated as soon as possible.

4.1.1.4 Notification

Based on the allocation of a donated kidney, it is important to decide what parties should be notified and involved, and what resources are needed. Usually, the participants in the kidney distribution include local police, provincial air ambulance system, potential recipients, physicians, members of retrieval team as well as different departments of donor hospital and transplant center. Sometimes kidney information may be needed to be released to other organ procurement organizations outside of the current organ sharing network for a better medical match. Such notification is guided by some predefined regulations and distribution plans. After the participants involved in the kidney distribution have been identified, to make them aware of current situation of the process, the tailored message (the current donor status, operation plan, schedule and so on) should be dispatched to them as soon as possible, proactively or on requests.

4.1.1.5 Arrangement

The real-time arrangement usually includes task decomposition, planning and scheduling. The roles and tasks of related parties should be defined. All the identified resources would be organized. Considering this geographically distributed timecritical multi-party collaboration, it is complex to coordinate all parties and decisionmakings with so many uncertainties involved in the overall process. So dynamic organization and planning are needed. The operation plan should be formed to satisfy problem-solving goals by resolving schedule conflict and exception. Those many individuals organized in different teams for different tasks should be able to quickly exchange relative information. Information sharing is also critical for reducing confusion and delay and help personnel in planning, coordinating and carrying out various activities in response to kidney distribution. The up-to-date information should be supplied to keep the latest status available, make timely response and handle exception. Both action items and information messages should be tracked to ensure that resources were properly deployed. The effective and efficient resource allocation, organization and arrangement are very important to support the cadaveric kidney distribution.

Five major tasks in cadaver kidney distribution are summarized in Table 6, in terms of their contents and key issues.

Tasks	Description	Key Issues
Registration	 Create donor record Register donor information to organ share network 	 Accuracy of data and information, as detailed as possible Timely data sharing
Matching	 Gathering information of donor and waiting transplant patients Choose geographic level of kidney allocation (local, regional, national and international) Generate the list of potential recipients in the chosen area for kidney matching by the matching schemes 	• Based on medical and equity principle, finding better medical matching within a big enough region
Allocation	 Identify the available resources Choose the candidates and their physicians for further contact Schedule contact activities Perform information exchange with the parties contacted Constantly monitor the progress of contact Collect and analyze retrieved information and data 	 Quick decision-making about the further contacts based on the generated list of kidney transplant candidates and nephrology expert consult or knowledge-based system Efficiency of communicating and information sharing Real-time interaction Accurately and timely analyze

Table 6 Five major tasks of kidney distribution

	• Make the final choice of the recipient and associated resources	 the collected information from different parities Quick decision-making on solutions of resource allocation for a particular kidney
Notification	 Notify the relevant participants about the latest status, distribution plan or schedule Quickly dispatch specific information to the right person and right parties Respond to information request Integrate and present all information requested 	 Defining explicit rules of information dispatching Quick decision-making about what and how information is to be dispatched Keeping the participants informed about the up-to-date information Effectively integrate requested information according to the unique preference or habits of the user
Arrangement	 Defining roles of related parties Dynamic organization of teams Dynamic planning and scheduling Efficiently support the coordination of tasks among parties Monitoring the executions of scheduled activities 	 Rapidly organizing identified resources Quickly assigning appropriate tasks Collecting and disseminating up-to-date, relevant information Real-time tracking the status Handling exception effectively and efficiently

4.1.2 Identification of the roles of agents in cadaver kidney distribution

Beyond the general discussion of agents' potential in improving cadaver kidney distribution, the roles of agents in the kidney distribution are further identified and discussed in this section, especially in assisting the coordinator for kidney distribution. Each agent has different roles in terms of information access, security, different kidney distribution tasks it is involved in.

4.1.2.1 Agents for kidney registration

Intelligent agents interact with the person who has information about a new available donated kidney. They can work as assistants of human coordinator to register donor information on an organ sharing network. They can communicate with other agents about the new donor to trigger the process of donated kidney distribution. Agents can quickly record and disseminate information in an electronic format.

4.1.2.2 Agents for kidney matching

Within a defined allocation region, allocation agents perform analysis on the data of each possible recipient based on different criteria and generate a list of potential recipients who are medically matched and ranked by a kidney matching algorithm. A multi-agent system is designed and implemented to support the human decision-maker with the pre-processing of the data and the suggestion of the best candidates (Valls et al. 2002).

4.1.2.3 Agents for kidney allocation

A number of agent-based systems have already been developed for information searching. After generating the matching list of potential recipients, based on allocation sequence policies, the agent chooses parts of potential recipients

or hospitals as further contacts to identify their availability, find out the final recipient and allocate corresponding resources. Through searching related database or web sites to retrieve donor and transplant candidate data as well as contact information of corresponding individuals and hospitals, agents then interact with human coordinators and set up the contact plan. Based on the contact plan, agents can automatically and simultaneously send notice or request to the human contacts that should be aware of the latest status. After collecting information, response and knowledge from related sources, intelligent agents with built-in reasoning capabilities such as probability-based reasoning or cased-based reasoning would be able to assist coordinators in finding the final recipient and even generate possible solutions for human decision-makers.

4.1.2.4 Agents for kidney distribution notification

Agent facilitates dispatching messages to corresponding teams or individuals involved in the process and keeping all the different parties aware of the current distribution situation. They also can response the requests for particular information from different parties in the process. Agents can easily automate such kind of notification. Agents can also automatically select alternative communication channels as phone calls, email, fax, and contacting relatives or friends in order to reach targeted recipients (Fricke et al, 2001). Typically, 100 phone lines only can notify 1,500 people in ten minutes. Agents are capable of augmenting the volume of communication channels and simultaneously contacting many people, facilitating
massive interactions, and also helping track those interactions, which could not be handled by traditional human-operated contact activity.

4.1.2.5 Agents for kidney distribution arrangement

Arrangement of a variety of identified distributed participants for kidney distribution is a very difficult task. Agent will help organize those identified participants in efficient ways, search related database to match mission requirements with peoples' profiles, assign them to medical teams and dynamically schedule activities in the distribution process. Agents can also register those individuals and teams to enable them to have authorities to access information and request for assistance and resources, and also make them as on site information resources for tracking the status of kidney distribution situation. To monitor kidney distribution, agents collect and review data to be certain that the distribution system is being followed and that it is achieving its goals. Agents are able to work real-time to aggregate and disseminate information based on user profile, communication traffic condition, and the current location of the users to facilitate information sharing between participants (Shek et al. 2000). Agents enable the participants during the kidney distribution to have the whole picture of the distribution situations and to make appropriate decisions. Onsite real-time needs for various resources could be facilitated through a distributed agent-based system, in which agents are able to constantly coordinate with each other to request, verify and use available resources. Agents for two issues, transportation and surgical operation arrangement, in the kidney distribution arrangement procedure have already been discussed, designed

and implemented by other researchers. One such a multi-agent system is designed for finding the most efficient way of transporting an organ, suitable to be transplanted, to the hospital where it must be implanted (Moreno et al. 2001a). The other is to solve scheduling task in the management of team that is going to make the surgical operation to implant an organ to a patient (Moreno et al. 2001b).

Roles of agents in five tasks of kidney distribution are summarized in Table 7

Tasks taken	Roles
by agents	
Registration	Create donor record
	Register donor information to organ sharing network
Matching	Generate the candidate lists of kidney recipient
Allocation	• Generate contact list for further identification and confirmation.
	• Select alternative communication channel such as phone calls, email and SMS
	Set up contact plan
	• Contact the persons in the contact list to check their current availability
	Tracking those interactions
	Collects response information
	• Process and analyze the data further
	• Interact with human coordinators
	Generate the identified resource list
Notification	• Notifying the relevant participants about the current status
	Tailor messages to parties
	• Dispatch specific information to the right person
	• Send request for action to personnel, department or organization
	• Respond the requests for particular information from different parties in the process
Arrangement	Facilitate information exchange among parties
l .	• Match individuals and groups to the corresponding roles (e.g.
	retrieval team, physician, transplant team and so on)
	Organize identified participants
	• Schedule activities in the kidney distribution process
	Receive tasks from human coordinators
	• Update and notify team assignment dynamically
	Offer resource allocation and logistic support
	Monitoring process
	Handle exception

Table 7 Roles of agents in cadaver kidney distribution

4.2 Development of a multi-agent system for cadaver kidney distribution

In this section, a distributed, agent-based system combined with mobile for improving coordination in donated kidney distribution is presented.

4.2.1 Three types of agents

Based on the general distributed agent architecture developed by Katia Sycara and Dajun Zeng (1996), in my system agents may be classed as *user agents*, *task agents* and *information agents* according to their different types. User agents assist users (e.g. physicians, patients, coordinators etc.), know their preference and may act on the user's behalf. Task agents have their beliefs and goals to help people perform tasks by communicating with other agents to reach mutual agreements. They are identified by the roles they take in a given task. And task agents used to solve distributed problems (e.g. informing all related staffs for the operation, scheduling the operation, arranging the organ transportation, exchanging information with others (man or agents), etc.). Task agents can be organized on-demand to cooperate with other agents for different tasks. Information agents provide intelligent access to a heterogeneous collection of information sources (Sycara and Zeng 1996).

The relations among three types of agents in my system are shown as follows.



Figure 12 Three types of agents in the multi-agent system

Functions of three types of agents:

- User Agent
 - 1) Making decision on the user's behalf based on the knowledge of user's preference
 - 2) Asking for user confirmation, when necessary

- 3) Asking the user questions for the information needed for decision making
- 4) Reporting the relevant information that the user wants to know
- 5) Collecting the relevant information from user to initiate a user profile

• Task Agent

- 1) Receiving new task from user agent and decompose the task
- 2) Making a plan for realizing its goal
- 3) Identifying what information needed
- 4) Coordinating with relevant agents for plan execution, monitoring and result composition
- Information Agent
 - 1) Responding to the query from task agents or other information agents
 - 2) Accessing and bundling distributed information sources
 - 3) Monitoring the occurrence or change of particular information

4.2.2 Architecture of the Multi-agent System for kidney distribution

The definition of agents in this system in terms of their roles and functions is assisted through conceptual models, which make up understanding of kidney distribution organization. This framework provides the conceptual basis for identifying the roles and related missions during kidney distribution. This model contains various basic entities represented as objects with specific properties and relations. Use case diagram and sequence diagram are illustrated in Figure 13 and Figure 14 respectively. Collaboration diagram presents the structure of a hierarchy of different levels in the co-ordination process in Figure 15. Definitions of objects, attributes and relations are specified in UML (Unified Modeling Language), which is a modeling language for specifying, visualizing constructing and documenting the artifacts of a system-intensive process.

4.2.2.1 Use case diagram



Use Case Diagram of kidney distribution process

Figure 13 Use case diagram of kidney distribution process

4.2.2.2 Sequence diagram



Figure 14 Sequence diagram of kidney distribution process

4.2.2.3 Collaboration diagram of the structure of a kidney distribution organization





4.2.2.4 Class diagram of intelligent agents

Based on this understanding with regard to kidney distribution organization and a typical cadaver kidney distribution process, agent-based system is proposed to facilitate the interactions between those parties. A class diagram of agents is illustrated in Figure 16. The collaboration diagram of agents is presented in Figure 17. This multi-agent architecture can be easily extended or tailored to any type of kidney distribution organization structure.



Figure 16 Class diagram of agents



4.2.2.5 Collaboration diagram of intelligent agents

Figure 17 Collaboration diagram of agents

4.3 Communication in KQML message Syntax

In my system, agents communicate with each other by KQML (Finin et al, 1994a; Finin et al, 1994b; Finin et al, 1994c; Labrou et al, 1994; Labrou 1996).

The Knowledge Query and Manipulation Language (KQML) is a language and protocol for exchanging information and knowledge. KQML is both a message format and a message-handling protocol to support run-time knowledge sharing among agents. KQML focuses on an extensible set of performatives, which defines the permissible operations that agents may attempt on each other's knowledge and goal stores. The performatives comprise a substrate on which to develop higher-level models of inter-agent interaction such as contract nets and negotiation. In addition, KQML provides a basic architecture for knowledge sharing through a special class of agent called communication facilitators which coordinate the interactions of other agents (KQML)

I will give two examples of agent communication using KQML in my proposed multi-agent system.

1) Example 1

• After Identification agent gets a new donor information, it formulates a goal ("confirming final recipient and relevant resources") and instantiates it with "donor-number = xxxxxx". That goal has 4 subgoals, "finding out the possible choices of recipient and relevant resources", "collect contact information", "producing contact plan" and "generating list of the identified final recipient and relevant resources". First of all, Identification agent contacts with Allocation agent for "finding out the possible candidates of recipient". So the Identification agent sends the following message to Allocation agent

(ask

:language

:ontology kidney-distribution

:in-reply-to identification-agent-ask-allocation-agent

:sender identification-agent

:receiver allocation-agent

:content (Need top-ranked-recipient-candidate

(donor-number="xxxxxx")

(ABO)
(HLA)
(PRA)
)	

)

• To find the recipient candidates, Allocation agent sends a KQML message to Qualification agent to rule out unsuitable choices preliminarily. So the scope of searching recipient is minimized.

(ask

:language

:ontology kidney-distribution

:in-reply-to allocation-agent-ask-qualification-agent

:sender allocation-agent

:receiver qualification-agent

:content ((Need qualified search condition)

(donor-number="xxxxxx")

```
(hospital )
(age )
```

(race)

)

)

2) Example 2

• The Identification agent processes the recipient candidates list and contacts Data retrieval agent to find more detailed recipients' information (e.g. telephone number, address, physician, physician's cell phone number...) and then produce the contact plan to contact candidates and their physicians. It decides the contacts, contact contents, the sequence of contact execution steps and selects alternative communication channels as phone calls, email and pager. Parts of contact task might be completed by the human-coordinators but most of them might be executed by Contact agents.

(evaluate

:language

:ontology kidney-distribution

:reply-with identification-agent-ask-coordinator-agent

:sender identification-agent

:receiver coordinator-agent

:content (contact plan = ?confirmed

(((time)(contact-name)(channel)(contents)(executor))
((time)(contact-name)(channel)(contents)(executor))
((time)(contact-name)(channel)(contents)(executor))
....
)

)

)

(stream_all (ask_all

:language

)

)

:ontology kidney-distribution

:in-reply-to identification-agent-ask-contact-agent

:sender identification-agent

:receiver contact-agent

:content (Need responses

(((time)(contact-name)(channel)(contents))
 ((time)(contact-name)(channel)(contents))
 ((time)(contact-name)(channel)(contents))

)

• The Coordinator agent asks the human coordinators about the contact plan. Then it returns the confirmed information or the changes provided by the human coordinators.

(tell

:language

:ontology kidney-distribution

:in-reply-to identification-agent-ask-coordinator-agent

:sender coordinator-agent

:receiver identification-agent

:content (Changed

(((time)(contact-name)(channel)(contents)(executor))
((time)(contact-name)(channel)(contents)(executor))
((time)(contact-name)(channel)(contents)(executor))
....
)

)

• In order to communicate with the contacts, the Contact agent spawns multiple inquiries collecting responses from different contacts in parallel. After the contacts' responses get collected, the Contact agent sends them to identification agent to make decision on the final recipient.

(reply

:language

:ontology kidney-distribution

:in-reply-to identification-agent-ask-contact-agent

:sender contact-agent

:receiver identification-agent

:content (

)

```
(((time )(contact-name )(response ))
 ((time )(contact-name )(response ))
 ((overtime)(contact-name ))
 ....
)
```

Chapter 5

Implementation of agent-based prototype system for assisting coordinator to identify the final recipient

It will take a great effort to implement an agent-based collaboration system for assisting coordinator in kidney distribution process. Since the importance of identifying a final recipient, confirmed inefficient communication problem by human coordinators and no other researches on the allocation task of the organ distribution process, I thereby only focus on one critical task, allocation task, to develop a prototype system for testing my solution. From my research findings, I found that identification of resources, particularly the final recipient, is one of the most timeconsuming tasks in the kidney distribution process. In some cases the final recipient can't be determined until the final crossmatch is complete at the recipient center and it is certain that this center will use the kidney. If the final recipient or the recipient center could be identified earlier, it will be easier and earlier to identify other related resource for the kidney transport and transplant. I believe that if the efficiency of critical task can be improved the performance of whole distribution system will be improved. Therefore, an agent-based prototype system was designed and developed to assist coordinator to identify the final recipient. This implementation utilizes Short Message Services (SMS) that is embedded into this system for improving the efficiency of communication task between agents and persons.

Before describing the prototype system, simplifying assumptions are made as followings:

- In this system, I only consider the issue of finding the final recipient and the transplant center. The issues of kidney allocation algorithm and coordination in kidney transportation and kidney transplant operations will not be considered here. The solutions for those issues have been proposed and discussed by other researchers. (Yuan et al. 2001a)
- After generating the optimal transplant candidate list by matching algorithm, all factors to influence the final decision on the recipient of a particular kidney are assumed to be opinions of patients and their physicians as well as availability of transplant center for the transplant operation.
- We suppose the waiting transplant patients and physicians responsible for the care of those patients have mobile phones. And all the mobile phones they use have Short Message Services. Moreover, all their phone numbers are stored in database that agents could access.
- Considering the use of cellular phone emulator, I have to use IP address and port number to identify different mobile phones instead of actual phone number.
- The availability of transplant center (bed, operation room, hospital equipment, medical personnel etc.) can be checked by agent through hospital legacy system or by coordinators through one-to-one voice communication.
- Agents help coordinators identify the availabilities of the most suitable recipients (not just one), then coordinators or specialists make the final decision on the recipient of a particular kidney.

5.1 Decomposition of goals in the agent-based prototype system

The goal of this prototype system is decomposed as follows (see Figure 18):



Figure 18 Goal tree of the prototype system

5.2 Tasks and roles of agents in the kidney distribution prototype system

Based on the goals analyzed in previous section, the agent-based prototype system consists of seven agents: Registration agent, Coordinator agent, Contact agent, Candidate matching agent, Recipient identification agent, Data retrieval agent and Publisher agent. The tasks and roles of different agents are described in Table 8.

Tasks	Agents	Roles
Registration	Registration agent	 Create donor record Register donor information to organ sharing network
Matching	Candidate matching agent	• Generate the candidate lists of kidney recipient
Allocation	Recipient identification agent Coordinator agent Contact agent	 Generate contact list for further availability identification and confirmation. Accept instruction from user (coordinator) to adjust its decision strategy Schedule contact activities Continuously record message exchanged among agents and coordinators Analyze the response information collected by contact agents Make final choice for recipient Interact with human coordinators Report current situation and execution plan Receive instruction from human coordinators Contact the persons in the contact list to check their availability Select alternative communication channel such as phone calls, email and SMS Collects response information Tracking those interactions
	Data retrieval agent	 Access information sources (Database) Retrieve and filter information according to other agents' requests Monitoring the occurrence or change of particular information
Notification	Publisher agent	 Respond the request for particular information from different parties in the process Integrate and present up-to-date information requested by users

Table 8 Roles of agents in my implemented multi-agent system

5.3 The architecture of the multi-agent prototype system

The architecture of the multi-agent prototype system has been designed, implemented and is shown in Figure 19.



Figure 19 Collaboration diagram of agents

I will now provide a brief description of each of the basic agents of this system. In the next section I describe in detail the coordination of agents and coordinator, illustrate the functioning of the distributed, cooperative intelligent agents through a scenario. • Registration Agent

This agent presents the interface of the multi-agent system. When it receives a message with the donor information, it initiates the coordination process by sending this information to the Recipient Identification Agent. If the donor record is registered into kidney sharing network successfully, Registration Agent will receive from Recipient Identification Agent a confirm message.

Coordinator Agent

This agent presents the interface of the multi-agent system with transplant coordinator. It is responsible for the communication with Transplant coordinator to receive coordinator's request, send this information to Recipient Identification Agent, and proactively or passively provide useful information to coordinators. Transplant coordinator can control the behavior of the agent through the coordinator interface.

• Recipient Identification Agent

This is the central agent of the system. It receives from Registration Agent the basic data necessary for identifying the recipient, and passes it along to the Candidate Matching Agent and Coordinator Agent. When Recipient Identification Agent receives the transplant candidate list from Candidate Matching Agent, it gets in touch with the Data Retrieval agent to find out the contact information of candidates and their physicians as well as relevant information of transplant center. Considering the opinion from Transplant Coordinator through Coordinator Agent, Recipient Identification Agent makes the contact plan and then sends it to Contact agent for

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execution. After receiving the contact results from Contact Agent, Recipient Identification Agent tries to match them (the decisions from patients and their physicians as well as availability of transplant center) and balance the criteria to find the most suitable recipient among those candidates. If this matching is successful, Recipient Identification Agent will send recipient suggestion to Coordinator Agent.

• Candidate Matching Agent

This agent receives from Recipient Identification Agent the information about the donor. It communicates with the Data Retrieval Agent to collect data of waiting transplant patients and then it will apply kidney allocation algorithm (multi-criteria decision) to rank the list of patients. The possible recipient list generated by Candidate Matching Agent will be send to Recipient Identification Agent.

• Data Retrieval Agent

This agent is responsible for access to a heterogeneous collection of information resources. It makes hospital legacy information resource available to other agents. Data retrieval agent retrieves information in response to a query from Recipient Identification agent, Candidate Matching Agent or Publisher Agent

• Contact Agent

This agent receives from Recipient Identification Agent the information about contact plan (contact ID, contact method, phone number, contact content and the period of time permitted for waiting reply). According to the contact plan, Contact Agent

selects alternative communication channels as phone calls, email and sends contact information (SMS or email) to receivers simultaneously. Contact Agent can also help tracking those interactions. After collecting response (SMS or email) from the patients and their physicians, it sends response results to Recipient Identification Agent for the decision on the final recipient.

• Publisher Agent

This agent is responsible for accepting requests on particular information from distributed authorized persons involved in this process and keeping updating information in the information-sharing network. It efficiently integrates the data and information to give a whole picture of the distribution situation.

5.4 An illustrative scenario

In order to demonstrate how agents would be able to assist coordinator to identify the final chosen recipient during cadaver kidney distribution, a scenario of the identification process with the help of agents as well as mobile and wireless technologies is illustrated in the following:

1) Registration

When there is a kidney available for transplant, the Registration agent receives a message with donor information (see Figure 20).

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	Donor recor	d has been submitted su	ccessfully
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_ast Name	Albers	Area	Ontario 💌
First Name	Mike	Hospital	Hamilton-St. Joseph 💌
Age	45	Death Date	04/06/2003
		a tit ai bedavan	
Blood Type) <u>A</u>		

Figure 20 Registration Agent interface

That means that the system must find a compatible kidney recipient of a transplant center for this donor as soon as possible.

2) Matching

The Registration Agent sends the same message to the Recipient Identification Agent and the Recipient Identification Agent sends this message to Coordinator Agent (see Figure 21) and Candidate Matching Agent that will pass it along to the transplant coordinator and Data Retrieval Agent. As soon as Data retrieval Agent retrieves enough laboratory test data of donor for kidney allocation, Candidate Matching Agent applies allocation schemes and algorithm to find the transplant candidate. Candidate Matching Agent will send candidate list to Recipient Identification Agent. The candidate list is also forwarded to Coordinator Agent for transplant coordinator review.

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Figure 21 Interface of contact agent

3) Contact (Allocation)

Recipient Identification Agent chooses several top-rank candidates to generate a contact list and Data Retrieval Agent collect the contact information related to these candidates such as patients' phone numbers, phone numbers of those patients' physicians and phone number of transplant centers that patients belong to. Based on this contact information, Recipient Identification Agent makes the contact plan in which the communication method (one-to-one voice communication, SMS, email or fax), sequence of contact activities, contact content, period of time permitted for waiting for reply and interval of repetition of calls are determined. The one-to-one voice communication task could be completed by transplant coordinators and the rest of communication tasks could be delegated to Contact Agent. Contact Agent could send different information or questions to different receivers simultaneously by SMS or email. The information could be shown in cell-phone or PDA of patients or physicians. (See Figure 22)



Figure 22 Contact information shown on cell phone and PDA

4) Information request (Notification)

After receiving the brief donor information, physicians could get online to request more donor information from donor information sharing network. Publisher Agent will process their request and present the information on the webpage.

5) Allocation

Then physicians could reply whether to accept the kidney or not by sending the short text messaging through their cell phones. In addition, patients could send their decision on the kidney and answers of questionnaire about their present health status to Contact Agents through their cell phones. Messages exchanged among parties will be recorded by Contact Agent for action tracing, situation assessment and later on investigation. In the case in which there is no answer received after the period of time permitted for waiting reply expires, the system will conclude that the contacted party gives up the chance to accept the kidney. Part of contact work may be done by transplant coordinators. After receiving the contact results from Contact Agent and transplant coordinators, Recipient Identification Agent tries to match them to find the available recipient. (See Figure 23)

Recipient Identification Result

1		and Announcements and a commence		Priysciari		Final choice
1	Mike	Albers	refuse	accept	accept	N
2	Mark	Andrews	accept	accept	accept	Y
3	Mark	Anna	accept	refuse	accept	N

Figure 23 Result of recipient identification

In case, all of contacted candidates are not available for the kidney, Recipient Identification Agent will select rank lower candidates on that potential recipient list to contact or ask Candidate Matching Agent to generate a new candidate list in a bigger area until finding the most appropriate available recipients. Recipient Identification Agent will send final recipient suggestion to Coordinator Agent. The coordinator who is in charge of the final kidney assignment will be told the final recipient suggestion by Coordinator Agent. Considering recipient identification result, patients' answers of health status questionnaire and other rules, coordinator will decide the final recipient for a particular kidney.

Although only parts of proposed multi-agent system are implemented here, the principles of implementation of other parts of system are similar to that of the developed part. The implemented prototype system is enough to demonstrate the agent technology for improving the efficiency of kidney distribution.

Chapter 6

Conclusions

The main contributions of my research are:

1. Identifying inefficiencies in donated kidney distribution

I investigate the process of donated kidney distribution through collected data and detailed records about the practical steps of kidney distribution and their execution time in different cases from TGLN and St. Joseph's hospital. The kidney distribution process is analyzed with the flowchart, Gantt chart and Critical path network chart. Based on the statistics data and analysis, I found the problems in current manual processing. Problems in coordination and contact management, particularly the delay problem, are the key challenges that I attempt to overcome

2. Proposing a suitable solution for improving the efficiency of donated kidney distribution;

A distributed multi-agent system operating in a mobile and wireless communication environment is proposed to assist transplanting coordinators in coordinating with multi-parties in the time-critical distribution process. In previous section this solution is justified by the nature of cadaver kidney distribution process and the advantages of agent technology as well as mobile and wireless technology. 3. Developing a multi-agent prototype system to help transplanting coordinators in allocating the kidney recipient.

The prototype system present in this thesis has been implemented in AgentBuilder. AgentBuilder is an integrated software toolkit that allows software developers to quickly develop intelligent software agents and agentbased applications. On that agent development platform, programming software agents (sometimes called Agent-Oriented Programming) is accomplished by specifying intuitive concepts such as the beliefs, commitments, behavioral rules and actions of the agent. The agents created with AgentBuilder can be distributed across machines (which not even need to share the same OS). I also developed a SMS (Short Message Service) emulator in J2ME (Java 2 Platform, Micro Edition). This emulator is integrated with Cellular Phone emulator for sending and receiving short messages. All the programming codes of this system are written in Java. In the implemented system, agents can assist the coordinator while they build their requests for actions, manage the contact process, send contact information, collect response information and suggest solution. The complexity of coordinator's contact work is reduced with the help of the multi-agent system.

I clarify the great potential of agents in supporting cadaver kidney distribution. The advantage of such a system is not only improving the efficiency of

this distribution process but also organizing the gathered information about kidney allocations using electronic format that can be analyzed later through data mining or machine learning procedure.

Moreover, the current work provides the discussion on agent technology application in health care area and would lead to the future research on exploring the roles of agents in facilitating other collaborations which involve time critical, urgent decision making, as well as the distributed entities, information and control. Ultimately, the patients will benefit greatly from my research.

Clearly, there are many issues need to be further investigated. Due to the time limitation, I didn't develop the entire multi-agent system I proposed. Although I have just implemented part of the functions of the whole system, the rest parts still follow the principle of the developed part and could be developed with similar methodologies. In future work, this prototype system should be extended and completed in order to deal with more complex situations that could happen in practical kidney distribution process.

A significant improvement of the efficiency of donated kidney distribution is expected, but I did not have time to run an experiment to verify the expectation in my thesis. A simulated case could be conducted with a fully implemented multiagent system.

Due to the availability and familiarity of AgentBuilder, I have used AgentBuilder to develop the agent-based prototype system. While AgentBuilder provides an advanced suite of graphic tools for supporting all phases of the agent

construction process, after evaluating this toolkit through this practical development project, I found that AgentBuilder does not integrate well with imported Java classes and packages I defined. Considering its weaknesses in standard compatibilities, security policy, agent mobility, usability and documentations, I will not recommend AgentBuilder toolkit for future large-scale distributed agent-based applications.

In my implemented multi-agent prototype system, agents communicate with each other using the Knowledge Query and Manipulation Language (KQML). Although in Distributed AI (DAI) research KOML offers a standard language and protocol that intelligent agents can use to communicate among themselves, it is not highly accepted by industry in comparison with another agent communication language, FIPA (The Foundation for Intelligent Physical Agents) ACL. FIPA was established as a not-for-profit organization in the middle of 1996 for producing standards for the interoperation of heterogeneous software agents. FIPA's normative specifications address such areas as agent management, agent communication language, agent-software integration, mobility, ontology, human interaction, nomadic applications and architecture. FIPA ACL is based on speech act theory. In KQML, each expression is a speech act described by a performative (Finin et al. 1994). The two languages have similar syntax. To ensure my agent application implementation to be integrated with agents constructed using other methods, tools, and/or architectures, I would move the system to a more standard and popular multiagent platform like JADE (Bellifemine et al. 2001). JADE (Java Agent DEvelopment Framework) is free software and is distributed by TILab. JADE has good GUI, accessible use and good documentation. The agents built by JADE use FIPA

specifications and support for inter-platform messaging with plug-in MTPs (RMI, IIOP, HTTP, WAP), ACL (Agent Communication Language) and XML codec for messages. It also has very good security features (Nguyen and Dang, 2002). By now JADE has been used in many development projects such as INRIA, Nice-Sophia-Antipolis, ATOS Sophia Antipolis agency within the European CoMMA project etc.

In order to improve the quality of communication between agents and mobile devices, it would be better to use the Wireless Messaging API (WMA). For future Mobile device program development WMA provides a porting/testing platform for sending and receiving SMS messages and have more functions than my developed SMS emulator. WMA is supported by J2ME Wireless Toolkit 2.1, a cell-phone emulator.

The architecture and functions of my proposed agent-based system presented in this thesis focus on the kidney transplant coordination task. Other research fields that I should study are the reasoning mechanism behind the decision making process for each agent and the incorporation of learning methods.

I did not implement privacy, security into my prototype system design. After the building of the prototype, user needs and interests will be more clearly defined, and then security constraints and medical legal issues will be studied in detail.

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Appendix A – Medical Background

In the following, I will provide a general introduction to the medical terms needed to follow the thesis.

Kidney transplant

Kidney transplant is a surgical procedure to implant a healthy kidney into a patient with kidney disease or kidney failure. The kidney transplant may be taken from a living donor or from a recently deceased donor.

Graft Survival

When a transplanted tissue or organ is accepted by the body and functions properly. The potential for graft survival is increased when the recipient and donor are closely matched.

Rejection

An immune response against grafted tissue, which, if not successfully treated, results in failure of the graft to survive

HLA (Human Leukocyte Antigen) Matching

HLAs are antigens that are present on human white blood cells (leukocytes) and tissues. Each HLA is determined by a locus on gene, and thus every body inherits two antigens per locus, one from each parent. The significant loci in terms of kidney allocation are referred to as the A, B and DR loci. Over 40 distinct HLA antigens have currently been identified for each of these loci. An HLA "mismatch" occurs when the donor possesses a particular HLA at one of these loci that the recipient does not have. Simplistically, the recipient "sees" something foreign to be attacked. Since a close HLA match between donor and recipient lowers the possibility of graft rejection, in an ideal scenario, the number of mismatches between the donor and the recipient should be at a minimum.

Crossmatching

A test in which donor and recipient blood samples are mixed together. A "positive" crossmatch shows the donor and recipient are incompatible. A "negative" crossmatch shows there is no reaction between the donor and the recipient. This means that the donor and recipient are compatible and the transplant may proceed.

CIT (Cold Ischemic Time)

Time between taking the organ out and placing it into a recipient

PRA (Panel Reactive Antibody)

A way of measuring immune system activity within the body. Serum is extracted from each patient, and each serum is then allowed to react with blood cells taken from a panel representing a supposedly random population. If the patient contains antibodies for an HLA antigen found on the cells of one of the members of this panel, the serum and cell will react. The percentage of people in the population with whom the patient's serum will react is the patient's PRA percentage number. PRA is higher when more antibodies are being made.

Survival Rates

Survival rates indicate how many patients or grafts (transplanted organs) are alive/functioning at a set time post-transplant. Survival rates are often given at one, three and five years. Policy modifications are never made without examining their impact on transplant survival rates. Survival rates improve with technological and scientific advances. Developing policies that reflect and respond to these advances in transplantation will also improve survival rates.

Waiting List

After evaluation by the transplant physician, a patient is added to the national waiting list by the transplant center. Each time a donor organ becomes available, the computer generates a list of potential recipients based on several criteria that include HLA matching, ABO blood group, PRA, waiting time on the waiting list and so on. Through this process, a "new" list is generated each time an organ becomes available.

Waiting Time

Waiting time is the length of time that a patient has been on a particular waiting list waiting for a suitable donor kidney. In order to allocate the donor kidney equally, a patient who has been waiting longer for a kidney is given priority over another patient who has been waiting for a shorter amount of time.

Appendix B – Description of the interactions of the various agents in the multi-agent system

• Registration Agent is informed a new donor available for kidney distribution.

Donor's basic and relevant medical background information, such as name, age, sex, race, hospital, declared death date, cause of death, blood type and laboratory data (PRA, CMV, HBsAG, HIV, HCV, HTLV1, Heb B Core Ab(lgG)) are necessary for the kidney allocation.

• Registration agent processes the kidney offer, assign the donor a unique donor number and extracts donor's information to Scheduling agent.

(insert

:language :ontology kidney-distribution :in-reply-to registration-agent-inform-scheduler :sender registration-agent :receiver scheduling-agent :content (insert donor (donor-number) (first-name) (last-name) (age) (sex) (hospital (declared-death-date) (ABO))

)

• The Scheduling agent informs coordinator agent about the kidney offer.

(Insert

```
:language
:ontology kidney-distribution
:in-reply-to scheduling-agent-inform-coordinator-agent
:sender scheduling-agent
:receiver coordinator-agent
:content (insert donor
(donor-number )
(first-name )
(last-name )
(age )
(sex )
```

```
(hospital )
(declared-death-date )
(ABO )
```

-)
- The Coordinator agent asks the Scheduling agent for the current status of kidney procurement and distribution process.

(Subscribe

:language :ontology kidney-distribution :in-reply-to coordinator-agent-subscribe-scheduling-agent :sender coordinator-agent :receiver scheduling-agent :content (Need updates of the current progress

)

• The Scheduling agent formulates a goal ("arrange the kidney distribution to the recipient's transplant center") and instantiates it with "donor-number = xxxxxx". This goal has two subgoals, "identifying the final recipient and relevant resources" and "produce kidney distribution schedule". The Scheduling agent will plan to contact the known task agent or information agent for "identifying the final recipient and relevant resources". So in executing the first plan step, the scheduling agent formulates a KQML message to the Identification agent conveying the donor's medical background information and ask it to find the final available matched recipient satisfying the allocation criteria.

(achieve

```
:language
:ontology kidney-distribution
:in-reply-to scheduling-agent-ask-identification-agent
:sender scheduling-agent
:receiver identification-agent
:content (Need final-recipient
(donor-number = "xxxxxx")
)
```

)

• The Identification agent formulates a goal ("confirming final recipient and relevant resources") and instantiates it with "donor-number = xxxxxx". This goal has 4 subgoals, "finding out the possible choices of recipient and relevant resources", "collect contact information", "producing contact plan" and "generating list of the identified final recipient and relevant resources". First of all, the Identification agent contacts with Allocation agent for "finding out the

possible candidates of recipient". So the Identification agent sends the following message to the Allocation agent

(ask

:language :ontology kidney-distribution :in-reply-to identification-agent-ask-allocation-agent :sender identification-agent :receiver allocation-agent :content (Need top-ranked-recipient-candidate (donor-number="xxxxxx") (ABO) (HLA) (PRA) (Xmatch))

)

• To find the recipient candidates, the Allocation agent send a KQML message to Qualification agent to rule out unsuitable choices preliminarily. So the scope of searching recipient is minimized.

(ask

:language :ontology kidney-distribution :in-reply-to allocation-agent-ask-qualification-agent :sender allocation-agent :receiver qualification-agent :content ((Need qualified search condition) (donor-number="xxxxxx") (hospital) (age) (race)

)

)

• The Qualification agent returns qualified search condition to allocation agent based on the distribution rules and newest notices from different parties which have the alternative resources needed for the kidney distribution. The message is as follow.

(tell

:language :ontology kidney-distribution :in-reply-to allocation-agent-ask-qualification-agent :sender qualification-agent

)

• After the qualified search conditions have been communicated to the Allocation agent by the Qualification agent, according to a kidney allocation algorithm, the Allocation agent will execute next step to generate a list of potential kidney recipients from a recipient waiting list through Data retrieval agent.

(ask

:language :ontology kidney-distribution :in-reply-to allocation-agent-ask-data-retrieval-agent :sender allocation-agent :receiver data-retrieval-agent :content (Need recipient-candidate (donor-number="xxxxx") (ABO) (HLA) (PRA) (PRA) (Xmatch) (Qualified condition) order by score)

)

• The Data retrieval agent queries the potential recipient database and returns basic information of the potential recipients who match the donor medically.

(tell

:language :ontology kidney :in-reply-to alloca :sender data-retrie :receiver allocatio	-distribution ation-agent-ask-data-r eval-agent	etrieval-agent		
:content (respond				
((rank)(recipient-number)(recipient-name)(hospital)
(rank)(recipient-number)(recipient-name)(hospital)
(rank)(recipient-number)(recipient-name)(hospital)
)				

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)

After Allocation agent generates a list of potential recipients, it completes kidney allocation task and returns top-ranked recipient candidates to identification agent.

(tell

:language :ontology kidney :in-reply-to ident :sender allocation receiver identifi	-distribution ification-agent-ask-al 1-agent	location-agent		
	ation-agent			
:content (((rank)(recipient-number)(recipient-name)(hospital)
(rank)(recipient-number)(recipient-name)(hospital)
(rank)(recipient-number)(recipient-name)(hospital)
•••••				
)				

-)
- The Identification agent processes the recipient candidates list and contacts Data • retrieval agent to find more detailed recipients' information (e.g. telephone number, address, physician, physician's cell phone number...) and then produce the contact plan to contact candidates and their physicians. It decides the contacts, contact contents, the sequence of contact execution steps and selects alternative communication channels as phone calls, email and pager. Parts of contact task might be completed by the human-coordinators but most of it might be executed by Contact agents.

(evaluate

)

```
:language
      :ontology kidney-distribution
      :reply-with identification-agent-ask-coordinator-agent
      :sender identification-agent
      :receiver coordinator-agent
      :content (contact plan = ?confirmed
                (((time )(contact-name )(channel )(contents
                                                                )(executor ))
                ((time )(contact-name )(channel )(contents
                                                                )(executor ))
                ((time )(contact-name )(channel )(contents
                                                                )(executor ))
(stream all (ask all
      :language
      :ontology kidney-distribution
      :in-reply-to identification-agent-ask-contact-agent
```

```
:sender identification-agent
```

• The Coordinator agent asks the human coordinators about the contact plan. Then it returns the confirmed information or the changes provided by the human coordinators.

(tell

)

```
)
```

• In order to communicate with the contacts, the Contact agent spawns multiple inquiries collecting responses from different contacts in parallel. After the contacts' responses get collected, the Contact agent sends them to identification agent to make decision on the final recipient.

(reply

)

After the response information has been collected, the Identification agent then executes the last step of the "generating list of the identified final recipient and relevant resources" plan. The identification agent asks the qualification agent to process and analyze the collected response information so it can identify the final recipient or the conflicts and compose further contact plan.

Rank	Recipient No	Patient	Physician	Hospital
1	5031	Y	N	Y
2	2342	N	Y	Y
3	4543	Y	Y	Y
4	894	timeout	timeout	Y
5	345	timeout	timeout	N

Table B-1 Collected response information for identifying final recipient

Table B-1 shows an example of response analysis. The columns correspond to different kinds of contacts that are related to each potential recipient. The rows are the potential recipients for identification. The marks of "Y" and "N" indicate which information source return answers for which potential recipients. "Y" represents "accept the kidney" and "N" represents "can't accept the kidney". The mark of "timeout" indicates no answer within the specified period of waiting time. The candidates, who have all the information sources marked with "Y", could possibly be chosen as the final recipient. At last, the decision depends on the rank of all available recipients, from whom the top-ranked one will be selected as the final recipient. From Table B-1, I observe that the third rank candidate is the final recipient.

• If the identification agent identifies the final recipient and relevant resources it passes the list of final recipient and relevant resource to Scheduling agent.

(tell

(tell

```
:language
:ontology kidney-distribution
:in-reply-to scheduling-agent-ask-identification-agent01
:sender identification-agent
:receiver scheduling-agent
:content (response
((recipient-no))
(name))
(hospital))
)
```

:ontology kidney-distribution

...)

)

• Now the Scheduling agent executes the second subgoal as the "produce kidney distribution schedule". It composes the distribution schedule through subsequent interaction and negotiation of scheduling conflicts with participants through identification agent, contact agent and coordinator agent. Due to the high uncertainty in the kidney distribution event, Scheduling agent will adjust his schedule frequently so it can not make a final schedule at once and only have a temporary schedule with estimated time on each step. An example of the schedule is shown in the following table.

	ЕТА	Plan	Execution
Nov 23	11:45am	Flight is ready for kidney	Nov 23 12:00 pm
Nov 23	12:00 pm	Retrieval team leaves for donor hospital	Nov 23 12:10 pm
Nov 23	12:45 pm	Retrieval team arrive donor hospital	Nov 23 12:50 pm
Nov 23	13:20 pm	Donor surgery begins	Nov 23 13:42 pm
Nov 23	15:00 pm	Recipient arrives transplant center	Nov 23 15:09 pm
Nov 23	15:48pm	Kidney arrives	Nov 23 16:52 pm
Nov 23	18:00pm	Surgeons arrive transplant center	Nov 23 18:00 pm
Nov 23	19:20pm	Operating Room, Anesthesia, Blood Bank, Biochemistry and transplant laboratories are ready for transplant	Nov 23 20:18 pm

Table B-2 Estimated time schedule

Any exceptional input by the human coordinator will affect the schedule managed by the Scheduling agent. It integrates the information, tries to find the conflicts and resolve it again. Scheduling agent repeats all above-mentioned activities till no conflicts exist in the schedule.

• The Scheduling agent passes the schedule to Notification agents for generating the notification plan. Notification agent collects the contact information through

the data retrieval agent and produces the notification plan. That plan is then executed by Contact agents.

• Based on the donor and recipient information in database, log file and kidney distribution schedule, Report agent generate the reports at the users' request.

Since the agent-based system just facilitates coordinator to manage kidney distribution, it needs interact with the user, getting user input, confirmation of suggestion, asking for user advice, and advising the user of the state of the system and its progress.

Appendix C – Structure of The Database

Table Donor – Stores donor information.

Column Name	Туре	Size	
DonorId	Long	4	
Name	Text	20	
Age	Integer	3	
Hospital	Text	50	
City	Text	50	_
Area	Text	50	
DeathDate	Date/Time	8	
BloodType	Text	2	

<u>**Table** *Patient*</u> – Stores waiting list patient information.

Column Name	Туре	Size
PatientId	Long	4
Name	Text	20
Birthdate	Date/Time	8
Physician	Text	50
Hospital	Text	50
Area	Text	50
Address	Text	50
PhoneNumber1	Text	20
PhoneNumber2	Text	20
PhoneNumber3	Text	20
BloodType	Text	2
Pra	Integer	2
Date_on	Date/Time	8
Date_off	Date/Time	8
AMismatches	Integer	2
BDRMismatches	Integer	2

<u>**Table** *Hospital*</u> – Stores hospital or transplant center information.

Column Name	Туре	Size
HospitalId	Long	4
Name	Text	20
Area	Text	50
PhoneNumber1	Text	20
PhoneNumber2	Text	20
PhoneNumber3	Text	20

Column Name	Туре	Size
PhysicianId	Long	4
Name	Text	20
Hospital	Text	50
Area	Text	50
PhoneNumber1	Text	20
PhoneNumber2	Text	20
PhoneNumber3	Text	20

<u>**Table** *Physician*</u> – Stores physician information

Table Area – Stores kidney sharing area information.

Column Name	Туре	Size
AreaId	Long	4
Name	Text	20
Country	Text	50

<u>**Table** *BloodType*</u> – Stores blood type compatibility information.

Column Name	Туре	Size
BloodType	Text	2
Compatibility	Text	2

<u>**Table** *Kidney*</u> – Stores information about the kidney(s) being donated by a particular donor and the kidney allocation information.

Column Name	Туре	Size
DonorId	Long	4
Organ	Text	20
PatientId	Long	4
TransplantDate	Date/Time	8

Table Candidate Temp# – Stores temporary kidney candidate list patient information.

Column Name	Туре	Size
RecipientId	Long	4
Name	Text	20
Physician	Text	20
Hospital	Text	50
Area	Text	50
Address	Text	50
PhoneNumber1	Text	20
PhoneNumber2	Text	20
PhoneNumber3	Text	20
Rank	Integer	4

Appendix D – Agent Definition

Agent toolkit: AgentBuilder Pro 1.3

Kidney Distribution Agents

Recipient Identification Agency

Registration Agent

Recipient Identification Agent

Data Retrieval Agent

Contact Agent

Rule definition

Registration Agent

- Wakeup notify
- Build RegistrationFrame
- Start Registration Panel
- Receive message from control panel
- Forward message from control panel to Recipient Identification Agent
- Receive DonorId
- Change DonorRegister status

Recipient Identification Agent

- Wakeup notify
- Build Recipient Identification Frame
- Connect actions to Recipient Identification Frame
- Clean up after launch
- Receive new donor Message
- Finding out the candidates
- Receive recipient candidate list
- Designate Contact agent to send message
- Receive Donor Id
- Forward Donor Id

Data Retrieval Agent

- Wakeup notify
- Build data retrieval agent
- Connect actions to Data Retrieval Agent
- Clean up after launch
- Receive request for candidate list
- Forward candidate list

- Clean up after sending candidate list
- Display candidate
- Reply Donor Id

Contact Agent

- Wakeup notify
- Build Contact Agent Frame
- Start MultiContactServer
- Clean up after launch
- Connect actions to Contact Frame
- Receive Contact list
- Get the number of candidates
- Queue outgoing messages
- Send message to Cell phone
- Clean up after queue outgoing messages
- Receive response forwarded from server
- Display received questionnaire answers
- Add Response Record

Appendix E – Agent Program and MIDP Application

Development environment:

- WINDOWS XP/2000
- AgentBuilder Pro 1.3
- Builder 9 Enterprise
- JDK java version 1.4.1-02-b06
- J2SE
- Forte For Java 4 ME
- J2ME

System Requirements:

- WINDOWS XP/2000
- JDK 1.4.1
- J2ME Wireless Toolkit 1.0.4_01
- Java 2 SDK, Standard Edition(J2SE SDK)1.3 or higher
- AgentBuilder JRE
- AgentEngine
- At least 35MB disk spaces for software installation

Package:

• CoordinatorAssistant

Description:

This is the implementation of user-defined classes used as Project Accessory Classes (PACs), which are custom classes coded in Java and designed to perform some specific tasks that augment the agent's behavior. These provided classes allow agent to instantiate and manipulate. The agent can invoke any of methods specified in PACs

The purpose of the implementation is to:

- > Provide Graphical User Interface for the Agent
- Provide database access for the Agent
- > Provide connection between Agent and mobile phone emulator
- Provide Java classes that will implement the action defined in agent activities and behavior.

Package specification:

The classes in this package need to access classes in the AgentBuilder package (com.reticular.agentBuilder.agent.perception)

<u>UML – Class Diagram:</u>

NO.	Class
1	Registration Frame
2	Recipient Identification Frame
3	Data Retrieval
4	Contact Frame
5	Donor
6	Donor Register
7	Recipient
8	Recipients
9	Hospital
10	Physician
11	Response
12	Send Message







Figure 1-2 RecipientIdentificaationFrame.class













Figure 1-5 Donor.class







Figure 1-7 Recipient.class



Figure 1-8 Recipients.class



Figure 1-9 Hospital.class

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Figure 1-10 Physician.class

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Figure 1-12 Response.class

• Mobile device programming

Description:

This package is a basic implementation of J2ME MIDP (Mobile Information Device Profile) application (MIDlet) to emulate SMS (Short Message Service) behavior and customize the GUI (Graphical User Interface) on MIDs (mobile information devices) such as cellular phones and entry level PDAs.

The purpose of the implementation is to:

- Provide datagram communication that is used for UDP in the Generic Connection Framework to receive inbound wireless messages. Datagram connection is opened in a "server" mode.
- Provide TCP/IP socket communication to send wireless messages back to an agent through a remote server. A socket connection is the most basic low-level reliable communication mechanism.
- Provide standardized GUI, which is saved on the client devices will be triggered only by incoming messages from the agent.

Package specification:

The package is dependent on package (javax.microedition.io) which includes the platform networking interfaces to defines the framework and supports input/output and networking functionality in J2ME profiles.

NO.	Class
1	ContactClient
2	ContactClient.DatagramServerHandler
3	ContactClient.ListenerThread
4	MIDPConnector
5	OpinionChoice
6	Questionnaire

<u>UML – Class Diagram:</u>





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Figure 2-3 ContactClient.ListenerThread.class
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Figure 2-5 OpinionChoice.class



Figure 2-6 Questionnaire.class

SocketServer

Description:

This package is the implementation of a server that waits for messages sent to port 8080 from Cell Phones and responses to them.

The purpose of the implementation is to:

- ➢ For receiving messages, the server supports Multi-Threaded message process mechanism.
- > Provide communication with agent via messages.

Package specification:

The MultiContactServer class in this package needs access the classes in the com.reticular.agentBuilder.agent.perception package. The built-in PAC class PacCommSystem class is used to simplify communication between an agent and an interface PAC.

UML – Class Diagram:

NO.	Class
1	MultiContactServer
2	DispatchServer
3	ContactServer



Figure 3-1 MultiContactServer.class







Figure 3-3 ContactServer.class

È.

Appendix F – List of factors that influence the cadaver kidney distribution process

Donor Factors

- 1. No consent
- 2. Not declarable
- 3. Hep. B/C or HIV Pos
- 4. Size (too small/large)
- 5. Increased CIT
- 6. Unstable/Crashed
- 7. Infection/Sepsis
- 8. Poor 2D echo/12 lead
- 9. Increased Inotropes (heart)
- 10. Poor ABG's (lung)
- 11. Poor CXR/Bronchi (lungs)
- 12. Organ contused / lacerated
- 13. Medically unsuitable e.g.cancer, high risk donor etc.

Recipient Factors

- 14. No recipient
- 15. No suitable recipient (size of kidney)
- 16. Recipient died- organ en route
- 17. Recipient not ready
- 18. Problem with Primary recipient no time to bring in back-up recipient

Team Factors

- 19. No surgeons
- 20. Team too tired
- 21. No ICU bed
- 22. No blood for transplant
- 23. No reason given

Other Factors

- 24. Technical storage/flush
- 25. Organ retrieved, but not suitable upon biopsy
- 26. Organ declined in O.R.
- 27. Logistical transportation
- 28. Other