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ABSTRACT

Kidney transplantation is an effective treatment for an end-stage renal disease. The donor kidneys need to be matched with appropriate patients, distributed and transplanted very quickly (less than 40 hours) in order to achieve optimal medical results. So far, most researches focus on developing algorithms to satisfy genetic matching between the donor and the recipient and waiting time criteria. The actual kidney distribution process however, is quite complex but still being handled manually which often results in unnecessary delays. In this paper we analyze the bottlenecks in current deceased donor kidney distribution process and investigate how agent technology can be applied to improve this process. We propose a distributed multi-agent system operating in a mobile communication environment to assist transplant coordinators in coordinating with multi-parties in this time-critical distribution process. A prototype system has been developed to demonstrate the feasibility of such system.

Keywords

Kidney transplanting, Multi-agent system, Mobile communication, Multi-party collaboration, Operation efficiency

INTRODUCTION

Kidney transplanting is an effective treatment for an irreversible renal disease. The demand for donor kidneys, however, far exceeds the supply. To enhance graft outcome, better HLA match between donors and recipients can be achieved by improving the matching algorithms (Yuan et al, 1994; Yuan et al, 2002), providing incentives to both donors and providers to participate and contribute (Yuan et al, 1997), and by expanding the organ retrieval and sharing networks. However, enlarging the organ sharing pool also increases the complexity of the distribution and coordination process. In some instances the benefits from increased levels of HLA matching with transported kidneys from long distance may be outweighed by the harmful effects associated with increased CIT (cold ischemic times). CIT are affected by the transportation time and the complexity of kidney distribution process. Thus, an efficient and effective kidney distribution system is critical to support optimal utilization of kidneys. In this paper, we investigate if an intelligent agent approach can be used to improve the efficiency and effectiveness of kidney distribution process.

Medical domain has been always a fertile area for Artificial Intelligence applications. In fact, European researchers have already provided wide discussions on the feasibility and utility of deploying software agents and multi-agent systems in today's medical environment (Nealon et al. 2002; Cortés et al. 2000; Moreno et al. 2001c). The agent technology has been proposed to perform tasks such as optimizing the recipient allocation problem (Valls et al. 2002b), optimizing the organ transportation routing problem (Moreno et al. 2001a), and optimizing the transplanting scheduling problem (Moreno et al. 2001b). However, in reality, the optimal solutions based on simplified models may not be followed due to the complexity of the collaboration required. For instance, the physician of the candidate recipient may be away from his desk and cannot be reached, the optimal recipient patient may not be in a good condition for operation, the ambulance needed for the task may not be available due to other emergency tasks, etc. Unexpected delay is often caused by great uncertainly and inefficient collaboration process but so far no research has addressed this type of collaboration problems.

Our objective, therefore, is to investigate what are the bottlenecks in current organ distribution process and how software agents can be deployed to overcome these bottlenecks. The paper is organized as follows: in Section 2, we identify the collaboration problems in current kidney distribution process. In section 3, we discuss how agent technology can be used to enhance the collaboration of kidney distribution process. In the last section we summarize our study and provide a conclusion.

PROBLEMS IN CURRENT KIDNEY DISTRIBUTION PROCESS

With the expansion of kidney retrieval and sharing networks, national and international co-operation is desirable to help maximize the use of donated kidneys, optimize kidney graft outcomes and enhance the fairness of accessing kidney transplants. However, the coordination of the preliminary activities involved in an organ transplant operation is still a very challenging, complex, and not yet well understood process. (Council of European Consensus Document, 1999)

The distribution process consists of three key tasks: 1) identify the best of available recipients for a particular organ, 2) transport it to the transplant center where the recipient is and 3) arrange the transplant operation. To understand the current kidney distribution process, we interviewed transplant coordinators in a single medium sized transplant center. Based on the duration of the activities, we use a critical path approach to identify the key activities that determines the total duration of the kidney distribution process. To analyze what factors will cause the delay of CIT, we requested statistics data from UNOS (United Network of Organ Sharing) and collected detailed records from TGLN (Trillium Gift of Life Network) in Toronto and St. Joseph's Healthcare in Hamilton, Ontario. Based on those collected data some major problems were identified.

Critical path analysis

We want to identify which activities can be shortened or started earlier in order to reduce the total time delay. The critical path is a chain of activities from the start to the end of the process. It highlights 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 1 shows an activity network for kidney procurement and distribution process. Uncertain factors haven't been considered into building the critical path of the network.

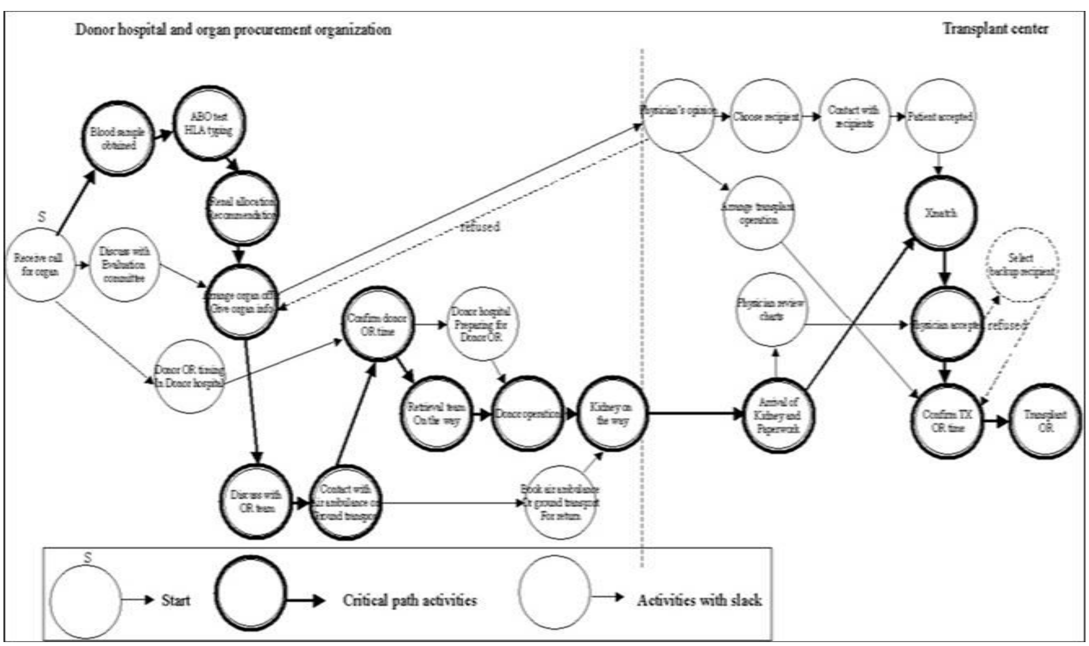

Figure 1. Network for cadaveric kidney procurement and distribution

The critical activities are listed in Table 1.

The critical activities are listed in Table 1. **Activities**	**Duration**
Blood sample obtained	< 1 hour
ABOtest HLA typing (biopsy)	1 hour 10 hours~12 hours 4 hours ~6 hours
Generate renal allocation recommendation	10 mins
Arrange organ offer and give organ information	30 mins ~18 hours
Discuss with organize retrieval team	1 hour ~ 2 hours
Contact with (booking->departure) air ambulance or ground transport	15 mins ~ 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 ~ 3 hours
Kidney Arrived and Physician reviewed charts	10 mins ~ 30 mins
Cross match	6 hours ~ 8 hours
Physician made decision	5 mins ~ 20 mins
Confirm transplant operation time	1 hour ~ 3 hours
Transplant operation	3 hours ~ 5 hours

Table 1. Critical Path Activities

From Table 1, we 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. The most significant variation is for arrange organ offer and give organ information (30 mins ~ 18 hours). Although renal allograft allocation algorithms can generate a list of optimal candidate recipients, due to a variety of uncertainties and response delays (patient's present health status, physician opinion, operating room availability, 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. We will devote more attention to the logistical efficiency as well as the cost issue in measuring the efficiency of this process.

Sample data analysis

In order to figure out the problems and bottlenecks in the current cadaver kidney distribution process, we collected statistical data about kidney transplant from UNOS. We also interviewed transplant coordinators and gathered detailed data on the practical steps of kidney distribution and their execution time in different cases from TGLN and St. Joseph's Healthcare.

Studies demonstrate that the deleterious effect of a longer CIT owing to an increased organ exchange and shipping would diminish the benefit of a better HLA match (Mange et al 2001). Geographical 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.

Figure 2 shows the Kidney transplant performed by CIT-by distance between donor hospital and transplant center based on UNOS and OPTN data as of June 28, 2002. It seems that the distance does affect the CIT.

From the graph, it is clear that statistically, longer distance usually leads to longer CIT. However, the distance alone cannot explain all the CIT variations.

To make more detailed investigation, we also collected some data from Canada. A total of 45 donor files were retrieved from the TGLN center in Toronto and a total of 31 donor files were reviewed from the transplant center at St. Joseph's Healthcare in Hamilton. Some records were excluded from statistical analysis because of missing important information (CIT time, enough detailed activity records and reasons of delays). The known characteristics of our excluded records were not significantly different from those of records included in our analyses. The data is summarized in Table 2.

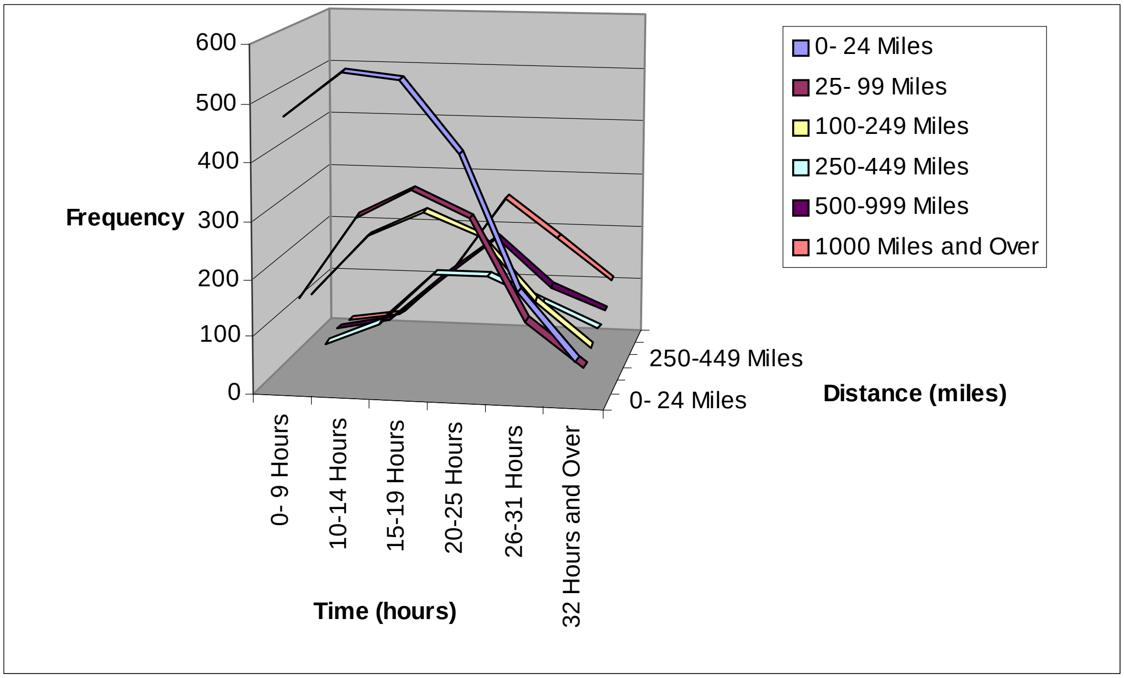

Figure 2. Kidney transplant performed by CIT - by distance between donor hospital and transplant center

Source	Distribution	Cases	Average CIT	Range of CIT
TGLN	Local	22	14 hr 23 min	4 hr 11 min to 28 hr 13 min.
TGLN	Regional	13	16 hr 59 min	6 hr 54 min to 27 hr 40 min.
St. Joseph	Local	16	15 hr 3 min	8 hr 55 min to 30 hr 25 min.
St. Joseph	Regional	15	24 hr 11 min	11 hr 45 min to 27 hr 58 min

Table 2. CIT at TGLN and St Joseph

In the records gathered from St. Joseph's hospital, a donated kidney had the longest CIT (30 hr 25 min) among all collected cases there. The deceased kidney was from a 9-year old child. Many potential recipients turned it down for this reason. The kidney allocation was delayed. Usually, if the donor has 'marginal' characteristics, the time of kidney distribution will be prolonged markedly (Matas and Delmonico, 2001). From the TGLN records, we noted that two kidneys from the same donor were transported to the same place (Barrie -Toronto) but had big difference in CIT (one was 20hr 30 min and the other was 12hr 45 min, the difference was about 8 hr).

Besides necessary transportation time between the places of the donor and the recipient, the complexity and inefficiency of co-ordination and co-operation also account for the increase of CIT. At transplant centers, especially the smaller transplant centers like St. Joseph's, the coordination of kidney distribution is still manual. Coordination is mainly achieved by telephone calls, pagers and/or other highly human-dependent means to contact physicians and transplant centers and to track down suitable recipients. The bottlenecks we identified are as follows:

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 becomes 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; non-heartbeating 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 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 individuals turn down a kidney, the actual allocation is delayed, further for organ reallocation (Oniscu et al. 2002) If numerous OPOs, centers and physicians are involved, this results in prolonging the CIT. Due to the increased use of kidneys from older deceased donors (“non-ideal” donors), delay increases in current kidney distribution. It is important to rule out an unsuitable donor 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.

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, reporting 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 “retrieval” 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 monitor the whole distribution process and respond to unexpected emergency events. To share information about the process of the kidney distribution, many calls need to be made among the people involved. Sometimes the coordinator has to pass through many people in order to reach the right person and the same information has to be repeated many times to different people. Currently, information exchange is mainly through telephone calls. 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 has to keep calling every 10-30 minutes in order to check the current status.

The complexity of multiparty coordination and cooperation

The donated kidney is not only shared locally but also shared regionally, nationally and internationally. The cooperation in kidney distribution therefore has to extend across different tasks, functional areas and organizational boundaries. Under time pressure of 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 3 shows the cooperation in the kidney distribution.

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 3, 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 optimize kidney procurement and distribution management.

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. 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 coordinators have many things to do and they are at the risk for making mistakes under time pressure. 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 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 decision. If they could easily access the information they needed earlier, the decisions could be made sooner and actions could be taken more quickly.

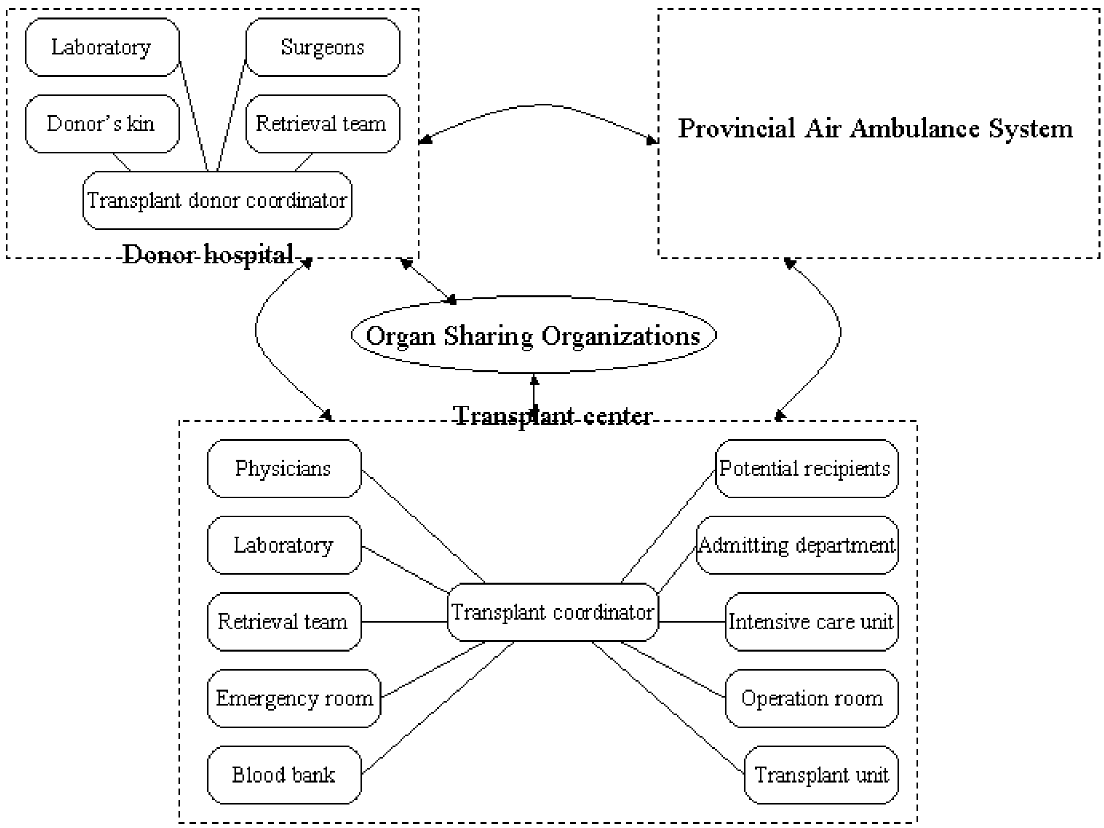

Figure 3. Cooperation in the donated kidney distribution

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.

AN AGENT-BASED MOBILE SOLUTION

Enabling technologies

Agent technology combined with mobile communication brings a potential solution to help improve the efficiency of donor kidney distribution. 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 coordination and improving the effectiveness of interactions. 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).

We 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. All participants have their own resources and decision-making tasks. They coordinate and co-operate each other to combine their resources to create capabilities needed to achieve a better outcome of kidney distribution. The coordination is cross-functional, geographically distributed 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.

Other enabling technology is mobile communication. Handheld mobile devices such as cell phones enable ubiquitous communication anywhere anytime and deliver information services to the person rather than the place (Yuan & Zhang 2003). Based on our analysis, we know that a kidney can be available anywhere and at any time and people such as physicians and patients may be moving around and can not be reached by their fixed-line home or office telephones. So with the help of mobile communication, the people involved can be reached immediately thus reducing unnecessary delay. .How the features of agent and mobile communication technologies help solving the bottlenecks are shown in table 3.

Bottlenecks	Solutions	Features of agent and mobile technologies used
Delay caused by the sequential confirmation process	Parallel working mode for decision making	Autonomy
Time-consuming contact process	Multiparty contact Message dispatching and real-time interaction	Autonomy Anytime anywhere Pro-activeness
The complexity of coordination and cooperation	Monitor and streamline the coordination process	Autonomy Collaboration and communication ability Reactive and pro-activeness
Inadequate and poor information sharing	Collect, analyze and disseminate information quickly, pro-actively and autonomously	Autonomy Reactive and pro-activeness

Table 3. Overcoming bottlenecks in the kidney distribution process

It will take a great effort to implement an agent-based collaboration system for assisting coordinators in kidney distribution process. From our research, we found that identification of the final recipient is one of the most critical and time-consuming tasks in the kidney distribution process. Therefore, an agent-based prototype system was designed and developed to assist coordinators to identify the final recipient. This implementation utilizes Short Message Services (SMS) in mobile phone system for improving the efficiency of communication between agents and people.

Tasks and roles of agents in the kidney distribution prototype system

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 4.

Tasks	Agents	Roles
Registration	Registration agent	• Create donor record • Registers donor information to organ sharing network
Matching	Candidate matching agent	• Generates the candidate lists of kidney recipient
Allocation	Recipient identification agent	• Generates contact list for further availability identification and confirmation. • Accepts instruction from user (coordinator) to adjust its decision strategy • Schedules contact activities • Continuously records message exchanged among agents and coordinators • Analyzes the response information collected by contact agents • Makes final choice for recipient
	Coordinator agent	• Interacts with human coordinators • Reports current situation and execution plan • Receives instruction from human coordinators
	Contact agent	• Contacts the persons in the contact list to check their availability • Selects alternative communication channel such as phone calls, email and SMS • Collects response information • Traces those interactions
	Data retrieval agent	• Accesses information sources (Database) • Retrieves and filters information according to other agents' requests • Monitors the occurrence or change of particular information
Notification	Publisher agent	• Responds the request for particular information from different parties in the process • Integrates and presents up-to-date information requested by users

Table 4. Roles of agents in my implemented multi-agent system

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 4.

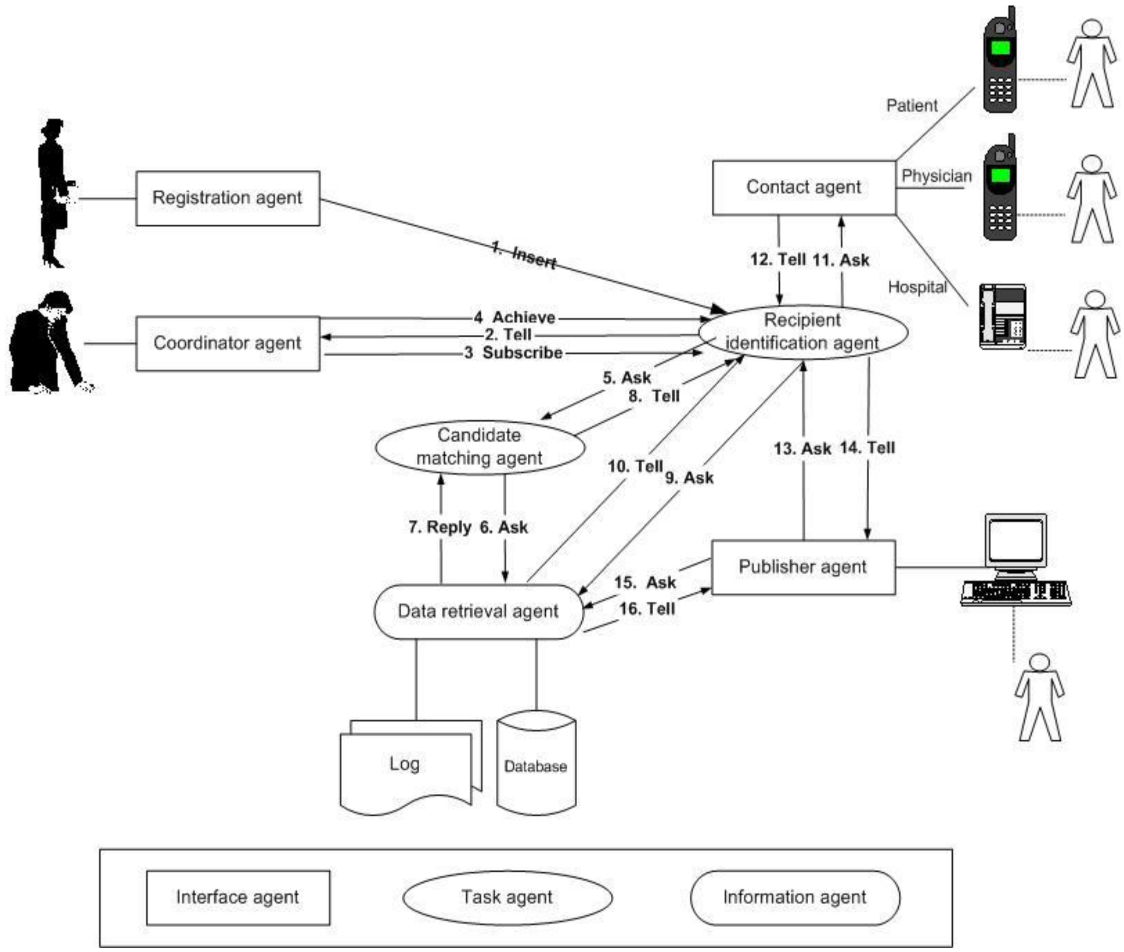

Figure 4. Collaboration diagram of agents

In the next section we describe in detail the coordination of agents and coordinator, illustrate the functioning of the distributed, cooperative intelligent agents through a scenario.

Runtime environment

Considering the availability and familiarity of agent development tools, we implemented the prototype system by using AgentBuilder (an agent toolkit, http://www.agentbuilder.com) and J2ME wireless toolkit. In our multi-agent prototype system, agents communicate with each other using the Knowledge Query and Manipulation Language (KQML). Both agents and cell phone emulator are coded in JAVA. Therefore agents could run on different computers that are connected by internet. Cell phone emulator could run on a computer to emulate SMS (short message service). The runtime environment is shown in Figure 5.

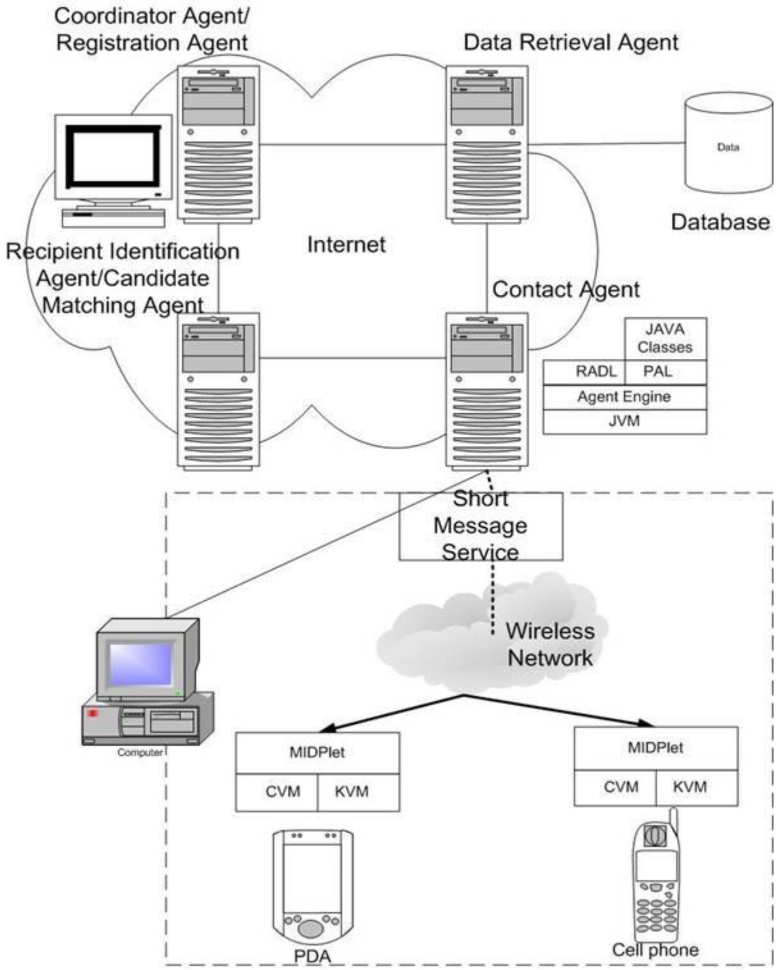

Figure 5. Runtime environment

An illustrative scenario

We use a scenario to demonstrate how agents would be able to assist coordinator to identify the final kidney transplanting recipient.

Registration

When a donor kidney becomes available for transplanting, the Registration agent receives a message with donor information.

Matching

The Registration Agent sends a message to the Recipient Identification Agent indicating the need to identify a suitable recipient. The Recipient Identification Agent sends this message to the Candidate Matching Agent. The Candidate Matching Agent asks the Data Retrieval Agent to retrieve laboratory test data of the donor and the patients in the waiting line for kidney allocation. Candidate Matching Agent applies allocation schemes and algorithm to generate the transplant candidate list and pass it to the Recipient Identification Agent. The candidate list is also forwarded to Coordinator Agent for transplant coordinator review.

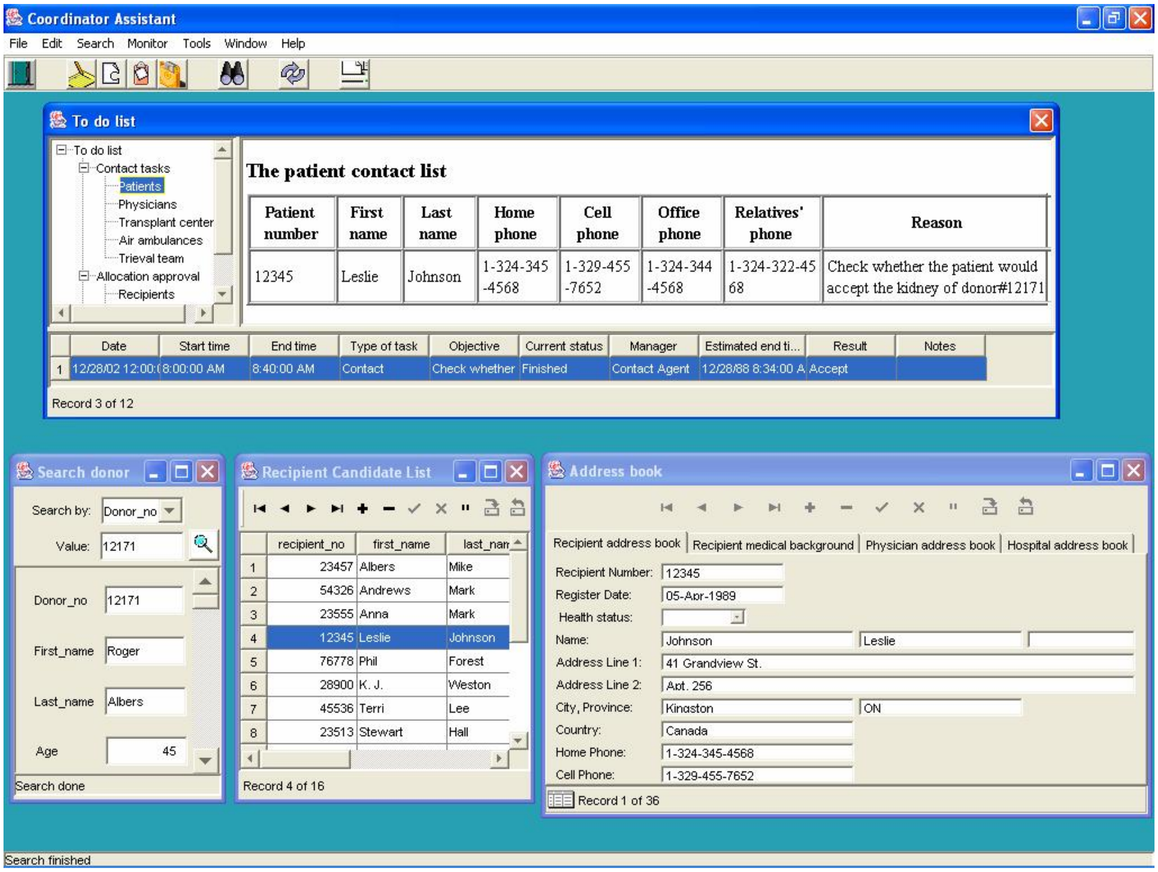

Figure 6. Interface of contact agent

Contact (Allocation)

With the received candidate list, the Recipient Identification Agent asks the Data Retrieval Agent to collect the contact information for 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), the sequence of contact activities, the contact content, the waiting time for reply, and the interval of repeating calls are determined. The one-to-one voice communication tasks could be completed by the transplant coordinators and the rest of communication tasks could be delegated to Contact Agent. The Contact Agent could send different information or questions to different receivers simultaneously by SMS or email. The information could be displayed on a cell-phone or a PDA of corresponding patients or physicians. (See Figure 7)

Figure 7. Contact information shown on cell phone and PDA

Notification and information sharing

After receiving the brief notification of donor information, physicians could go online to request more donor information from donor information sharing network. Publisher Agent will process their request and present the information on the webpage. This web-based information sharing can reduce repeatedly sending the same donor information to different parties involved.

Allocation

Based on the donor information, physicians can reply whether to accept the kidney or not by sending the short text messaging through their cell phones. Patients could also notify their own decision on the acceptance of the donor kidney and answer the questions 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. If there is no answer within the permitted waiting time period, the system will assume that the contacted party gives up the right to accept the kidney. After receiving the contact results from either Contact Agent or transplant coordinators, Recipient Identification Agent tries to identify the final recipient with the confirmation received from all the parties (the patient, the physician, and the hospital) involved. If all of contacted candidates are not available for the kidney, Recipient Identification Agent will request Candidate Matching Agent to generate a new candidate list with lower rank order or in a bigger area until finding the most appropriate available recipients. Recipient Identification Agent will suggest the final recipient to the Coordinator Agent. The Coordinator Agent then passes this information to the coordinator for final approval.

CONCLUSION AND FUTURE WORK

In this paper we investigated the donor kidney distribution process and identified bottlenecks that caused unnecessary delay. We proposed a suitable solution for improving the efficiency of donor kidney distribution by using a distributed multi-agent system operating in a mobile and wireless communication environment. A prototype subsystem system was developed to assist transplanting coordinators in coordinating with multi-parties for determining the final kidney transplanting recipient.

Clearly, there are many issues need to be further investigated. Due to the time limitation, we have not developed the entire multi-agent system we proposed. Although we have just implemented part of the functions of the whole system, the remaining parts still follow the principle of the developed part and could be developed with similar methodologies.

A significant improvement of the efficiency of donated kidney distribution is expected, but we did not have time to run an experiment to verify the expectation in our paper. A simulated case could be conducted with a fully implemented multi-agent system. Our investigations indicate that a fully implemented multi-agent system would be valuable in organ retrieval and allocation. Such a system would be amenable to initial experimental construction and validation through simulation. .

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