

A Use Case for Developing Meta Architectures with Artificial Intelligence and Agent Based Simulation in the Kidney Transplant Complex System of Systems

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Abstract— The gap between the demand for kidneys and the supply of kidneys keeps growing by approximately six percent per year. There is an opportunity to utilize discarded kidneys, with roughly twenty percent of kidneys discarded each year. A real-time generation of an optimized architecture is desired to assist kidney allocation. Current practice for allocating high-risk deceased donor kidneys requires organ procurement organizations (OPOs) to engage in a prolonged manual process, accruing cold ischemic time and exacerbating kidney quality. An interactive digital simulation tool is developed to identify high-risk kidneys that are hard to place and justify starting the accelerated placement process sooner. The simulation tool will estimate the increased likelihood of placement and improve the current allocation model by providing a systematic basis for changing the current process and demonstrating how simulation can be leveraged to evaluate a policy change before implementation. The simulation meta-architecture and AI were all integrated on the Anylogic platform to conduct real-time optimization and prediction of the kidney transplant system of systems. This integrated simulation allows UNOS to generate optimized policies for the kidney transplant systems of systems. Future work includes validating and verifying the platform with additional stakeholders and testing different policies with UNOS.

Keywords: meta-architecture, artificial intelligence, optimization, organ transplant, system of systems

I. INTRODUCTION

According to the U.S. Renal Data System, approximately 750,000 have end-stage renal disease (ESRD) [1]. The demand for kidney transplants far outpaces the supply of kidneys from both surviving and deceased donors. In 2019, over 24,000 kidneys transplant occurred while over 88,000 people were on the waiting list, leaving an additional 64,000 people waiting for a kidney transplant [2]. The growing gap between the demand for kidney transplants and the supply of kidneys is growing yearly. In Figure 1, the gap between the number of patients needing a transplant and the number of people getting transplants has widened and continues to grow in the past decade [1].

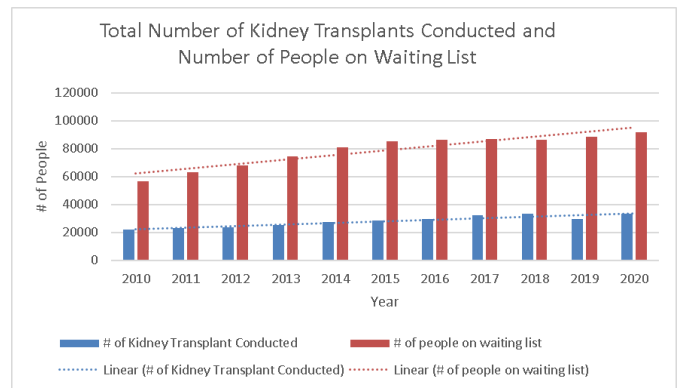


Fig. 1. Total Number of Kidney Transplants Conducted and Number of People on Kidney Transplant Waiting List 2010-2020 [1]

Despite the growing need, as seen in Figure 1, the percentage of discarded kidneys continues to grow and far outweighs the supply of kidneys. Figure 2 shows the kidney discard rate has increased in the last decade [1]. The demand for kidneys is expected to continue to grow based on previous trends of the past decade. Despite the growing demand for kidney transplants, approximately 20% of procured deceased donor kidneys are discarded in current practice [3]. These discarded kidneys are typically lower quality but have been proven cost-effective and life-extending in the appropriate candidates [4].

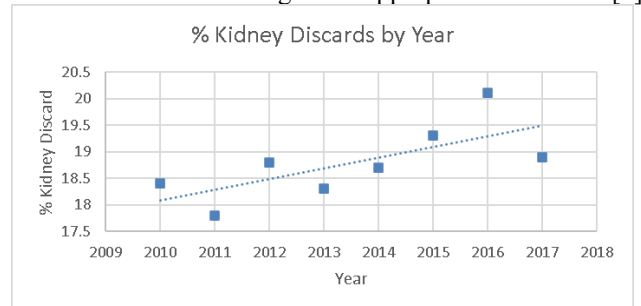


Fig. 2. Percent Kidney Discard by Year 2009-2018 [1]

Even with the great demand for kidney transplants, approximately 20% of procured deceased donors' kidneys are discarded in current practice. These lower-quality kidneys (KDPI >85) have a high probability of being discarded [4]. Although some of the high-risk kidney discards are unavoidable, even lower-quality kidneys have been life-extending and cost-effective for the appropriate candidates [5]. The discard rate of kidneys rises with the Kidney Donor Profile Index, a regressor of several donor characteristics into a single value denoting the graft failure after transplant [6].

Digital health technologies, such as telehealth, telemedicine, wearable devices, etc., have significantly contributed to equitable and affordable health care to improve population health. Since nearly half of the US population suffers from one or more chronic conditions, chronic diseases dominate as the leading cause of death [7]. Chronic kidney disease affects 14.9% of the US adult population, and about 800,000 people are diagnosed with end-stage renal disease (ESRD) at present [8]. Roughly 70% of ESRD patients receive renal replacement therapy through dialysis and possibly enlist as candidates seeking kidney transplants. As opposed to dialysis, kidney transplants offer higher survival benefits and improved quality of life [9]. However, as the number of patients with incident ESRD exceeds 100,000 per year, the number of transplants for the year 2019 recorded slightly higher than 23,000, of which 7,000 came from living donors [10]. About a third of the deceased donor kidneys are high-risk kidneys affiliated with a kidney donor profile index (KDPI) greater than 85. KDPI is calculated from several parameters and is an index score for the quality of the kidney. The deceased-donor discard rate of recovered kidneys is 20%, and most discards are from high-risk donors [11]. Unfortunately, this shortage of kidney donors leads to longer wait times and leads to increased waitlisted candidate mortality rates. To address this challenge, we aim to develop a digital simulation platform to identify opportunities to reduce kidney discards. Digital twins include modeling and simulation technology to study the dynamic effect of proposed changes on existing processes. The development of a digital simulation platform to address this challenge and identify opportunities to increase high-risk deceased donor transplants and reduce kidney discards. Simulations include modeling and simulation technology to study the dynamic effect of proposed changes on existing protocols. Similar efforts have been developed in the "digital patient" to accelerate heart diagnosis, assess treatment options, and support medical decisions [12]. The digital patient technology facilitates work for cardio-specialists and is improving health outcomes. The high impact and high effort tasks for autonomy have been initially identified for the kidney transplant systems [13-14]. Various machine learning algorithms have been proposed and developed to identify missed opportunities that may increase deceased donor kidney placement [13].

On the other hand, detection, and prediction deep learning models, such as brain segmentation for Parkinson's disease, are used to diagnose early diagnosis and differentiate

between Parkinson's disease and atypical parkinsonism [15-16]. Deep learning is a subfield of AI representing models through hierarchical feature learning and requires architecture and hyperparameter optimization. A regularized genetic algorithm with parameter sharing guided deep architectures that provided higher validation accuracy for early diagnosis of Parkinson's disease [17-18]. This approach would serve as a basis to search for efficient architectures in developing the kidney allocation decision-support tools. Incorporation of two artificial intelligence (AI) models in simulation will serve as decision-support systems to facilitate interactions between OPO and transplant centers. An OPO AI model will focus on transplant center possible kidney acceptance based on match probability to support order of contact, development of back-up plans, and potential for accelerated placement [17]. The need for Deep Neural Networks (DNN) in healthcare [19] and a transdisciplinary approach has been identified [13] and could assist in the problems of healthcare. The kidney discard problem in the kidney transplant community has the potential for optimization and using DNN tools to help decisions. Neural Networks have successfully evaluated kidney acceptance [20] and heart transplants [21].

The agents involved in the kidney transplant system are patients, surgeons, kidneys, OPOs, Transplant Centers (TCs), United Network for Organ Sharing (UNOS), air transportation, and ground transportation. The OPO is the agent that is responsible for the capability of providing kidney offers to transplant centers. The OPO consists of several personnel participating in the workshops to address workflow, including directors, managers, and kidney coordinators. The OPO's primary goal is to maximize the number of kidneys transplanted and deliver multiple offers to different TCs. UNOS is the governing body of the entire kidney system of systems. It provides policy changes constraining the system and the patient merit list that determines the order in which patients receive kidney transplants. The TC's primary goal is to perform kidney transplants and obtain an ideal kidney for the given patient, maximizing life-years gained for the patient. The TC personnel interacting with the system are the kidney coordinator and the transplant surgeon. All these agents are systems with conflicting goals in the kidney system of systems. These agents and personnel formed the basis for developing the Key Performance Attributes (KPA) and the systems' capabilities.

Various simulations have been developed and tested, attempting to simulate and predict changes in the kidney allocation system. Arena simulation language software packages simulate different policies that affect survival ratings, deaths, and wait times [22]. The multiple listing strategy where patients enlist at one-to-many transplant centers is deemed effective the larger the distance they could enroll in [23]. The KARES-CBR system was used from medical knowledge, social information, and expert involvement to recommend patients for transplants [24]. The UNOS Kidney Allocation Model is used to simulate and analyze allocation policies [25]. A discrete event simulation KSIM was developed to analyze geographical distance for allocation policies [26]. While these simulations solved parts of the problem, a systems decision supporting all

stakeholders and available data to make decisions is still a gap within the kidney allocation system.

II. METHODOLOGY

Design-A-Thons and Interviews with Stakeholders

The initial step was understanding and analyzing the stakeholders involved in the kidney allocation process and the work processes, capabilities, metrics, and current pain points. The research team conducted three Design-a-thons, which are events interacting with the stakeholders, to host tens of stakeholders from the kidney transplant community. The stakeholders involved in the kidney transplant system are Organ Procurement Organizations (OPOs), the United Network of Organ Sharing, Transplant Centers (TCs), and patients. The OPO is a stakeholder but also a system that owns the capability of providing organ offers to transplant centers. The OPO had in attendance several key personnel in the workshops, including directors, managers, and organ coordinators. The OPO wants to maximize the number of kidneys transplanted and sends organ offers to various TCs around the United States. UNOS is the governing body of the kidney SoS and develops policies and the patient merit list. The transplant center's primary capability is

their KPAs in the kidney allocation SoS. Figure 3 shows the simulation Overview.

Key Performance Attributes

The KPAs were developed and defined from the Design-A-Thons and the interviews with OPO stakeholders of the kidney allocation system. Two primary KPAs are added to calculate an objective function optimized via genetic algorithms. Equations 1 and 2 can be defined as systems, $S(X, i) = 1$ if the i system is participating in chromosome X , meta-architecture, and 0 if not. Interfaces, $I(X, i, j) = 1$ if the i and j system has an interface connection in chromosome X , and 0 if not. The C_{xxx} represents system characteristics, i value of performance where 'xxx, i ' indicates the characteristic value for the system i . Variable δ represents the interfaces between active systems to be calculated in the objective function.

$$\text{Kidney Utilization} = \frac{\sum_i^{Ns} S(X, i) * C_{\text{kidneytransplanted}, i} \prod_j^{Ns} [1 + \delta S(X, j) I(X, i, j)]}{\sum_i^{Ns} S(X, i) * C_{\text{totalkidneyallocated}, i} \prod_j^{Ns} [1 + \delta S(X, j) I(X, i, j)]} \quad (1)$$

$$\text{Kidney Transplant O/E} = \frac{\sum_i^{Ns} S(X, i) * (C_{\text{Observed}, i} \prod_j^{Ns} [1 + \delta S(X, j) I(X, i, j)])}{\sum_i^{Ns} S(X, i) * (C_{\text{Expected}, i} \prod_j^{Ns} [1 + \delta S(X, j) I(X, i, j)])} \quad (2)$$

The kidney utilization KPA calculates the total number of kidneys utilized and transplanted as a percentage. This KPA is desired to be maximized and would be 100% in an ideal SoS.

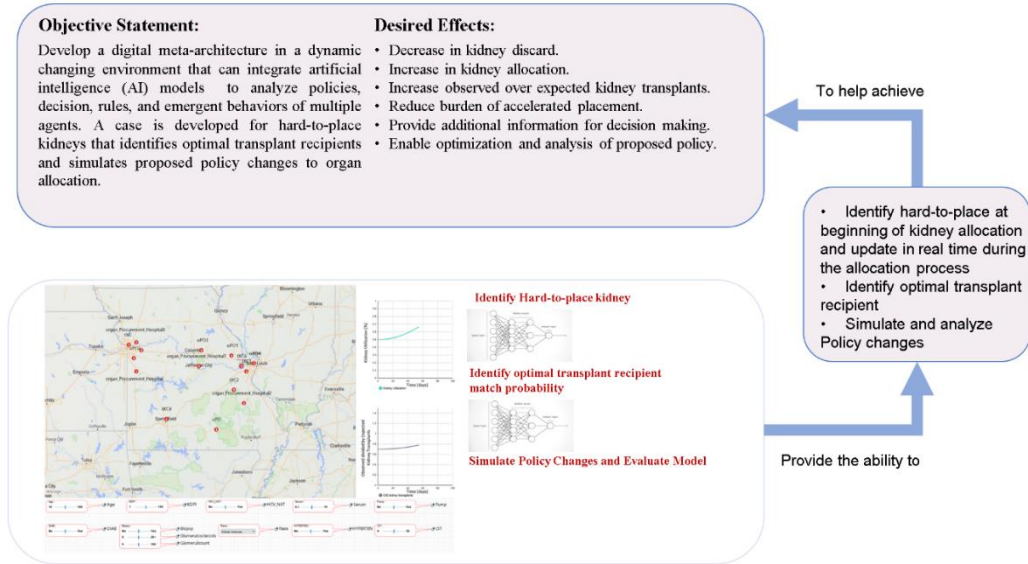


Fig. 3. Simulation Overview

to perform a kidney transplant that maximizes life years gained and is suitable for a given patient. The direct personnel involved in the design-a-thons were the kidney coordinator and the transplant surgeon. All these stakeholders are systems within themselves and have diverging interests and emergent behavior in the kidney SoS. The Design-A-Thon results are discussed with initial pain points and decision support systems [16]. The current simulation developed in this paper focuses on the OPO stakeholder to determine KPAs, policies, and dashboards that the OPO can utilize to analyze various approaches to optimize

The kidney transplant O/E is the number of kidneys observed that are successfully transplanted divided by the kidney transplants expected to be transplanted. The expectation of kidney transplants is provided by UNOS and is based on the average rate of all OPOs. The optimal meta-architecture is calculated using SoS Explorer utilizing a simple SOGA genetic algorithm with 10,000 maximum evaluations.

Systems of Systems Explorer

SoS Explorer is a software tool written by the Engineering Management and Systems Engineering Department at Missouri S&T. It provides a framework for defining system of systems problems such that metaarchitectures may be produced computationally. The overall performance of the architecture is determined by the KPAs. These objectives may be defined using Python, MATLAB, or F#. The selected optimizer can then be used to generate optimum architectures which are displayed in the Graphical User Interface (GUI) and may be interacted with by the user. Solutions may also be stored as Excel Open XML files (XLSX) or graphically as Portable Network Graphics (PNG) images. For evaluation, the objectives require an architecture which, in this framework, is a set of systems and interfaces and information about the systems in terms of their characteristics, capabilities, and feasible interfaces. The objectives are evaluated by an optimizer, of which three evolutionary algorithms are included: NSGA-III, MaOEA-DM, and Simple SOGA. Both single and multiple objective optimizations are supported. Furthermore, constrained optimization is supported, and constraints may be added using Python, MATLAB, or F#.

Membership Functions & Fuzzy Assessor & Rules

To quantify the ambiguity of the KPAs a fuzzy assessor and membership functions were developed using MATLAB's fuzzy designer. The membership functions were chosen based upon the Design-A-Thons and interviews with stakeholders but can be updated with additional KPAs or update the membership functions based upon how the stakeholders' definitions of Low, Below Average, Average, Above Average, and High for the KPAs. The process is repeated with each KPA with the group of stakeholders to quantify the KPA.

A set of rules are generated based upon stakeholder input for the fuzzy assessment of the objective function is created based upon each of the KPAs. Each of the KPAs are assessed to assess the desirability of the meta-architecture. An example would be if performance is low, discard rate is low, OoverE is low, credibility is low, affordability is below average, and acceptability is low, then the overall assessment is that the meta-architecture is very unacceptable. Another side of the spectrum example is if performance is high, discard rate is high, OoverE is high, credibility is above average, affordability is above average, acceptability is high, then the meta-architecture is very desirable. These rules create a KPA dimensional surface to determine the objective function of the meta-architecture of the system of systems. This methodology is as applied to the kidney allocation is described in a previous paper [27].

Anylogic Simulation Creation

Anylogic utilizes multiple methods for developing a modeling environment. The modeling environment is used to develop models using all three modern simulation methods of discrete

events, agent based, and system dynamics. The three methods can be utilized in any combination, with one software, to simulate complex systems. Anylogic can utilize several different visual modeling languages including process flowcharts, statecharts, action charts, and stock & flow diagrams. This platform was chosen to model the architecture of the kidney transplant systems of systems and to execute via agent-based simulation.

Artificial Intelligence Integration

Currently, the OPO assesses hard-to-place kidneys, and utilizing accelerated kidney placements relies heavily on the kidney donor profile index (KDPI) and the number of declines. A Deep learning optimization approach to quickly identify kidneys at risk for discard is integrated within the simulation. These deep learning approaches use Organ Procurement and Transplantation Network data to model kidney disposition. The model is developed to predict the transplant and discard of recovered and not transplanted kidneys. Kidneys with a higher probability of discard are deemed hard-to-place kidneys, which require early adoption of accelerated placement. The deep learning models aid in identifying hard-to-place kidneys before or after procurement and support OPOs to deviate from the match-run for accelerated placement [28]. Artificial intelligence algorithms that were developed to assist in identification of hard to place kidneys and identify aggressive transplant centers were integrated into the Anylogic simulation. They provide recommendations to the simulation on which transplant center and patient is the best for a given hard to place donor kidney.

III. RESULTS

The initial results shown in Figure 4 include the current architecture of kidney allocation from the OPO perspective, agents, kidney characteristics, and KPAs. The agents are represented in the middle of the screen with a geo-referenced map of the agent's current location. The bottom of the dashboard consists of the current donor kidney's selected characteristics. On the right are the OPO KPAs over time. This tool estimates the system-level performance of OPO efforts to increase kidney utilization. The tool allows for changes within various policies of UNOS and the OPO, such as donor type, Cold Ischemic Time (CIT) to accelerated placement, TXC Offer to send, distance for match run offer, and a percent discard to conduct accelerated placement. Donor type can change between live and deceased donors.

CIT to accelerated placement is the time that has passed since the kidney has been clamped (surgically removed) from the body. The accelerated placement bypasses the list of patients that UNOS has provided and offers the kidney to any available transplant center. TXC offers to send is the number of offers on average sent until the final acceptance has been made for a given batch of offers. Distance for match run offer is the distance from the OPO to the patient's transplant center that is

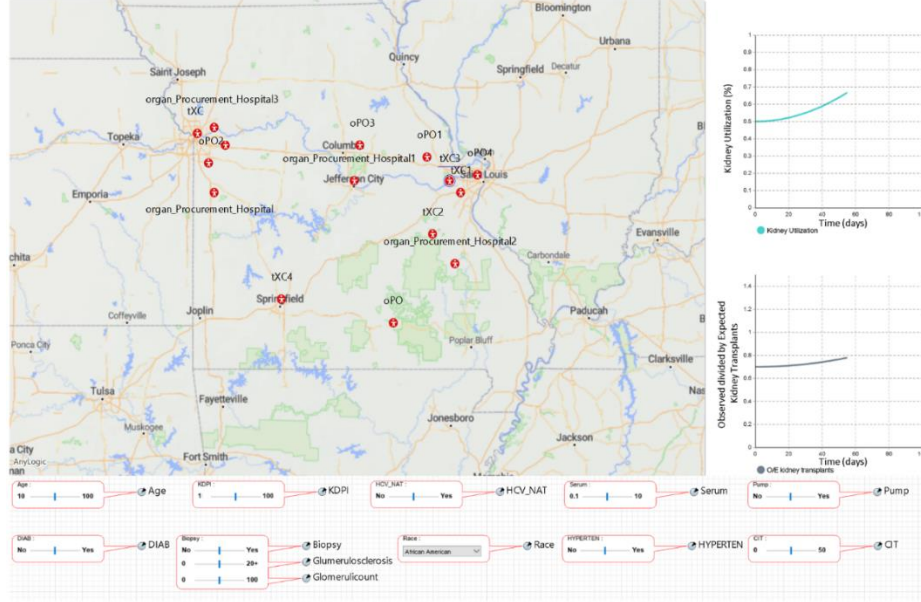


Fig. 4. Simulation Dashboard Example

allowable for a given match run. The match run patient must be within this distance unless accelerated placement is utilized or the list is exhausted. Percent discard to conduct accelerated placement is the percent chance of discard given by the artificial intelligence algorithm to conduct accelerated kidney placement. All policies can be changed, and the KPA observed within the agent-based simulation consists of all the stakeholders of the kidney allocation SoS. The effectiveness of the digital simulation tool is measured by KPAs of kidney utilization and observed/expected kidney transplants. Other calculated measures and statistics of interest to the OPOs include:

- Allocation time
- Sequence number allocation
- Cold ischemic time all
- Cold ischemic time placed
- Cold ischemic time non-utilization
- Logistical time

Allocation time is the amount of time from when the kidney becomes available to when the transplant surgeon accepts the final offer. Sequence number allocation is the number that the patient who received the transplant was on the UNOS waiting list. Cold ischemic time is the amount of time from clamp time to transplant or the last denial of the kidney offer for all kidneys. Cold ischemic time placed is the amount of time from clamp time to transplant for all transplanted kidneys. Cold ischemic time non-utilization is the amount of time from clamp time to the last denial of the kidney offer for all nonutilized kidneys (discarded). Logistical time is the amount of time the kidney is transported from the origination site to the transplant center via ground or air.

IV. FUTURE WORK

Future work involves the integration of logistics and the integration of updated and additional artificial intelligence aid for different stakeholders such as the transplant center into the simulation. Degradation of the kidney occurs over time, and it is important to know how long it will take a kidney to travel to get to the transplant center. If the time is too long, the kidney will end up discarded. A simulation is desired to let the OPO know how long the kidney will be traveling to ensure the kidney is not discarded. Additional validation and verification events with different realistic policy testing are planned with Mid America OPO and transplant centers within the year.

V. CONCLUSION

The study analyzes the impact of amended kidney allocation practices and identifies best practices for high-risk kidney allocation. KPPs are used to measure the effectiveness of new kidney allocation policies for high-risk kidneys. The digital simulation tool predicts an increased deceased donor kidney utilization for early engagement in accelerated placement for out-of-sequence allocation, hence supporting high-risk kidney allocation policy changes. Future work will include incremental updates to the simulation and AI models for data-supported aggressive transplant centers willing to transplant high-risk kidneys.

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