Robotic Kidney Transplantation with Regional Hypothermia: Evolution of a New Procedure using the IDEAL guidelines

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Background

The need to innovate in the field of transplantation

- Minimally invasive surgery reduces postoperative pain and minimizes perioperative morbidity/complications in comparison to conventional surgery.
- Being fragile and immunocompromised, patients undergoing kidney transplantation (KT) are at a greater risk for developing perioperative complications than the average patient.
- Complications affect not only short-term patient convalescence but also compromise long-term graft and patient survival. Thus, transplant recipients may gain substantially from minimally invasive surgery.

How to innovate in an evidence-based manner with minimal risk to the patient

- IDEAL guidelines for surgical innovation.
Our experience:

Robotic Kidney Transplantation with Regional Hypothermia
Overview

Development Phases of Robotic Kidney Transplantation with Regional Hypothermia (IDEAL model)

- Phase 0-1:
  - Phase 0: Simulation of pelvic hypothermia in the robotic radical prostatectomy model.
  - Phase 0: Cadaver lab ➔ establishment of preclinical procedural feasibility.
  - Phase 1: Treating a highly select group of patients (n=7) ➔ establishment of clinical feasibility.
  - Prospective and objective patient safety and surgeon-learner assessment, utilizing techniques of Statistical Process Control (ongoing from phase 1 onwards).

- Phase 2a:
  - Technique modification and standardization.
  - Outcomes (technical and 6 month functional).

- Phase 2a-b:
  - Dissemination and evolution of individual approaches, and Mentoring.
Phase 0: Preclinical

- Phase 0:
  - Innovating the technique to cool the graft kidney during minimally invasive KT
    - Why: To provide a broader ischemic window during the initial cases of robotic kidney transplantation (learning phase) and preservation of the graft function.
    - How: In the robotic radical prostatectomy model, we devised a technique to achieve regional pelvic hypothermia (for neurovascular bundle protection) by delivering the ice-slush directly into the pelvic cavity using a GelPOINT device and modified Toomey syringes (n= >300 patients over a 2-3 year period).
    - Result: Effective regional hypothermia without any significant change in the core temperature of the patient.

Jeong et al. BJUI 2013
Phase 0:

Establishing the technical feasibility of robotic kidney transplantation in a preclinical setting

Why: To avoid the pitfalls associated with trial and error in the initial patients.

How: Cadaver lab (n=2 cadavers, with interval review between the two lab sessions). Performed 4 kidney auto-transplants using the 2 cadavers.

Result:

- Preclinical procedure feasibility established.
- Optimal patient position, port placement and robot docking established.
- Easy introduction of the graft kidney via the GelPOINT established.
- Robotic instrumentation and suture selection.
- Standardization of vascular and ureterovesical anastomoses technique.

Creation of a prospective database

- Recorded 138+ data points for each patient (available as a supplement with the paper).

Menon et al. Eur Urol 2013 (IDEAL Phase 0-1)
Phase 1: Idea

Phase 1:

- Technical and data collection protocols registered at the institutional level.
- IRB clearance obtained and informed consent taken in each case.
- Treatment of a highly select group of patients by a team of surgeons experienced in both KT and robotic surgery.

  For the initial cases very stringent inclusion/exclusion criteria were used to select the best candidates for the procedure. But, as the feasibility became apparent these criteria were relaxed.

  Safeguards: During the phase 1 – the foremost concern was patient safety. To protect the graft harvested from a living donor, the ability to convert robotic KT to open surgery was ensured by having the open surgeons and open surgical instruments available. Causes for open conversion would include failure to progress, inability to cool the graft adequately, concern regarding the quality of the vascular anastomoses, or other concerns regarding our ability to provide a result at least as favorable as the standard of care. *Though the conversion to open surgery was never needed.

Results:

- Established clinical safety and feasibility.
- Effective pelvic cooling using ice-slush hypothermia.
- Early outcomes comparable to outcomes achieved with open KT as reported in the literature.

Menon et al. Eur Urol 2013 (IDEAL Phase 0-1)
Phase 1: Idea (continued)

 Prospective patient safety monitoring (Phase 1 onwards)

- Statistical Process Control (SPC)
  - Why: To ensure patient safety by allowing objective and prospective monitoring of patient outcomes in a comparative manner.
  - How: We utilized techniques of SPC (recommended by the Balliol Collaboration); one such technique is the Shewhart Control Charts.
  - SPC methods are time trend analytic techniques that allow comparative effectiveness evaluation of new techniques, with ones that are already established (For example in our case, comparison of outcomes after Robotic KT to open KT).
  - Using outcomes from the OKT literature and retrospective analysis of OKT data from the participant institutions, we derived our desired target outcome values for the RKT (“target value”) and also set the threshold limits (“alert and alarm limits”). If the outcomes for any patient fell outside these threshold limits – this raised concern for an insult that cannot be attributable to random variation and prompted a causal examination.
  - See figures on next slide for illustrative examples (only showing functional outcomes). More details can be found in the paper.

Sood et al. Eur Urol 2014 (IDEAL Phase 2a-b)
Phase 1: Idea (continued)

(a) Shewhart Control Chart: Serum creatinine POD 7

- **Alarm Line:** If the results deviates 3 SD from expected (derived from the OKT results)
- **Alert Line:** If the results deviates 2 SD from expected (derived from the OKT results)
- **Target Value:** expected outcome (derived from the OKT results)

(b) Shewhart Control Chart: Estimated GFR POD 7

- **Group-1:** Extensive robotic surgery experience but limited KT experience
- **Group-2:** Extensive robotic and KT experience
- **Group-3:** Extensive KT experience but limited robotic experience

⭐ Groups 1 and 2: In Control from the start
Prospective learning curve evaluation (Phase 1 onwards)

Again utilizing the techniques of SPC:

- **Why:** To provide an objective assessment of duration of mentorship a surgeon learner might require, if any. (This evaluation is more important in Phase 2b of the study when more surgeons are adopting the new procedure, to ensure competency of the surgeon learner, which will in turn ensure patient safety).
- **How:** Using the cumulative summation (CUSUM) method.
- Competency is said to be achieved when the plateau is reached and with further experience a person achieves proficiency and mastery.
- See figures on next slide for illustrative examples (only for technical outcomes). More details can be found in the paper.

Sood et al. Eur Urol 2014 (IDEAL Phase 2a-b)
Phase 1: Idea (continued)

(a) CUSUM Graph: Venous anastomosis

- Competency achieved
- Groups 1 and 2: competent from the start

(b) CUSUM Graph: Arterial anastomosis

- Competency achieved
- Groups 1 and 2: competent from the start
Phase 1: Idea (continued)

(c) CUSUM Graph: Uretero-vesical anastomosis

- Learning phase continues
- Groups 1 and 2: competent from the start

(d) CUSUM Graph: Re-warming time

- Competency achieved
- Groups 1 and 2: competent from the start
Phase 2a: Development

Phase 2a:
- Technique evolution and standardization at one center
- Minor technical changes during this phase (and phase 1) made the procedure more efficient.

**TIMELINE – TECHNICAL MODIFICATIONS**

- Started utilizing Aortic Punch, introduced through the GelPOINT™: to make the circular arteriotomy
- Icostlush delivery becomes more systematic: 120cc delivered just before the graft kidney introduction, 120cc immediately following the graft introduction and an additional 120cc after completing the venous anastomosis (Total of 360cc)
- Started utilizing the V-Loc CV23 6” barbed suture to perform the detrusor layer closure: decreased the average time taken to perform the ureteroneocystostomy from 26 minutes to 15 minutes
- Started retroperitonealizing the graft kidney using peritoneal flaps, instead of leaving the graft kidney intraperitoneal with simple fixation to the lateral wall

**CASE NUMBER**

- Preparation of the vessel-bed before bladder take-down
- Limited dissection of EIA only to the degree required for vascular anastomosis
- GelPOINT™ now placed after preparing the vascular bed and bladder
- Omission of continuous temperature monitoring
- Use of robotic-scalpel for linear-arteriotomy
- Omission of routine Doppler-flow measurements
Phase 2a: Development (continued)

Phase 2a:

- >50 patients underwent RKT with regional hypothermia successfully.
- >6 months follow-up data available for 25 patients:

  TECHNICAL OUTCOMES: Key Points
  - No need to convert to the open setting in any case (out of all 50).
  - No need for anastomotic revision in any case (out of all 50).
  - Equal degree of graft cooling achieved in both open and robotic KT (*data not published).
  - Significantly smaller incision size (*data not published).
**FUNCTIONAL OUTCOMES: Key Points**

- No need for dialysis in any case (out of the 25).
- Mean serum creatinine at time of discharge 1.3 mg/dl, @1 month 1.1 mg/dl and @6 month 1.1 mg/dl.
- No graft torsions, wound complications/ infections, urine leaks, vascular thrombosis were noted during the 6 month follow-up period (out of the 25).
- Pain and Narcotic use significantly reduced in patients undergoing robotic KT when compared to open (*data not published; out of the 25) .
- One patient developed acute cellular rejection treated with good response to Steroids (out of the 25).
- One patient died of congestive heart failure 1.5 months post op, secondary to underlying cardiac conditions (pre-operative Charlson’s Comorbidity score of 11).
Phase 2b: Exploration

Phase 2b: In progress

- Adopted by another center in India where >60 procedures have been performed.
- Centers in the U.S. and Europe are in the process of starting robotic transplantation programs.
- Creation of a multi-institutional registry is underway for uniform data collection.
RKT with Regional Hypothermia Development (IDEAL Model)

**IDEAL Phase 0**
- Demonstration of the ability to achieve effective pelvic hypothermia (in the RALP model)
  - Feasibility demonstration: > 300 patients underwent RALP with pelvic hypothermia (to minimize inflammatory insult to the NVB) successfully, using soft surgical ice-slush introduced via GelPOINT™
  - Efficacy demonstration: In all cases, pelvic temperature between 15-20°C was consistently achieved, with no change in core temperature
  - Demonstration of the ability to retrieve/handle organs (excised prostate specimen) through the GelPOINT™ with ease, without the need for de-docking

**IDEAL Phase 0**
- Cadaver Lab – helped establish:
  - Feasibility of the procedure (pre-clinical)
  - Optimal patient positioning, port placement and robot docking
  - Robotic instrumentation and sutures of choice
  - Renal allograft can be comfortably introduced via the GelPOINT™
  - Standardization of the vascular and uretero-vesical anastomoses

**EVOLUTION TIMELINE**
- June 2011
- December 2012
- January 2013
- February 2013

**IDEAL Phase 1**
- Informed consent, IRB clearance, protocol registration and safeguards
- Peri-operative patient data – helped establish
  - Feasibility and safety of the procedure (clinical)
  - Effective hypothermia using the ice-slush in the RKT
  - Early functional outcomes equivalent to open kidney transplant
- Broadening Indications
- Minor changes in surgical technique

**IDEAL Phase 2a & b**
- Study development – NRCT with 2 arms (on-going)
- Early adopters