A Randomized Controlled Trial Comparing Efficacy, Ergonomics, and Safety of ILY Robotic System vs Manual Flexible Ureteroscopy in Patients Undergoing Laser Lithotripsy for Kidney Stones

iFURS Trial: ILY Robotic System vs Manual **F**lexible **UR**eteroScopy for Kidney **S**tone Treatment

Protocol Version 2.1

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Protocol Content

1.0 Abstract

Background: The rising prevalence of kidney stone disease (KSD) has increased the need for ureteroscopy (URS). Innovations like digital flexible URS and robotic technology have improved ergonomics and reduced surgeon radiation exposure. The ILY® robotic URS system, a novel wireless-controlled manipulator, has shown promising efficacy and safety, but no direct comparisons to manual flexible URS (fURS) exist.

Objectives: Our primary objective is to evaluate whether robotic ureteroscopic lithotripsy using the ILY® robotic system provides the same efficacy, measured by the stone free rate. Secondary outcomes will evaluate safety, measured by peri-operative and 30-day post-operative complication rate, in comparison with the manual fURS. Additionally, intra-operative ergonomics, surgeon safety in terms of radiation exposure, and intraoperative parameters like operative time and conversion rate will be evaluated

Methods: This is a multicenter, parallel group, randomized controlled noninferiority trial with a 1:1 allocation ratio between the treatment and control groups. The treatment group will undergo laser lithotripsy with robotic fURS utilizing the ILY® robotic system and the control group with manual fURS. The NASA Task Load Index will be used to assess ergonomics and "Instadose" badges will be measuring the surgeon's radiation exposure.

Analysis Primary analysis will follow an intention-to-treat approach. Stone-free rates between groups will be compared using the Chi-square or Fisher's exact test. Perioperative and 30-day postoperative outcomes will be compared using chi-square tests or logistic regression with adjustments for covariates. For the NASA Task Load Index scores, independent t-tests or Mann-Whitney U tests will be used, depending on normality. Secondary outcomes will be analyzed similarly to the primary outcomes.

Significance This is the first clinical trial to evaluate the ILY robot system in comparison to manual fURS, providing pioneering data on its efficacy, safety, and postoperative outcomes.

Source of funding: AUB Intramural Funding sponsored by the Medical Practice Plan

2.0 - Objectives:

Our primary objective is to evaluate whether robotic ureteroscopic lithotripsy using the ILY® robotic system provides the same efficacy, measured by the stone free rate*. Secondary outcomes will include safety, assessed by the perioperative and 30-day postoperative complications in comparison with the manual flexible ureteroscopy.
In addition, we will assess intra-operative ergonomics, surgeon safety in terms of radiation exposure, and intraoperative parameters (operative time, draping time, docking time, lasing time, conversion rate, etc...)

*Stone free rate will be defined as the absence of residual fragments on NCCT scan. [1]

3.0- Background and Innovation

The prevalence of kidney stone disease (KSD) has surged recently [2, 3] increasing the demand for therapeutic interventions, particularly ureteroscopy (URS) [4, 5]. In recent history, the development of digital flexible URS proved to be a significant leap in the field, with the addition of high-powered laser technology making laser lithotripsy via URS more viable and efficient. Currently, the introduction of robotic technology is making URS more comfortable and safer for the surgeon by improving its ergonomics and avoiding surgeon exposure to ionizing radiation [6-8].

Previous publications have shown that different URS techniques and equipment have differences in muscle activation as assessed by surface electromyography (EMG) [9]. This finding called for individual studies to assess different techniques and URS equipment. Studies looking at novel robotic URS systems explored the possible advantages of robotic URS over conventional URS, including increased range of motion, improved ergonomics, intuitiveness, and instrument stability [10-12].For instance, some robotic technologies improve ergonomics by introducing controllers or wireless consoles [11, 12], such as the Sensei robot (Hansen Medical, Mountainview, CA, USA) or the EasyUretero (ROEN Surgical Inc., Daejeon, Korea). Ergonomics and surgeon wellbeing have been shown to contribute to patient safety [13]. One study comparing the efficacy of

a robot designed by Elmed (Ankara, Turkey) for flexible URS to manual URS revealed better performance in some parameters by the new robotic flexible URS, such as less fragmentation/dusting time and higher stone-free rate at 3 months [14].

Moreover, wireless controllers allow surgeons a safe distance away from the source of ionizing radiation [15]. The harms of ionizing radiation are well known [16, 17] and have been studied in urologists [18] who might receive up to 1,100 mrem per one hour of fluoroscopy time, while the United States Nuclear Regulatory Commision recommends an annual whole-body exposure of 5,000 mrem for radiation workers [19]. URS involves a lot of potential radiation exposure [20, 21] which led to studies looking at solutions to mitigate this risk [22, 23], including justification, optimization, and limitation of radiation. Distance and shielding can eliminate such risks completely, and the remote nature of some robotic URS techniques allows surgeons to distant and shield themselves more effectively [11, 12].

Such promising results highlight the potential of robotic flexible URS, considering that its wide-scale adoption has yet to be seen. ILY® (Sterlab, Vallaruis, France) is a novel robotic URS manipulator that is adaptable to multiple types of URS and access sheaths and is controlled by a wireless controller. ILY® uniquely addresses the challenges in manual fURS including surgeon fatigue, procedural variability, and ergonomic strain by introducing a remote control, which allows the surgeon to work easily at a distance from the patient and decreases the exposure to ionizing radiation[15]. Also, the ILY® robotic system integrates enhanced dexterity and precise laser guidance offering the potential for improved procedural efficiency and outcomes[15].

In its first prospective clinical experience, the ILY® showed efficacy and safety in the clinical setting [24]. In another clinical experience by Farré et al [25], no intraoperative complications or device-related failures were reported. To our knowledge, no direct comparative studies comparing ILY® to the standard of care (manual fURS) have been conducted or reported in the literature.

This study represents the first clinical trial to evaluate the ILY robot system in comparison to manual fURS, providing pioneering data on its efficacy, safety, and postoperative outcomes marking a significant advancement in the field.

4.0 – Device Description

ILY® (STERLAB, Vallauris, France) is a ureteroscope holder which can be telemanipulated by the surgeon with a wireless controller while placed close to the patient (**Figure 5**). Unlike the rest of the robots used in endourology, ILY has a remote

control similar to the PlayStation's joystick (Figure 6). This helps the surgeons keep a distance from the source of ionizing radiation.

Figure 5. ILY® robot.

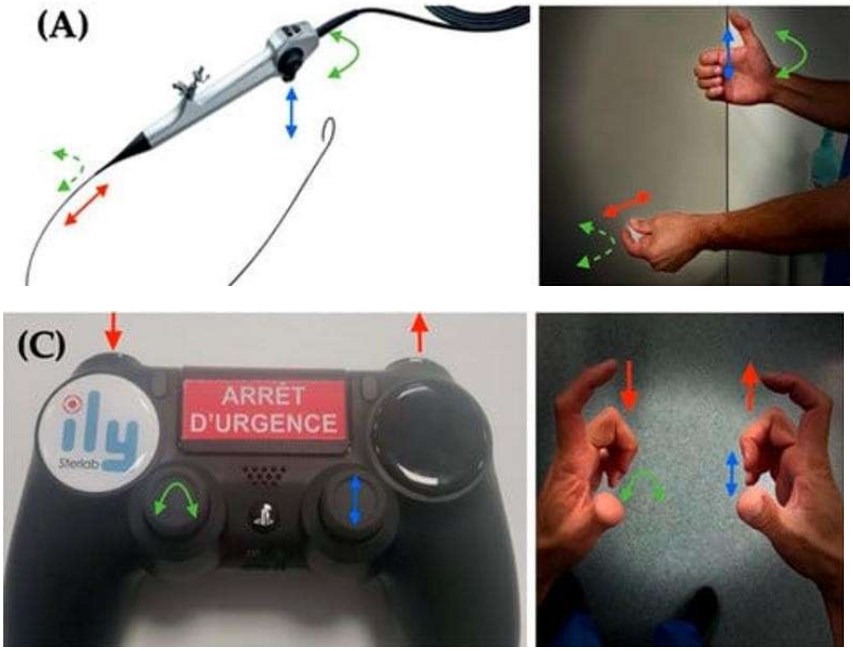


Figure 6. Placement of surgeon's hands and movements to manipulate (**A**): Flexible ureteroscope; (**C**): ILY® robot. Arrows represent how to perform different movements and the corresponding directions of hands, fingers, scope and movements.

The ILY® ureteroscope holder is compatible with all types of ureteroscopes available on the market. (reusable and single use). It is also compatible with most of the sheath brands and their different sizes. The type and size of the sheath can be selected on the tactile screen during the UAS placement, and the sheath holder modulates according to it.

Since there ILY robot has the advantage of maneuverability, it can be rotated +/- 360 degrees. In addition, placing the scope over a surface increases stability and accuracy which in turn reduces the movements of the scope and fiber tip during the renal stone's lithotripsy.

In terms of ergonomics in fURS, Ong et al. [26] mentioned that this device is of great importance for surgeons who perform several surgeries per day and for long procedures where the manual handling of the ureteroscope becomes tedious. The wireless console decreases surgeon fatigue and osteoarticular pain that may result from the manual ureteroscope handling because the ILY robot enables the surgeon to do the surgery from a seated position while performing limited hand movements with the remote control. Gauhar et al. [15] also noted that placing the robot is easy and quick, taking only 5 mins to set up and 3 mins to install.

One limitation to the ILY, however, is that using a video-game controller forces the surgeon to learn how to use the control buttons to replicate the expected flexible ureteroscope movement which might be time consuming [15].

The ILY® robotic platform has received CE marking which means that it complies with the European Union safety, health, and environmental protection standards for medical devices [24]. However, it has not yet obtained FDA approval for use in the US.

5.0- Study Design:

This study is a parallel group noninferiority trial in the form of a multicenter randomized controlled trial with 1:1 allocation in a treatment group (Group 1) and control group (Group 2). The treatment group will undergo laser lithotripsy with a robotic flexible URS utilizing the ILY® robotic system and the control group will undergo laser lithotripsy with manual URS which is the standard of care.

5.1- Participants:

The participating centers will have predefined inclusion and exclusion criteria for patient eligibility. Patients presenting to the clinic or emergency department (ED) with renal stones requiring laser lithotripsy will be identified by the treating physician (urologist) in the corresponding center. Physicians will assess the patient against the inclusion criteria and, if deemed eligible, notify a designated member of the research team.

Once a potential participant is identified, a member of the research team will approach them in a private and comfortable setting (urology clinics or PAU to ensure

confidentiality. During this interaction, the research team member will explain the purpose, procedures, risks, and benefits of the study in detail. Ample time will be provided for the patient (or their legal representative, if applicable) to ask questions and make an informed decision.

If the patient agrees to participate, they will be asked to sign an informed written consent form.

The patients will be enrolled prospectively from multiple centers between April 1, 2025, to April 30, 2027, or until the target patient recruitment is complete, whichever is earlier. The eligibility criteria for including a patient in the study is demonstrated in Table 1.

Table 1: Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
Males or females ≥ 18 years old	Children < 18 and pregnant women
Patients with a normal pelvicalyceal anatomy	Patients with anatomically anomalous kidneys, known case of stricture or stenosis, or recent 3-month history of ureteroscopy (DJ stent placement only will be accepted) or known history of complicated ureteroscopy
Patients with renal stone diagnosis confirmed by non-contrast computed tomography regardless of stone size, location, and multiplicity	Patients in whom stone measurement was not feasible on NCCT or those with concomitant ureteric stones.
ASA score I-III	ASA score IV
Intact mental and cognitive ability to provide informed consent and willingness to participate in the study with 30-day follow-up	Mentally incapacitated patients unable to provide informed consent

Patient data collected will be coded by giving the patients ID numbers. Coded data will be shared with the data analysts to minimize the risk of bias.

5.2- Sample Size Calculation:

With a type I error rate of 0.05, power of 0.8, case to control ratio of 1, drop outrate of 20%, expected proportion of outcome of interest in treatment group (Group 1) of 0.924 vs control group (Group 2) of 0.894 [13], and margin on risk difference scale of 0.10, the total sample size will be 152 , with 76 in each of the treatment and control groups. The expected proportions used in calculating sample size are from the results of a study looking at Roboflex Avicenna-assisted (Elmed, Ankara, Turkey) vs classical ureteroscopy's SFR, since there are no studies comparing ILY-assisted to classical ureteroscopy's SFR[14]. Both robots have similar technology, ergonomics, safety profile, and operative outcomes. Additionally, both systems have similar procedural workflows and surgeon learning curves.

Considering that the results from the initial prospective clinical assessment of the ILY® robotic system done at our center are similar to the results in the aforementioned study, we believe the results can be generalized.

Furthermore, a review of the literature showed the clinically relevant margin on risk difference was 8 to 10% and it was deemed that a margin of 10% will be clinically relevant for our study[27, 28].

5.3- Recruitment Strategies

1. Multi-Center Recruitment Approach

- The study will be conducted at **multiple high-volume urology centers** to maximize patient recruitment and ensure a diverse patient population.
- Sites will be selected based on **annual case volume of URS (ureteroscopy) and robotic kidney stone procedures**, ensuring access to eligible participants.

2. Patient Outreach and Education

- Patients undergoing **preoperative consultation for kidney stone treatment** will receive detailed study information, including potential benefits and risks of robotic vs. manual URS.

Participant Withdrawal:

Participants may be withdrawn from the study for the following reasons:

- **Loss to Follow-Up**: If a participant cannot be reached after three documented contact attempts, they will be considered lost to follow- up.

- **Voluntary Withdrawal**: Participants who choose to voluntarily withdraw from the study will be removed, and the reason for withdrawal should be documented.

Participants who are withdrawn from the study or lost to follow-up will not be replaced. Data collected up to the point of participant withdrawal will be retained and included in the analysis to ensure study integrity, in accordance with ethical guidelines and study protocol. No further data will be collected after withdrawal.

5.4- Blinding and Randomization:

Patients will be blinded as follows:

1- During the recruitment stage, patients will not be informed about which group they will be randomized into. Patients involved in the study are those already planned for surgery and eligible for both robot-assisted or manual URS.

The cost of the procedure, whether performed with the ILY robot or manual flexible URS, is covered under the same standard package for ureteroscopy. No additional charges are applied for robotic use.

2- During the operation, all equipment will be masked until the patient is under general anesthesia to prevent patient knowledge of the procedure type.

3- The physician and operating room (OR) team will not be blinded to the intervention because, by the nature of the procedure, they will inherently know which technique is being used during the operation.

4- Postoperative care teams cannot be blinded since the operation note will include details of the procedure. However, patients involved in the study will be flagged on EPIC to ensure procedure details are not disclosed to them. Care teams will be reminded during handovers to avoid revealing group allocation. Moreover, postoperative care protocols will be standardized to maintain consistency among the groups.

5- During follow-up, patients will receive the same postoperative care instructions regardless of the procedure type.

6-Regarding outcome assessors, they will be blinded to the group allocation to ensure there will be no bias in the evaluation of postoperative outcomes.

Randomization and Allocation Concealment:
REDCap (Research Electronic Data Capture) will be used to implement a centralized, web-based randomization system with built-in allocation concealment and stratification by center.A computer-generated randomization sequence for 1:1 allocation will be created and maintained by the lead site (AUBMC) using REDCap's randomization module. This system will ensure that allocation is concealed until after the participant has been enrolled and eligibility confirmed.
Urology treating physicians at the collaborating centers will have no access to or knowledge of the randomization sequence. Once a patient is confirmed eligible and consented, the collaborating site will access REDCap, which will automatically assign the treatment group based on the pre-generated concealed sequence. This process ensures that the person enrolling participants cannot predict or influence assignment.
Collaborating centers will be given REDCap access limited to their Data Access Groups (DAGs). REDCap will be password-protected with access restricted to the team of the study.

5.5- Intervention:
The treatment group will undergo flexible URS with a robotic URS manipulator ILY® (Sterlab, Vallarius, France) while the control group will undergo a routine flexible ureteroscopy performed manually. Both procedures can be performed under general anesthesia and the surgeon can use any scope brand and sheath depending on availability on the premises that all scopes used are 7.5 Fr disposable. It will be documented whether the sheath used is suction, non-suction, or if no sheath was used. In addition to the planned 1:1 allocation of patients in the treatment and control groups. Any laser type can be used...
Any positive urine culture will be treated preoperatively as per the center's own antibiogram/protocol. Any antiplatelet or anticoagulation will be stopped 5 days prior to surgery and documented as such. If stopping the antiplatelet or anticoagulation medications was not feasible, these patients will be excluded from the study. Any on table decisions such as the use of accessories, abandoning procedure, switching to another technique due to complications, switching equipment due to malfunction, or stenting the patient will be as per surgeons' discretion and will be documented. If intra-op

the stone was amenable to direct basketing without the need for lithotripsy laser, these patients will be automatically excluded from the study.

6.0- Study Measures:

Primary Measures: Efficacy will be assessed by measuring the stone-free rate (SFR). A patient is considered stone free if there are no visible residual stone fragments after the treatment. It will be assessed by an NCCT done at 4 weeks from the index procedure. Residual Fragments (RF) will be assessed using a **"bone window"** setting on the CT scan for better accuracy. Strict criteria will be used defining SFR as zero residual fragments.

Secondary Measures:
Safety outcomes will be assessed as perioperative and 30-day postoperative outcomes. Clavien-Dindo Classification (26) will be used for adverse events monitoring. This assessment will account for any complications related to the patient's clinical condition from the procedure through a 4-week postoperative period. The Clavien-Dindo classification system, which has been expanded on in Table 3, provides surgeons with a common platform for communication and will capture the safety or risks associated with each type of URS.

Grade	Description
1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Acceptable therapeutic regimens are drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections open at the bedside.
2	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions, antibiotics and total parenteral nutrition are also included.
3	Requiring surgical, endoscopic or radiological intervention
3a	Intervention under regional/local anesthesia
3b	Intervention under general anesthesia

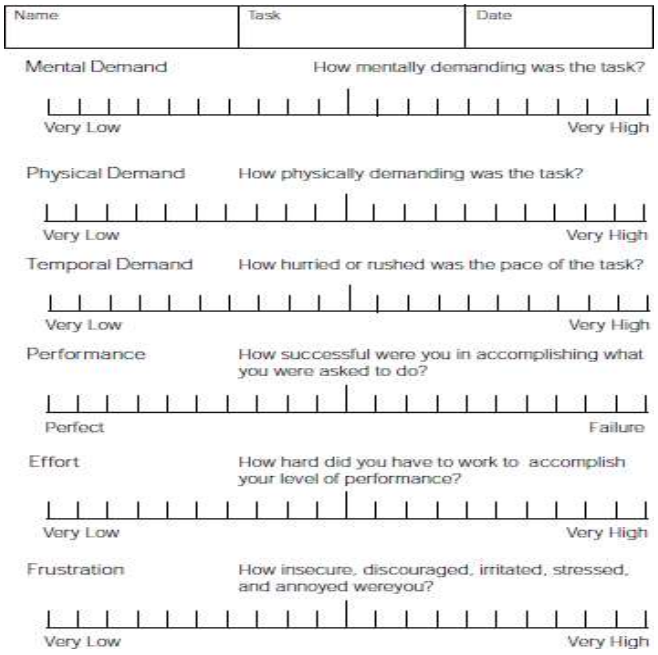
4	Life-threatening complication requiring intensive care/intensive care unit management
4a	Single organ dysfunction
4b	Multi-organ dysfunction
5	Patient demise

Table 3: The Clavien-Dindo classification system

Other secondary measures will be ergonomics, surgeon safety in terms of radiation exposure, and intraoperative parameters (operative time, draping time, docking time, lasing time, conversion rate, etc..)

The NASA Task Load Index (Figure 1) will be used to assess for ergonomics [29], which will be filled by the surgeon after each surgery. This measures workload by assessing 7 dimensions (e.g., physical demand or effort) using a scale with 21 graduations ranging from very low to very high (perfect to failure in the case of performance). Each dimension's scores will be added up in each of the treatment and control groups, calculating the mean of each group. Comparative analysis will be conducted between the groups on each dimension, as well as on the mean of all dimensions added together, which will be considered the workload score. The physical demand dimension will act as a subjective measure for ergonomics.

Figure 1: The NASA Task Load Index



Surgeon safety from ionizing radiation will be assessed by the surgeon wearing 3 dosimeter badges, one in each of the following: Around their neck, in their chest pocket, and on their pants' waistband to capture radiation exposure near organs that are at risk of malignancy. The areas on the body where they will be worn can be seen in Figure 2. The "Instadose" dosimeter badges will be used to detect and record exposure. These are small badges easily clipped on clothing (refer to figure 3) which function as a wireless dosimetry system consisting of three main components: a wireless dosimeter, a communication device (either a smart device with the *Instadose Companion* Mobile App or an InstaLink™3 Gateway), and an online reporting system accessed through a PC. The results will be available almost immediately by downloading the information on a computer, smartphone or mobile device and a comprehensive archive of official dose records will be maintained.

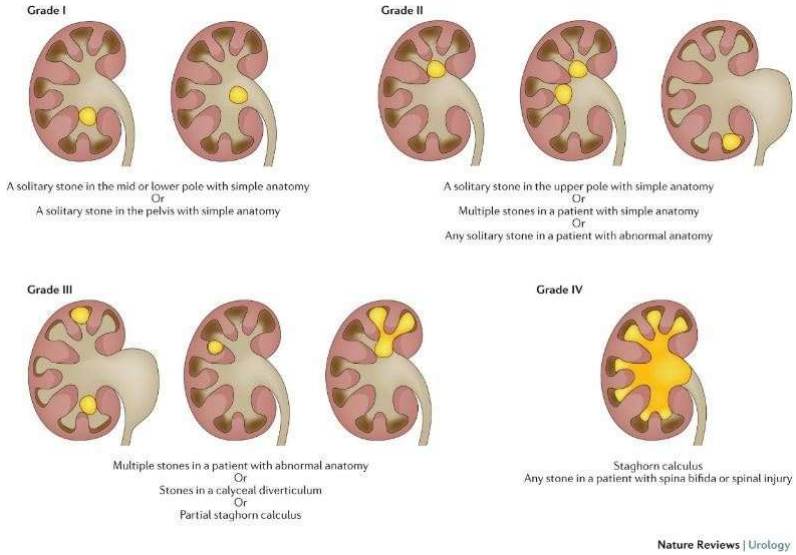
Two sets of 3 dosimeter badges will be kept in the same locker away from any sources of radiation other than background radiation. One set will be used by the surgeon exclusively during the treatment group's procedures, the other set will be used exclusively during the control group's procedures. The devices will be sent weekly to a technician to collect the data from the application and extrapolate it onto secured excel sheets in a radiation unit of measure, mrem. This will also ensure that any issue with the badges or the app will be detected early on and attended to.

Figure 2: Locations of tonometry badges

Figure 3: Instadose Wireless Dosimetry System

The Guy's Stone Score [30] will be used to assess the stones preoperatively and determine complexity. Since we are randomizing the patients into two groups, this should overcome the potential confounding effect of this variable. It will be included in the descriptive statistics section to assess how comparable the final two groups are. If the two groups were not balanced, then, this will be explored in the analysis section. Figure 4 [31] expands on the Guy's score which has been validated in multiple studies and is easy to apply. Higher Guy's stone score has been correlated with a lower stone free rate [30].

Figure 4: The Guy's Stone Score



7.0 Schedule of Activities

7.1- Pre-procedure Evaluation

The following assessments will be done prior to the procedure:

- Patient demographics
- Medical/Surgical History
- NCCT scan which is the standard of care
- Guy's stone score

7.2- Pre-discharge Evaluation

- Adverse events/Complications

- Length of hospital stay

If the subjects experienced prolonged hospitalization post procedure, any further assessments performed should be documented in addition to the reason for the extended stay.

7.3- Postoperative Follow Up

One month after the procedure (30 days) with an acceptable visit time frame of +/- 7 days
- NCCT scan will be done to assess SFR

- Adverse events/Complications

7.4- Unscheduled Follow Up Visits

If a subject visit occurs outside the protocol-specified time frame (one-month post-op), study sites are required to record data from that visit, especially if it is related to the procedure itself.

Possible reasons requiring data collection from the visit include:

- Subjects experiencing new symptoms and/or an adverse event

- Follow Up on an adverse event that occurred previously

8.0- Data Analysis and Significance

Primary analysis will be performed using an intention to treat (ITT) approach.

For our primary outcome, we will compare the two groups' stone free rates using the Chi-square test, or Fisher's exact test if appropriate. The P-value and effects size (Cohen's h) will be reported. Risk ratios with 95% confidence intervals will be calculated for the ILY-assisted ureteroscope with the classic approach as the reference group. 0.05 will be set as the p-value threshold.

Perioperative and postoperative complications within 30 days, as per Clavien-Dindo classification, will be compared the same way after stratifying the complications into their respective Clavien-Dindo group.

As for the NASA Task Load Index, the overall scores of the two groups will be compared using the independent t-test or Mann Whitney U test, according to the normality of the results assessed by Shapiro-Wilk test. The mean and 95% confidence intervals of the overall scores will be reported, alongside the P-values and effect size (Cohen's d). Individual factor scores within the NASA Task Load Index will be compared similarly. Surgeon safety, assessed by radiation exposure rate, as well as other intraoperative parameters like operative time, draping time, docking time, lasing time, and conversion rate will be compared using the same method.

Logistic regression will be employed, particularly interaction terms between intervention (ILY vs classical approach). This term will be included in the bivariate logistic regression of stone free rate and Clavien-Dindo complications. The term will also be used for the NASA Task Load Index scores and radiation exposure rate, in the context of linear regression.

Since stratification by laser type is not` performed at randomization, we will adjust for laser type as a covariate in all primary and secondary outcome analyses to control for potential confounding.

Regarding missing data, if the proportion is small, we will use complete case analysis where only participants with complete data are analyzed.

If the missing data comprises a big proportion, a systematic approach will be utilized through multiple imputations particularly for ergonomics and surgeon safety assessments. In addition, sensitivity analysis will be conducted to assess the impact of the missing data on the results.

The ILY robotic system represents technological advancement in the field of URS. There

is currently no noninferiority randomized controlled trial (RCT) comparing the ILY robot to manual flexible URS. This proposal addresses a significant gap by evaluating whether robotic assistance can provide equivalent or superior efficacy and safety, improving clinical outcomes, procedural consistency, and surgeon ergonomics and radiation exposure.

The successful completion of this study could have a significant impact on urological practice encouraging the adoption of the ILY robot in routine kidney stone management, potentially improving the standard of care.

In terms of methodology, the proposed RCT using the noninferiority design will yield key metrics including stone-free rate, peri and post-operative outcomes, ergonomics, surgeon safety in terms of radiation exposure, and intraoperative parameters. The trial will be conducted with strict randomization, blinding of outcome assessors, and adequate sample size calculations to ensure robust statistical power.

9.0- Maintaining Records

The study sponsor (AUBMC) will maintain hard and electronic copies of the data collected from the centers including the consent forms, adverse events, and other records related to the trial. Clinical sites will maintain study records for a minimum of 3 years after study completion.

The study investigators will maintain all relevant study documentation through entering the data into a secure electronic database (REDCap). Personal identifiers will be hidden, and the data will be labeled according to the Medical Record Number (MRN) of each patient to protect their identity and personal information. Each patient will be also given a study ID number. The coded data set will be provided to the statistician for analysis and the data will be analyzed and reported in that form. We will maintain an excel sheet with the Patient Name, MRN, and assigned Code to allow re-identification if necessary (for follow-up). This version will only be accessible by the local PI and will be secured and stored in a separate file on the computer of the PI with strong passwords to maintain access control and confidentiality.

The final trial dataset will be accessible only to the principal investigators and authorized research personnel at AUBMC. Collaborating centers will not have access to the full dataset. Data sharing is governed by institutional policies and ethical guidelines to ensure compliance with data protection regulations.

10.0- Adverse Events and Safety Monitoring

As discussed before, the ILY robot has a strong safety profile observed in the first two prospective clinical assessments done by Hajj et al. and Farre et al. This is why this study does not carry any additional risk on the patients and, therefore, we expect a low incidence of adverse events.

1. General Anesthesia

Both procedures require the same standard of general anesthesia for ureteroscopy.

2. Risks Specific to Manual Flexible Ureteroscopy (Standard of Care)

The known procedural risks include:

- Ureteral injury
- Infection or sepsis
- Hematuria

3. Risks Specific to Robot-Assisted Lithotripsy (ILY Robotic System)

Mechanical malfunction of the robotic system, although rare, could require conversion to manual ureteroscopy intraoperatively. This will have no impact on the patient.

At present, no evidence suggests that the ILY system increases overall risk compared to manual fURS, and preliminary studies have shown comparable safety profiles [24].

In case of any adverse events, prompt investigations will be done, and appropriate treatment plans will be implemented based on the standards of care.

Additionally, all equipment used will be routinely checked by the medical engineering department as per standard protocols. Also, before each procedure the OR nursing team will check the equipment as per standard practice.

<u>Plan for Handling Unexpected Intraoperative Events and Device Malfunctions</u>

During the Trial:

Common Intraoperative Complications:

1. Ureteral or Renal Pelvis Perforation

- Step 1: Stop the procedure and assess severity using imaging if necessary.

- Step 2: Place a ureteral stent or nephrostomy tube to divert urine and allow healing.
- Step 3: Postpone further intervention if clinically indicated.
- Step 4: Document and report to the trial coordination team.

Postoperative care:

Monitor with follow-up contrast imaging to confirm resolution.

2. Bleeding or Hematuria

Intraoperative management:

- Apply gentle irrigation to clear the field and identify the source of bleeding.
- If bleeding is localized, use tamponade with the ureteroscope or reduce laser power.
- Stop the procedure if bleeding is uncontrolled and ensure hemostasis.

Postoperative care:

Monitor hematuria and provide supportive care (e.g., hydration).

3. Stone Migration

Intraoperative management:

- Retrieve migrated fragments during the same procedure if possible.
- If inaccessible, schedule a follow-up procedure.

Postoperative care:

- Use follow-up imaging to monitor residual stones and schedule additional interventions if necessary.

4. Scope Damage

Intraoperative management:

- If the scope fails, switch to a backup device.
- Document the incident for follow-up maintenance or manufacturer feedback.

5. Device malfunctions:

- Step 1: Pause the procedure and attempt to troubleshoot using the provided user manual.

- Step 2: Notify the OR team and assess the patient's condition.
- Step 3: If unresolved within 10 minutes, convert to manual fURS or alternative method.
- Step 4: Document the issue and notify the trial coordination team.

Documentation and Reporting:

There should be immediate documentation of any intraoperative event, including:

  - Nature of the event.
  - Steps taken to manage it.
  - Outcome (e.g., resolved, conversion to another method).
- All events must be reported to the central trial coordinating team within 24 hours for review and analysis.

Post-Event Follow-Up

Patient Monitoring:

- Monitor the patients postoperatively and manage any complications according to the standards of practice.

To ensure that the same procedures are followed at all participating centers, a standardized and systematic approach will be implemented:

1. <u>Standardized Protocols:</u>
   - All study centers will follow a single, unified protocol that has been approved by the IRB at AUBMC.
2. <u>Regular Communication and Monitoring:</u>
   - AUBMC's study coordinator will oversee recruitment and adherence to protocols, acting as the main point of contact for any site-related queries.
3. <u>Data Collection and Quality Control:</u>
   - All data will be collected on RedCap.
   - The postdoctoral research fellows of Dr. Albert El Hajj will conduct remote monitoring for the data collection to ensure compliance with the protocol.

This is feasible through checking the data on RedCap monthly to assess data entry progress, missing fields, and data inconsistencies.

4. Data and Safety Monitoring Board (DSMB):

A DSMB will be established to oversee patient safety and the integrity of the study as mentioned in the protocol. The DSMB will be responsible for reviewing the data about the procedures and adverse events to ensure the safety of the subjects. It will also monitor adherence to ethical standards and trial conduct. This committee will be independent from the study investigators and will meet bi-annually.

The following members will form the DSMB:

1- Dr. Bassel Bachir, MD
Department of Surgery, Division of Urology, American University of Beirut Medical Center, Beirut, Lebanon
2- Dr. Marlene Chakhtoura, MD
Department of Internal Medicine, Division of Endocrinology, American University of Beirut Medical Center, Beirut, Lebanon.
3- Dr. Marianne Majdalani, MD
Division of Pediatric Intensive Care Vice-chair, Bioethics and Professionalism Program, American University of Beirut Medical Center, Beirut, Lebanon.

A uniform protocol will be shared with all centers for adverse event reporting and managing withdrawals.

11.0- Ethical Considerations and Dissemination

11.1- Ethical Considerations:

- This study will be conducted following the principles of Belmont Report and abiding by the principles of responsible research conduct and scientific integrity.
- Approval from AUBMC's Institutional Review Board will be sought, with regular audits taking place throughout the trial. Findings from these audits will be documented, and any necessary corrective actions will be implemented promptly.
- Written informed consent will be obtained from all the participants.
- Any modifications to the study protocol will be submitted for approval by the Institutional Review Board (IRB) prior to implementation. All approved changes will be promptly communicated to the collaborating centers and investigators to ensure compliance with the updated protocol.
- Regular progress reports will be submitted to the IRB according to their established guidelines. Upon completion of study, the IRB will be notified.

11.2- Data Sharing Plan:

Coded participant data, including baseline characteristics, primary and secondary outcome measures, and statistical analysis plans will be made available upon reasonable request from the corresponding author, beginning six months after publication and ending five years after the publication date, ensuring compliance with ethical guidelines and institutional review board (IRB) regulations.

The study protocol, statistical analysis plan, and informed consent forms will also be accessible upon request. Researchers seeking data must submit a methodologically sound proposal, which will be reviewed by the trial steering committee. Data will be shared in compliance with institutional and ethical regulations.

To facilitate data reproducibility and secondary analyses, study protocols, statistical analysis plans, and consent forms will also be accessible via [institutional repository or corresponding author]. Researchers requesting access must submit a formal proposal, which will be reviewed by the study steering committee.

12.0- Conflicts of Interest

The authors declare there are no conflicts of interest related to this study. Neither the manufacturer nor any affiliated company of the ILY Robot had any role in the study design, data collection, analysis, interpretation, manuscript preparation, or decision to publish the results. No financial or non-financial support, including grants, was received from the manufacturer.

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