Protocol Outline

Protocol Title: Intraop Cone-beam CT for Percutaneous Nephrolithotomy
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I. Abstract

Percutaneous nephrolithotomy (PCNL) is a first-line treatment for kidney stones >2cm. Frequently, patients require multiple procedures to address their stone burden. The decision to proceed with a second-look procedure is based on follow-up CT imaging, which is obtained postoperatively. In this study, we propose the use of a portable CT scan technology to obtain follow-up imaging while the patient is still under anesthesia for the initial procedure. The goal of this study is to determine whether this allows the surgeon to identify residual fragments and render the patient stone-free within a single anesthetic event.

II. Background and Significance/Preliminary Studies

Percutaneous nephrolithotomy (PCNL) is considered a first-line management option for kidney stones larger than two centimeters. Unfortunately, because of the large stone burden, up to 70% of these patients are left with residual stone fragments after their initial PCNL.[1] Additionally, an estimated 20% to 60% of such patients ultimately require further interventions due to residual stone fragments.[2] The need for a subsequent procedure is determined by postoperative abdominal computed tomography (CT) imaging, which is routinely performed on the first postoperative day at this institution. The decision to proceed with a second procedure is based on findings from this postoperative CT scan.

Cone-beam CT (CBCT) is a novel portable imaging technique that can allow cross-sectional imaging to be obtained intraoperatively, rather than post-operatively.[3] Incorporating this modality would allow the surgeon to determine whether the procedure should be continued, in the event of residual fragments, or if it can be safely concluded. This would obviate the need for dedicated postoperative CT scans and, more importantly, reduce the need for subsequent procedures and consequently decrease the patient's length of stay.

III. Study Aims

The purpose of this study is to determine whether using CBCT to perform an abdomen-pelvis CT scan immediately following initial PCNL, before the patient emerges from general anesthesia, allows the surgeon to determine whether additional work is needed or whether the procedure can be concluded without requiring further imaging or future interventions. Therefore, the primary outcome will be the rate of subsequent surgical intervention (i.e. "second-look" interventions) in patients undergoing CBCT.

IV. Administrative Organization

This study will be performed exclusively in the Main Operating Room area of Loyola University Medical Center.

V. Study Design

1. The study population will be patients undergoing initial PCNL, and they will be recruited to participate in this study prior to surgery.
2. Outcomes from this study will be compared with existing data on rates of second-look intervention at this institution.
3. **Our retrospective chart review of PCNL patients from 2018 and 2019 revealed a total of 178 PCNL patients, with a second-look intervention rate of 31.5%. We anticipate that use of CBCT will reduce our second-look intervention rate to 10%. However, despite being rendered radiographically stone-free with CBCT, we imagine patients may require second-look procedures for various reasons; we estimate the upper bound of this occurrence to be 15%. Assuming this, along with a power of 80% and a type I error rate of 5%, our study would be appropriately powered with 39 patients. We will aim to recruit 60 patients to allow for redundancy and unanticipated exclusions such as for reasons listed in VI.1.i.2.**

VI. Study Procedures

1. Subject selection procedures
    i. Sampling plan
        1. Inclusion criteria:
            a. Patients >18yo
            b. Undergoing initial PCNL
            c. Stone fragmentation (laser/ultrasonic/mechanical) was performed during the procedure
        2. Exclusion criteria:
            a. Patients who are deemed by the operating surgeon not to require any form of CT imaging, intra-operatively or post-operatively (for example, this can occur in the event of a single visible stone which is removed in its entirety under direct vision without requiring any fragmentation)
            b. Patients whose procedures are aborted for various reasons, including but not limited to bleeding, hemodynamic instability, equipment failure, and inadequacy of nephrostomy access
            c. Patients whose habitus does not allow for the use of the CBCT machine
    ii. Recruitment procedures
        1. Patients undergoing initial PCNL will be recruited and provided protocol/consent materials at a preoperative

outpatient clinic visit. Consent will be obtained by one of the research team members at the preoperative visit or in the preoperative area on the day of surgery.

2. The patient will not be required to attend any additional clinical appointments beyond standard care. The patient will not be compensated for their participation in the study.

2. Data collection procedures
    - **i. A retrospective chart review of first-look PCNL procedures from 2018-2019 will be performed to identify a matched-cohort (based on patient demographics and stone characteristics) that meets the inclusion and exclusion criteria.**
    - ii. Data will be prospectively collected for our study cohort. The determination of our primary outcome (need for repeat surgical intervention) will be made in our usual fashion: via shared decision-making between the patient and the surgical team on the day subsequent to the initial procedure.
    - iii. Data collected for both cohorts will include but not be limited to:
        1. Demographic factors (age, sex, race/ethnicity)
        2. Medical factors (patient height and weight, presence of medical comorbidities, surgical history, pertinent laboratory values)
        3. Stone factors (location, size, composition, and other characteristics)
        4. Surgical factors (length of procedure, blood loss, operative time, length of hospital stay, radiation dose)
        5. Surgical complications, ranked by Clavien-Dindo class
    - iv. All data will be entered into Loyola's secure RedCAP application.

VII. Safety Monitoring Plan

1. There are no additional anticipated patient safety issues associated with performing intra-operative CBCT when compared to standard post-operative CT imaging.
2. In another study using the same Medtronic O-arm CBCT system that is available at Loyola, it has been demonstrated that the radiation dose experienced by the patient from CBCT is lower than that from standard CT imaging.[4]
3. In regards to radiation safety for operating room staff, standard precautions will be taken which include but are not limited to: using lead aprons for sterile surgical staff, optimizing the placement of sterile and non-sterile surgical staff, using lead aprons for sterile surgical staff, and standing beyond a 2-meter distance from the iso-centre. Assuming one CT per surgical procedure, a liberal average of three procedures per week, and 48 work-weeks per year, an unprotected staff member would be expected to receive below 1.6 mSv a year at a distance of 2-meters from the iso-centre.[4] This is far below the occupational exposure limit set at 50 mSv per year by OSHA (Occupational Safety and Health Administration).

VIII. Analysis Plan

1. The historical cohort and study cohort will be compared on a variety of demographic and surgical factors to ensure homogeneity between the groups. Chi-squared and Student's t-tests will be performed as appropriate.
2. The proportion of patients requiring a second-look procedure would be calculated for both our cohort under study and our historical cohort. These proportions would be analyzed with a chi-squared test to determine statistical significance.
3. We would also perform subgroup analyses on a variety of patient characteristics, including but not limited to BMI, stone size, stone composition, and stone location, to determine if certain patient populations are more likely to benefit from CBCT.
4. Data will be analyzed by exporting tables from RedCAP onto Loyola's secure research network drives. From there, data will be imported into SPSS and analyzed as appropriate by the research team.

IX. Literature Cited

1. Pearle MS, Watamull LM and Mullican MA: Sensitivity of noncontrast helical computerized tomography and plain film radiography compared to flexible nephroscopy for detecting residual fragments after percutaneous nephrostolithotomy. J Urol 1999; 162: 23.
2. Nevo A, Holland R, Schreter E, Gilad R, Baniel J, Cohen A, Lifshitz DA. How Reliable Is the Intraoperative Assessment of Residual Fragments During Percutaneous Nephrolithotomy? A Prospective Study. J Endourol 2018; 32(6): 471-5.
3. Roy OP, Angle JF, Jenkins AD, et al. Cone beam computed tomography for percutaneous nephrolithotomy: initial evaluation of a new technology. J Endourol. 2012;26:814–818.
4. Pitteloud N, Gamulin A, Barea C, Damet J, Racloz G, Sans-Merce M. Radiation exposure using the O-arm® surgical imaging system. European spine journal. 2017 Mar 1;26(3):651-7.