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Near-Infrared Fluorescence Visualization of Iatrogenic Ureteral Injury Using Pudexacianinium Chloride (ASP5354) in a Porcine Model In Vivo

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INTRODUCTION

- Intraoperative ureteral injury (IUI) is a major surgical complication, which can lead to a poor prognosis in patients[1,2]
- IUI places a serious health burden on patients, can necessitate additional surgery, and increases healthcare utilization[3,4]
- Technologies such as ureteral stenting and intraoperative imaging have been developed to prevent IUI; however, ureteral stenting is invasive and can increase the risk of complications[1,5]

- Two ongoing phase 3 studies (NCT05754333, NCT05999747) are evaluating pudexacianinium chloride (ASP5354), a near-infrared fluorescence (NIRF) imaging agent, for ureter visualization during abdominal surgery[6,7]

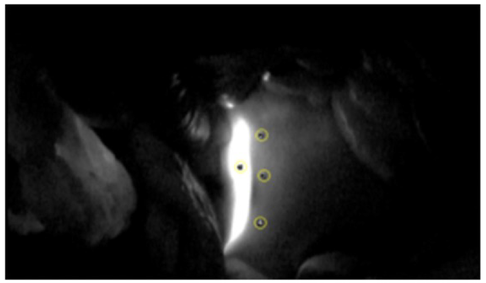
Objective

- To evaluate the effectiveness of pudexacianinium on detection of some types of IUI using NIRF imaging in a porcine model in vivo

METHODS

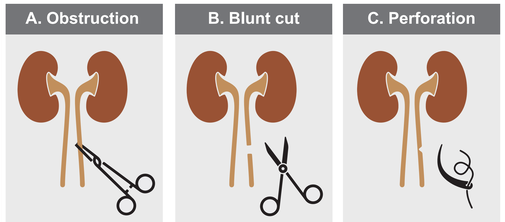
- Göttingen mini-pigs (n = 3) underwent laparotomy and were administered pudexacianinium (0.01 mg/kg) intravenously (IV)
  - Both left and right ureters were visualized using the clinically approved NIRF camera, pde-neo (**Figure 1**)
  - Indigocarmine (0.8 mg/kg IV, n = 3) was used as an agent to compare visual assessment
- After confirmation of urine flow by NIRF video image in the pudexacianinium group or by visual recognition in the indigocarmine group, various ureteral injuries were induced (**Figure 2**)
  - **Obstruction:** The ureter was injured by obstruction with forceps
  - **Blunt cut:** The ureter was injured by cutting with scissors
  - **Perforation:** The ureter was injured by puncture with a 18G needle
- In each case, a sponsor-designated urologist located and verified ureteral injury using images of the ureter and its vicinity taken with the NIRF camera system (pudexacianinium group) or macroscopically (indigocarmine group)
- The urologist stayed in another room while animals were prepared for an injury by puncture; thus, the urologist could not directly confirm the punctured site

Figure 1. NIRF visualization of mini-pig ureters using pudexacianinium



NIRF, near-infrared fluorescence.
Image adapted from Fushiki H et al. *Mol Imaging Biol*. 2023;25(1):74–84.

Figure 2. Ureteral injury model in this study: (A) obstruction with forceps, (B) blunt cut with scissors, and (C) perforation by needle



CONCLUSION

- These preclinical results suggest that intraoperative NIRF imaging with pudexacianinium, which is currently under investigation in phase 3 studies for ureteral visualization during abdominopelvic surgery, is potentially useful for detection of obstruction, blunt cut, and perforation ureteral injuries

RESULTS

- Results of visual evaluations and images of ureteral injuries are shown in **Table 1** and **Figure 3**
  - **Obstruction:** Ureteral injury was confirmed in 3/3 animals each in the pudexacianinium and indigocarmine groups
  - **Blunt cut:** Ureteral injury was confirmed in 3/3 animals each in the pudexacianinium and indigocarmine groups
  - **Perforation:** Ureteral injury was confirmed in 2/3 animals in the pudexacianinium group. In the indigocarmine group, no ureter injuries were detected in any of the 3 animals

Table 1. Ureteral injury in mini-pigs in pudexacianinium and indigocarmine groups

Group	Right ureter		Left ureter
	Obstruction	Blunt cut	Perforation
Pudexacianinium	+	+	+
	+	+	–
	+	+	+
Indigocarmine	+	+	–
	+	+	–[a]
	+	+	–[b]

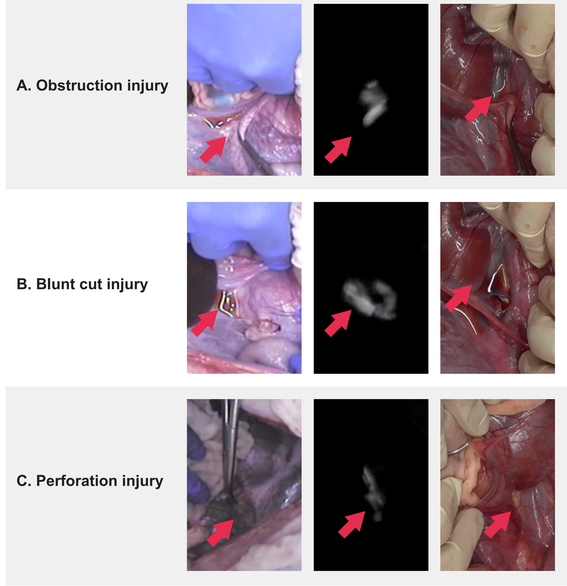
+, ureteral injury was confirmed; –, no ureteral injury was confirmed.
[a]Unable to confirm whether urine was leaking from the ureter due to hemorrhage in the vicinity.
[b]Unable to confirm conditions of injury because urine was mixed with blood.

LIMITATIONS

- Not all types of ureteral injury were recreated in this model
- All animals in this study had ureteral injuries, unlike the real-world setting for abdominopelvic surgery
- Indigocarmine was the only comparator used
- As ureteral injuries were induced in this model immediately following intravenous administration of pudexacianinium or indigocarmine, injuries sustained later in surgery were not evaluated

Figure 3. Representative images of ureteral injuries

Pudexacianinium	+	+	–
Indigocarmine	–	–	+
White light	+	–	+
NIRF	–	+	–



NIRF, near-infrared fluorescence.

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