



Poster
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Safety and Clinical Insights on Renal Papillary Tip

Biopsies for the Study of Lithiasis

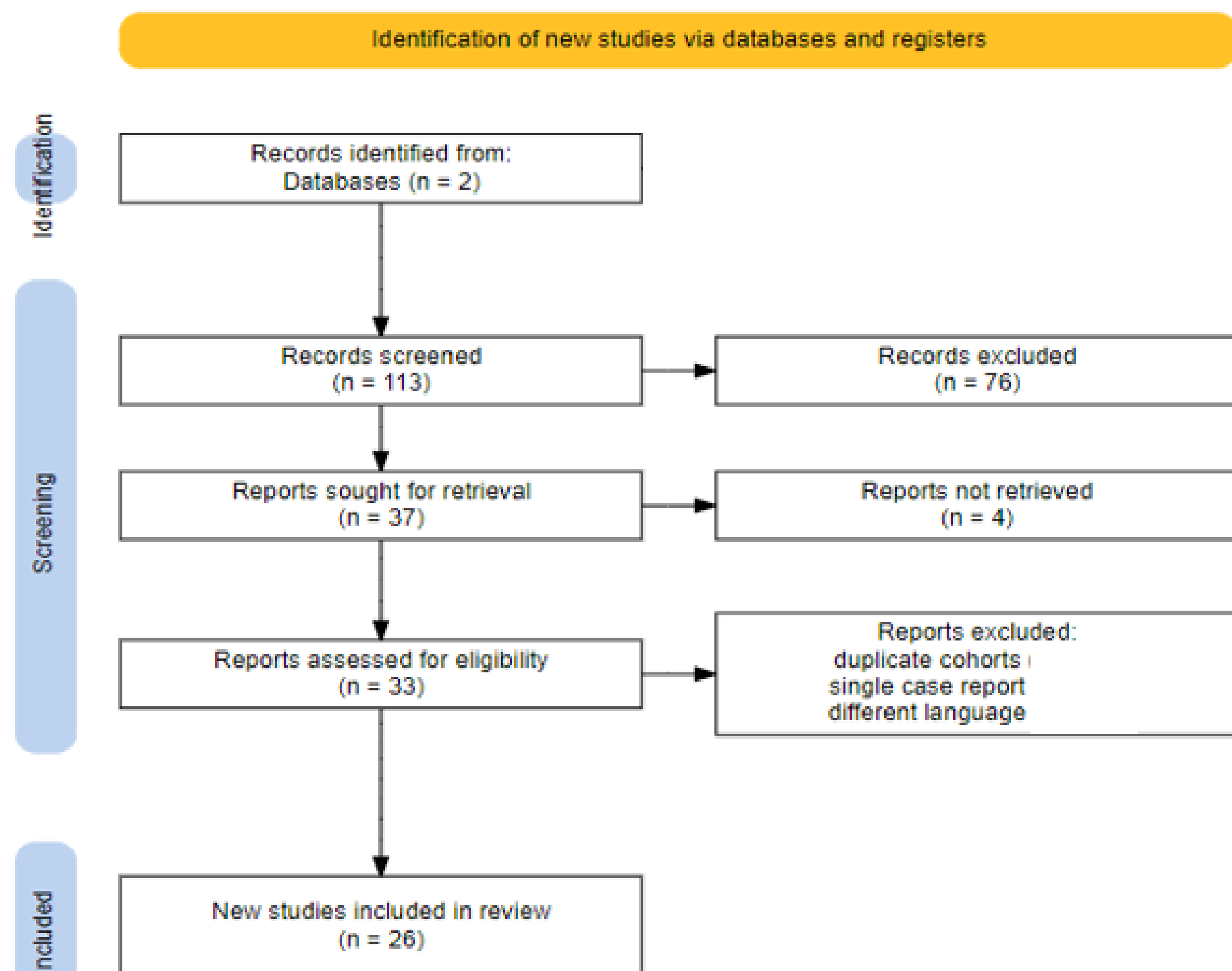
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INTRODUCTION

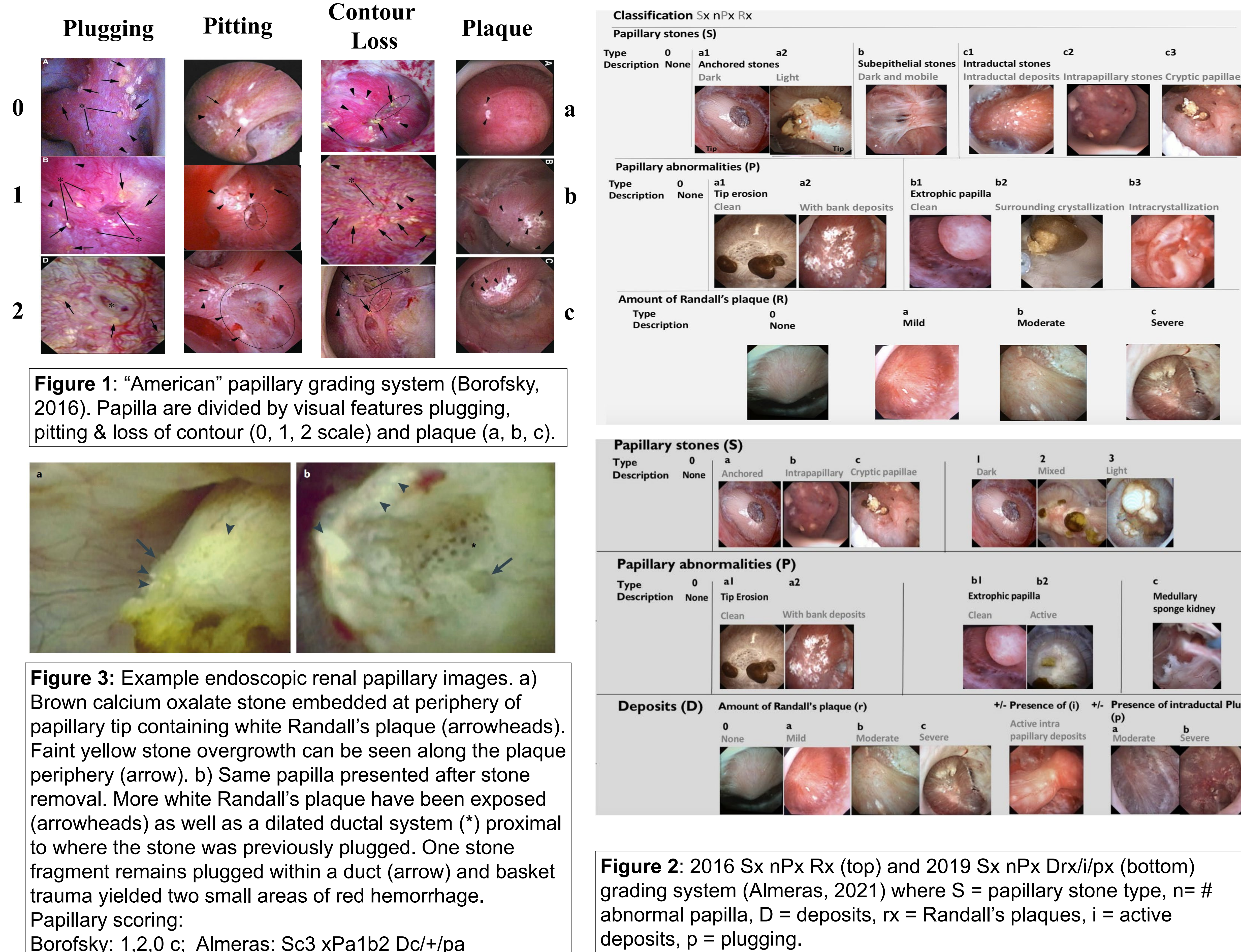
- 1937: Alexander Randall published renal papillary tip findings from cadaveric kidneys: 73/429 (17%) “inchoate precipitants”
- 1997: Low & Stoller: first modern endoscopic assessment of papilla, 43/57 (74%) stone formers + plaque
- 2003: Evan and Kuo, first report of papillary tip biopsy to investigate stone pathogenesis
- Since modern papillary biopsies are now performed on a live kidneys, we performed an exhaustive literature search to review the safety, value, and complications associated with this procedure

METHODS

- Predefined protocol developed according to PRISMA
- PubMed, Cochrane library, and Embase databases searched through September 2022 on endoscopic papillary biopsy using predefined terms. “stone” kidney “papilla” biopsy”. Manual searches of relevant articles were also performed.
- Primary outcomes** : 1) complications associated with papillary tip biopsy; 2) procedural type (ureteroscopy, PCNL) for biopsy; 3) value of endoscopic description of papillary abnormalities
- Two investigators initially screened relevant reports and reviewed full-texts. When populations overlapped, duplicates were removed. If no biopsy complication was reported, the procedure was assumed to be safe.
- For ease of review, data was divided into categories: Outcomes/Insights and Papillary Grading Scales



PAPILLARY GRADING SCALES



OUTCOMES AND INSIGHTS

Table 1: Summary of Literature Review and Key Findings

Name	Year	# biopsied	PCNL	URS	Outcomes	Findings
Evan AP	2003	19	19		No complications similar serum creatinine between biopsied patients analyzed	The origin of plaques in calcium stone formers is in the basement membranes of the thin loops of Henle at the urothelium. New endoscopic biopsy technique sufficient quality and size to allow for IHC staining of calcium deposits and infrared analysis.
Kuo RL	2003					Brushite SF share some bx characteristics with CaOx and intestinal bypass SFs with often more severe interstitial fibrosis. Cystine stone formers papillae histopathology most resemble brushite stone formers, however cystine stones are the only one so far to show thin loop of Henle apatite crystals.
Evan AP	2005	10	10		No significant hemorrhage or postoperative complications related to the biopsy procedures	SF w distal RTA have fibrosis around normal IMCD/BD whereas BR stone formers have fibrosis around crystal filled IMCD and BD.
Evan AP	2006	7	7		No significant hemorrhage or postoperative complications related to the biopsy procedures	Inter-alpha-trypsin inhibitor heavy chain 3 may stabilize renal interstitial matrix. Hypothesis: 1) disrupted epithelial attachment site, 2) denuded plaque attracting crystalline organic matrix, 3) CaOx crystal overgrowth.
Evan AP	2007	5	5		No significant hemorrhage or postoperative complications related to the biopsy procedures	PHP and CaP have flat retracted papilla along with dilation of the ducts of Bellini (BD) and inner medullary collecting duct (IMCD) plugs.
Evan AP	2007	10	7	0		SF w illeostomies demonstrate interstitial apatite plaque and IMCD apatite crystal plugs despite low urine pH.
Evan AP	2007	2	2	0		Small bowel resection pts w CaOx stones have lower density of IMCD plugging than ileostomy patients.
Evan AP	2008	5	5		No significant hemorrhage or postoperative complications related to the biopsy procedures	No difference between the percutaneous and transurethral renal papillary biopsy samples used for histopathologic analysis.
Evan AP	2008	16	16		No significant hemorrhage or postoperative complications related to the biopsy procedures	Histologic examination of papillary tip biopsy correlates with documented microcalcifications on endoscopic mapping.
Evan AP	2009	7	7		No significant hemorrhage or postoperative complications related to the biopsy procedures	HA and brushite stone formers demonstrate differences in papillary injury, deposits, and cortical injury.
Evan AP	2010	11	11		No significant hemorrhage or postoperative complications related to the biopsy procedures	Idiopathic CaOx stone formers with low plaque demonstrate less intralaseal and BM crystallization on histopathology.
Ruggerra L	2011	28	20	8	Statistically (but not clinically) significant differences in pre vs post-op Hb/Hct p (<.001). Fever in one PCNL patient	SF w medullary sponge kidney have IMCD ductal stones but do not demonstrate papillary interstitial fibrosis histopathologically.
Linnes MP	2013	78	78		No significant hemorrhage or postoperative complications related to the biopsy procedures	CaOx stone former have significantly more interstitial inflammation compared to UA stone formers.
Evan AP	2014	26	26		No significant hemorrhage or postoperative complications related to the biopsy procedures	Struvite stone formers histopathologically show an increased inflammatory response when compared to CaOx stone formers.
Wang X	2014	27	27		No significant hemorrhage or postoperative complications related to the biopsy procedures	First study demonstrating increased inflammatory gene expression in papillae from CaOx formers.
Evan AP	2015	12	12		No significant hemorrhage or postoperative complications related to the biopsy procedures	BiGopsy forceps for renal papillae biopsy was associated with increased quality of renal papillary tissues and better RNA yield.
Viers BR	2015	14	14		No significant hemorrhage or postoperative complications related to the biopsy procedures	Expression of inflammatory cytokines in papilla >> level of systemic inflammation, supporting theory of inflammation for RP.
Jaeger CD	2016	112	112		No significant hemorrhage or postoperative complications related to the biopsy procedures	UASF have plaque and plug formation but lack tubular deposits and anchored stones.
Taguchi K	2017	23	*NS		“Laser coagulation was performed if there was uncontrollable bleeding in the biopsied region by irrigation (# unspecified)”	Brushite SF RP have increased expression of inflammatory pathways in neutrophil activation when compared to CaOx SF.
Taguchi K	2017	49	16	33	Biopsy increased URS OR time by 22 minutes (p = 0.004)	SF urinary extracellular vesicles differ from non-stone formers in immune cell derivatives and regulatory proteins.
Sun AY	2018	92	92	0	N/A	Osteogenic differentiation of interstitial fibroblasts plays a critical role in the formation of RP with long non-coding RNA MALAT1.
Evan AP	2020	8	8		No significant hemorrhage or postoperative complications related to the biopsy procedures	SF have diffuse injury with matrix remodeling with potential markers of stone burden and progression being MMP7 and MMP6.
Makki MS	2020	20	16	4	No significant hemorrhage or postoperative complications related to the biopsy procedures	
Zhang J	2021	17	17	0	N/A	
Zhu Z	2021	57	32	0	N/A	
Canela VH	2022	5	3	0	N/A	
TOTALS: 26		660	562	45		

DISCUSSION

- Post-op labs were similar between biopsies and controls
- 1/660 (0.2%): fever >38°
- Papillary tip biopsies added 20”-30” to procedure time
- Various theories on RP formation continue to exist 1) inflammation 2) vascular 3) osteogenic transformation
- Pro-inflammatory genes, immune & cell apoptosis are more common in papilla of stone formers than controls
- Randall Plaque (RP) stone formers (SF) vs non-RP SF: higher uCa+, papillary plaque coverage
- Strohmaier: extent of RP correlates with # CaOx stone episodes
- Ciudin: papillae tip HU attenuation >43 HU correlates with stone recurrence

CONCLUSIONS

- Papillary tip biopsies are a safe method to sample renal tissue and can help elucidate stone pathogenesis
- Histological material from papillary tip biopsies varies by stone type
- The reliability of papillary tip endoscopic interpretation remains subjective with the potential for interpretation bias
- Future studies should test papillary grading models in a blinded fashion for further proof of concept