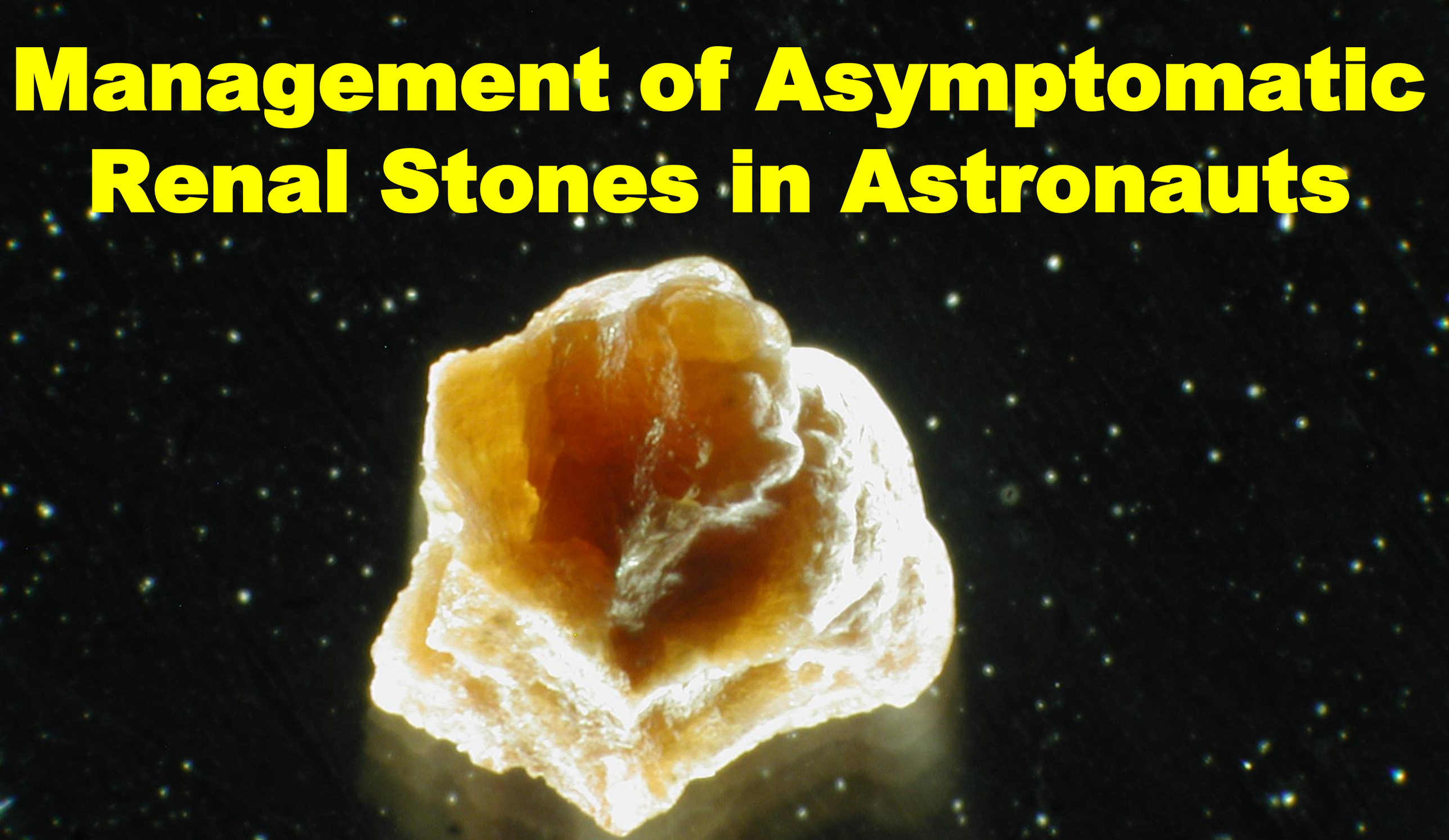
Management of Asymptomatic Renal Stones in Astronauts



For the NASA HRP Investigator's Workshop

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Galveston, Texas

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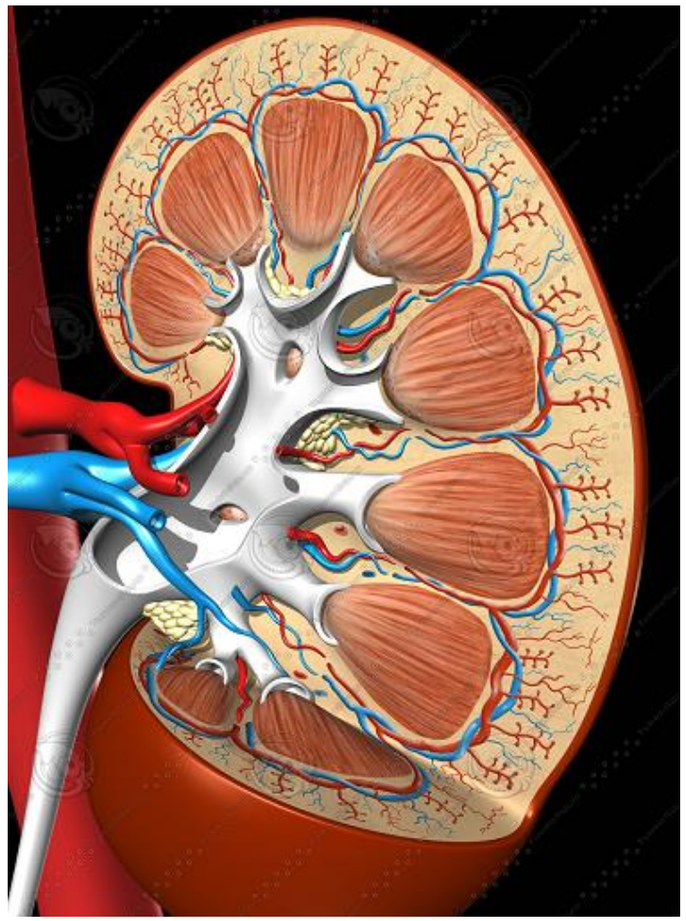
Overview

- The problem of small asymptomatic stones
- Background and risks
- Historical data
- How to screen for small stones
- Treatment and waiver

Small and Asymptomatic

- Small calcifications difficult to detect
- What is their significance?
  - Parenchymal or in the collecting system
  - Stable or growing
- Treat asymptomatic ditzels?
  - Or Leave them there?
- How to monitor over time?



Natural History

Size (mm)	Stone Free	Progression	Intervention
<= 5	28%	40.4%	5.3%
5 - 10	4.8%	52.4%	9.5%
>= 10	0%	71.4%	14.3%

Koh, et al. (2011), *Outcomes of long-term follow-up of patients with conservative management of asymptomatic renal caliculi*, BJU Int, 109:622-625.

Spontaneous Passage versus Stone Size

(Ueno, et al. (1977), Relation of spontaneous passage of ureteral calculi to size, Urology, 10(6):544-546.)

General Population

- Lifetime prevalence 10% male, 5% female
- Increasing incidence (20 - 74 y.o.)
- 3.2% to 5.2% (+ male)
- 3.7 % to 4.6% of commercial aviation pilots between 2000 – 2007 [2]

1. Hall, P. (2009) Nephrolithiasis: Treatment, causes and prevention, Clev Clin J Med, 76(10):583-591
2. Hyams, E., et al. (2011) The incidence of urolithiasis among commercial aviation pilots, J Uro, 186:914-916.

IMM Renal Stone Risk

	Probability (%)			
DRM	**No Events**	**Any Event**	**Best Case**	**Worst Case**
Lunar (21 Days)	99.979	0.021	0.013	0.003
ISS (6 months)	99.818	0.182	0.110	0.072
Mars (3 years)	99.092	1.090	0.659	0.430

IMM Data Request #: D-20150911-334

LSAH / EMR Review, April 2014

- At least 19 astronauts affected
  - 3 females, 16 males
- Treatment and prevention varied
- Monitoring parameters varied

LSAH Review, July 2015

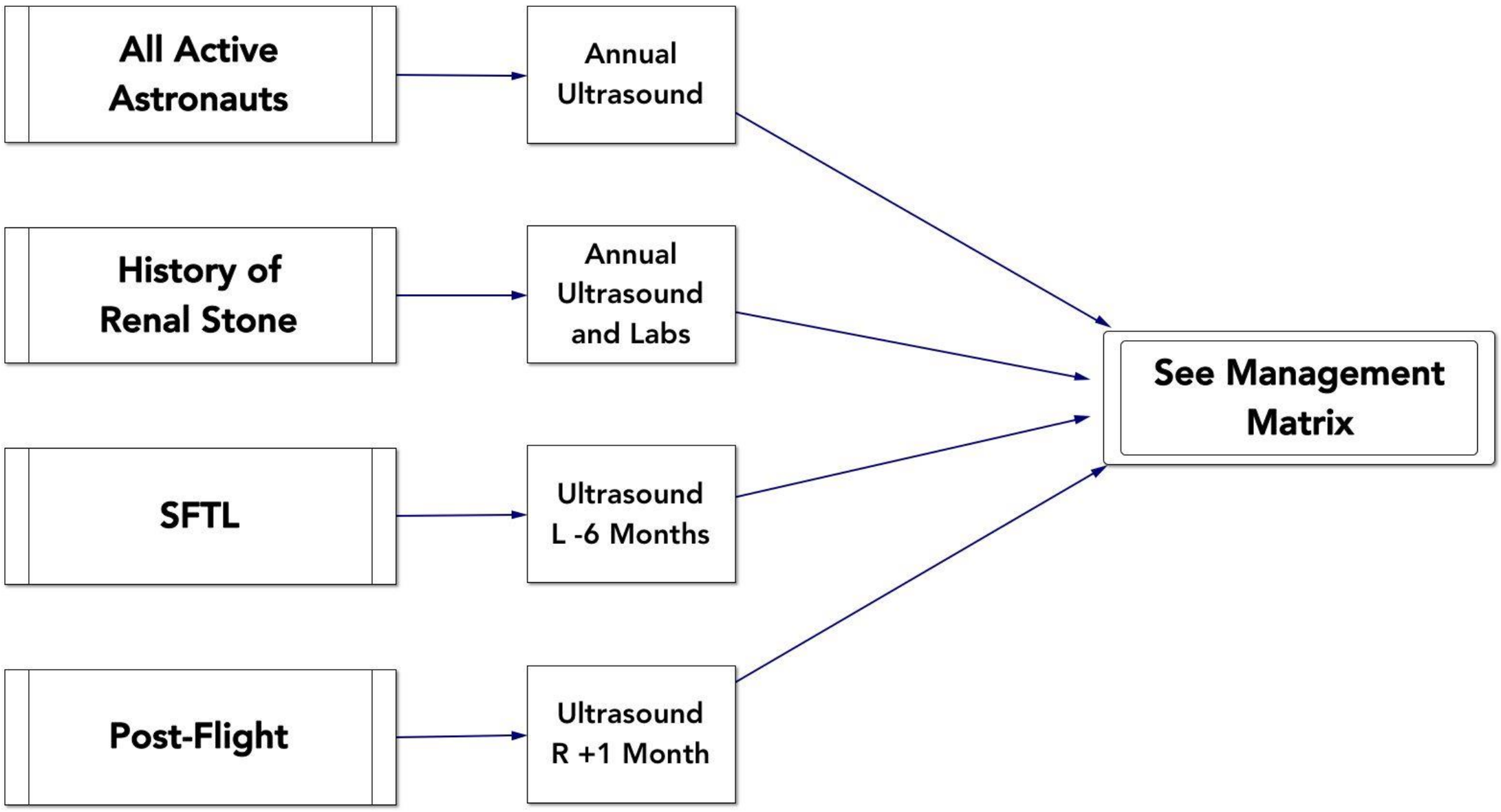
	# of Events	Long Duration	Short Duration
Preflight	4		
R+0-90 days	1	1	
R+90-180 days	3	1	2
R+180-270 days	1		1
R+270-365 days	2		2
Inter-flight	4	1	3
R>365 days	21		21
Grand Total	36	3	29

How to Screen?

- **Language matters**
  - Mineralized renal material or stone?
- **Ultrasound!**
  - No radiation
  - Almost as good as CT
- **CT for possible stones**
- **Flexible Ureteroscopy**
  - Both diagnosis and treatment
- What use are urine studies?

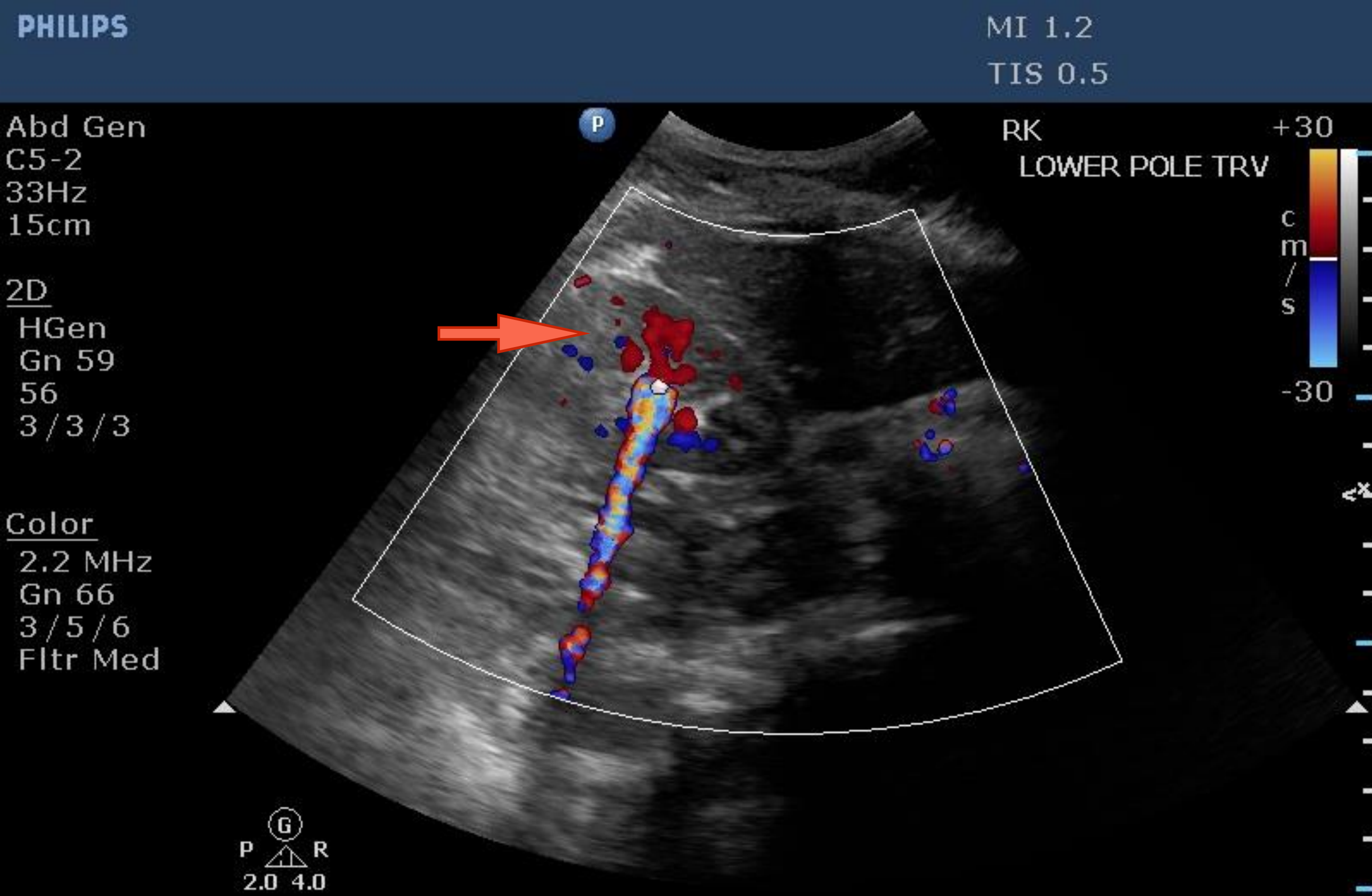
	Sensitivity (%)	Specificity (%)	Dose (mSv)
Ultrasound			
Average 2.6mm (1 – 9 mm, SD 1.15), n=51 pts, 114 stones [17]			
Shadowing alone	65 (PPV 90)	-	0
Twinkling alone	81 (PPV 94)	-	0
Shadowing + Twinkle	**88 (PPV 96)**	-	0
Average 3.9mm (1-20 mm), n=105 pts, 65 stones, CT as reference [18]			
Shadowing alone	48 (PPV 81)	99	0
Shadowing + Twinkle	**55 (PPV 67)**	**99**	0
X-Ray			
KUB	45 - 58	69 - 77	0.7
IVP	85	90	3
CT			
Low-dose, non-con.	97	95	3
Non-contrast	95 – 98	96 - 98	**10**
MRI			
	93 - 100	95 - 100	0

When to Screen?



Enhanced U/S Protocol

1. **Echogenic** → seen from 2 or more angles
2. **Twinkling** → frequency dispersion / “twinkling”
3. **Shadowing** → opaque to ultrasound
4. **Localizable** → papilla/collecting system
5. **Measurable** → >= 3 mm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HGen
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Color
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Gn 66
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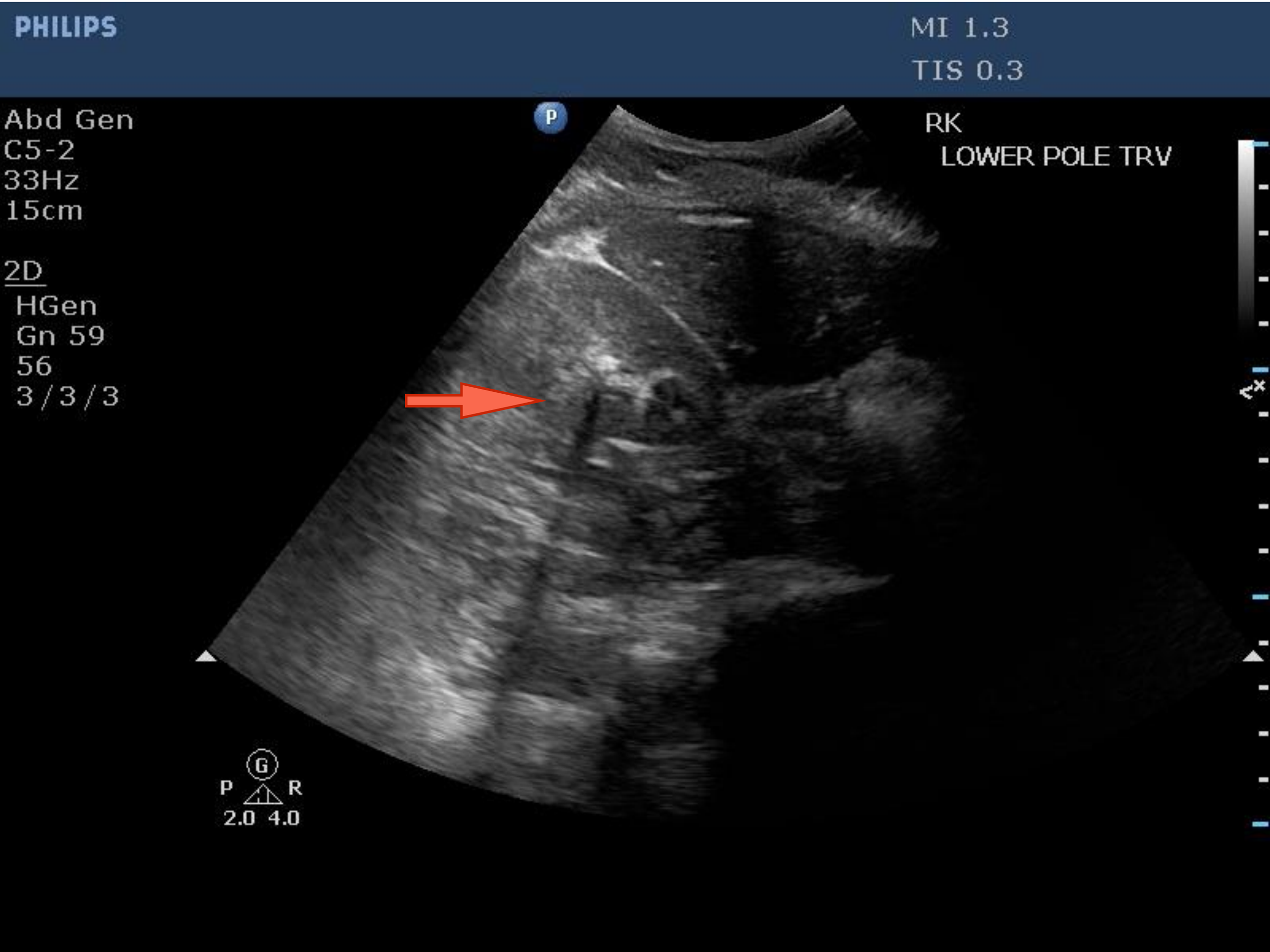
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2.0 4.0

Clinical Practice Guideline

- Use of specialized ultrasound protocol
- Yearly ultrasound for all astronauts??
- MRM by ultrasound may require…
  - Low-dose, high resolution CT
- MRM by CT…
  - then Flexible Ureteroscopy??
- Mission assignment affects treatment method
- Potential waivers for very small, stable MRM

US Navy Standards

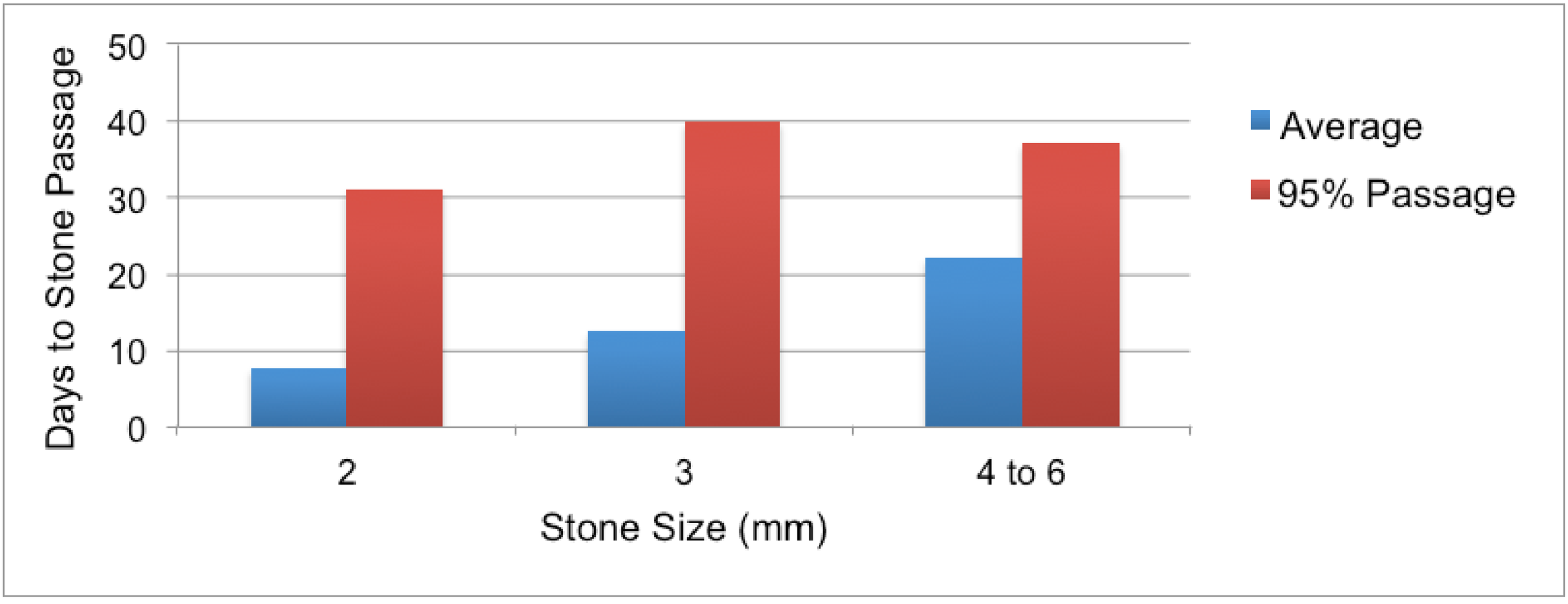
- Waivers given for...
  - calcium oxalate, calcium phosphate, uric acid and struvite;
  - retained stones in the renal parenchyma;
  - recurrent stones > 12 months apart.

- Medical evaluation & urology consult required

US Navy Standards

- Waivers NOT given for...
  - recurrent stones within one year,
  - cysteine stones,
  - hypercalcuria,
  - stones retained in the collecting system.

Exploration Missions?



Ureteral Stone Size and Time to Passage

Miller and Kane (1999), *Time to stone passage for observed ureteral calculi: A guide for patient education*, J. Urology, 162:688-691.

Back-Up

IMM – Renal Stone Events

DRM**	Probability Per Mission of One or More Event (%)		
	Any Event (95% CI)	Best Case (95% CI)	Worst Case (95%)
Lunar (21 day)	0.021 (0.017 – 0.026)	0.0127 (0.0074 – 0.019)	0.003 (0.0033 – 0.014)
ISS (6 month)	0.182 (0.149 – 0.222)	0.110 (0.064 – 0.165)	0.072 (0.029 – 0.122)
Mars (3 year)	1.090 (0.887 – 1.320)	0.659 (0.383 – 0.986)	0.430 (0.172 – 0.730)

Watch and Wait*

Application	Stone Free	Pros	Cons
best for renal or ureteral stones <5 mm	<5 mm // 28%	do no harm	time, stone growth (50%)

Koh, et al. (2011), *Outcomes of long-term follow-up of patients with conservative management of asymptomatic renal calculi*, BJU Int, 109:622-625.

Medical Expulsive Therapy

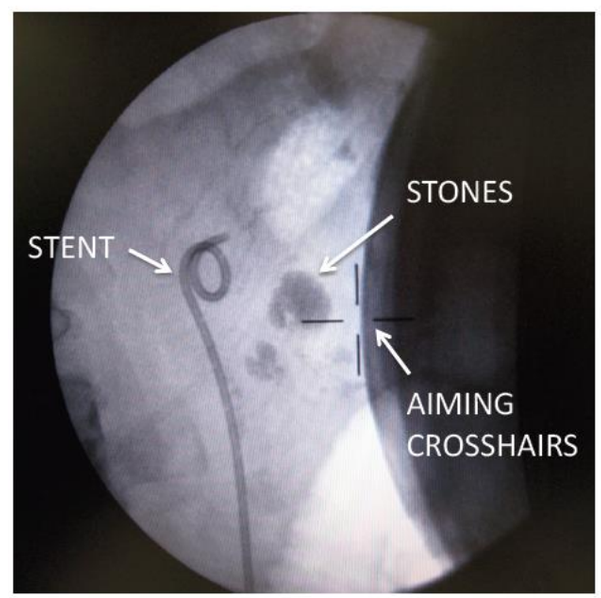
Application	Stone Free	Pros	Cons
best for distal ureteral stones	<4 mm // 55%	a bit better than waiting	need for treatment

Moe, et al. (2011), *Pharmacotherapy of urolithiasis: evidence from clinical trials,* Kidney Intl., 79:385-392.

Lithotripsy (ESWL)

Application	Stone Free	Pros	Cons
best for renal stones 10-20 mm	23 - 82% depend on size and location, better w/ MET	non-invasive, widely available	Radiation, no better for small stones, retained frags

Obek, et al., (2001), *The efficacy of extracorporeal shock wave lithotripsy for isolated lower pole calculi compared with isolated middle and upper caliceal calculi*, J Urol, 166:2081-2085.

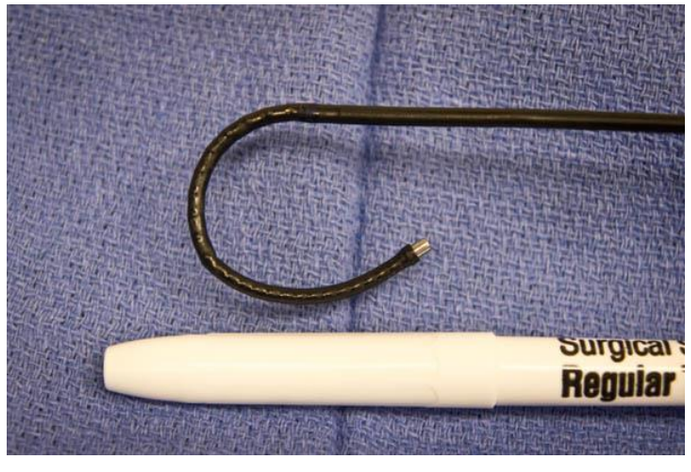


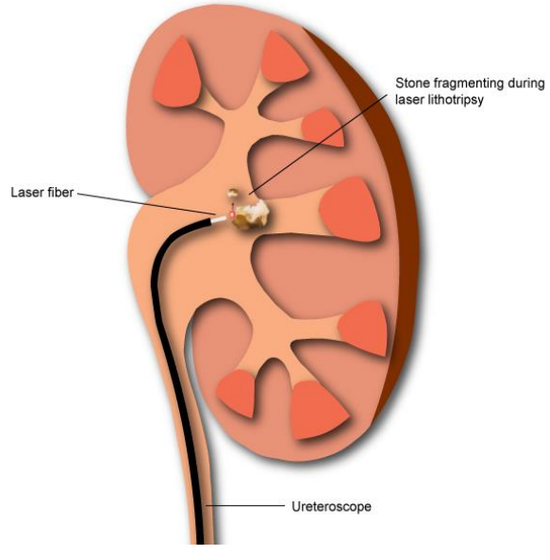
Images from: www.kidneystoners.org

Flexible Ureteroscopy**

Application	Stone Free	Pros	Cons
Can be used for any stone	>90%	high-stone free rate, low retreat rate	less widely available, operator dependent

Hussain, et al. (2011), *Redefining the limits of flexible ureterorenoscopy*, J Endourol, 25(1):45-49.



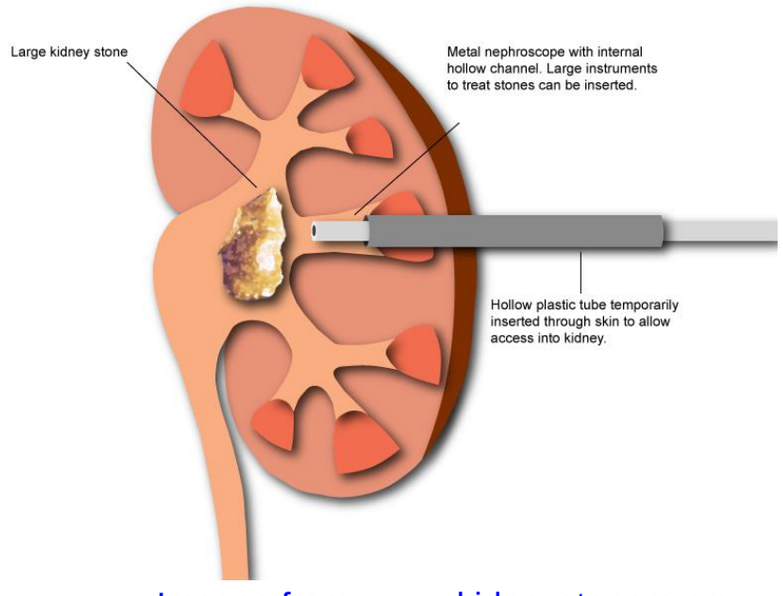


Images from: www.kidneystoners.org

Nephrostomy

Application	Stone Free	Pros	Cons
large, complicated, staghorn, other	>95%	definitive treatment	invasive, serious complications possible

Breda, et al. (2011), *Flexible uretroscopy and laser lithotripsy for single intrarenal stones 2 cm or greater - is this the new frontier?*, J Urol, 179:981-984



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