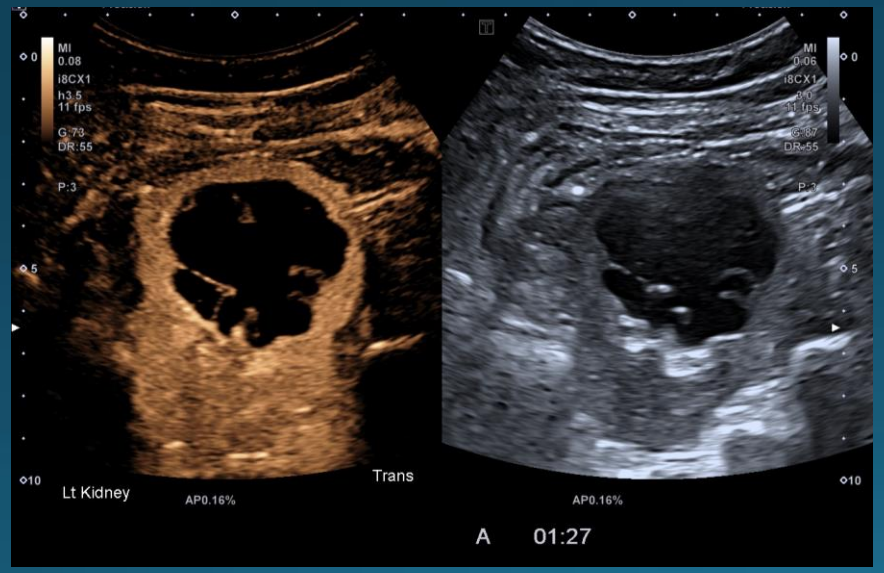
Renal Tract CEUS: Breaking out of the Bubble



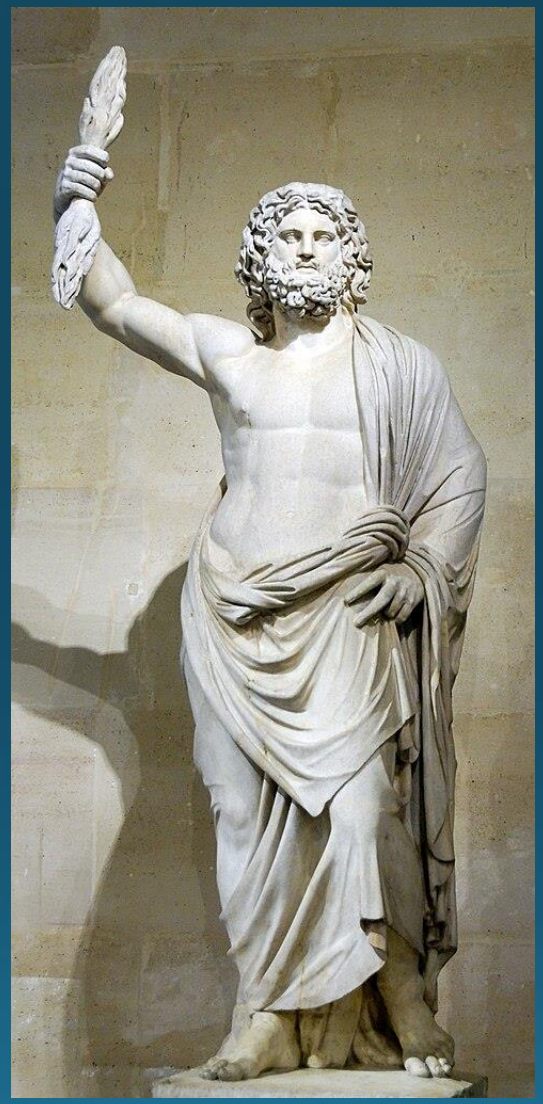
Dr Dean Rabinowitz

POWH Medical Imaging Department

Spectrum Medical Imaging

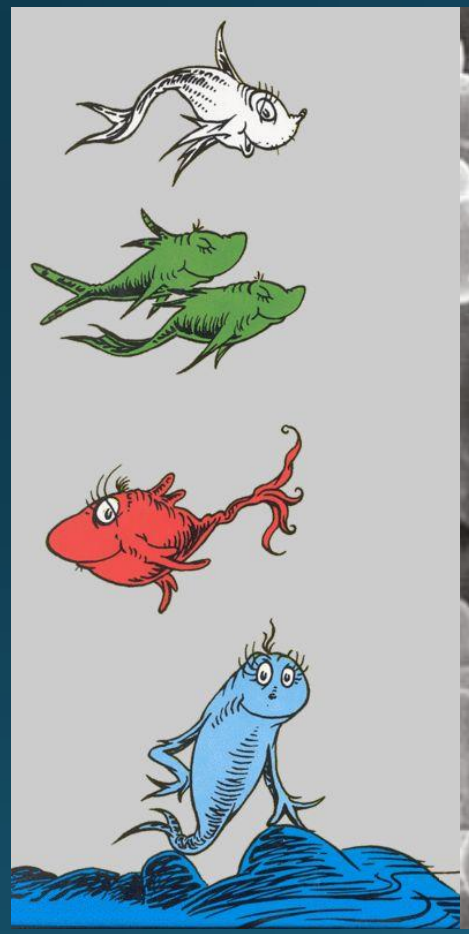
Outline

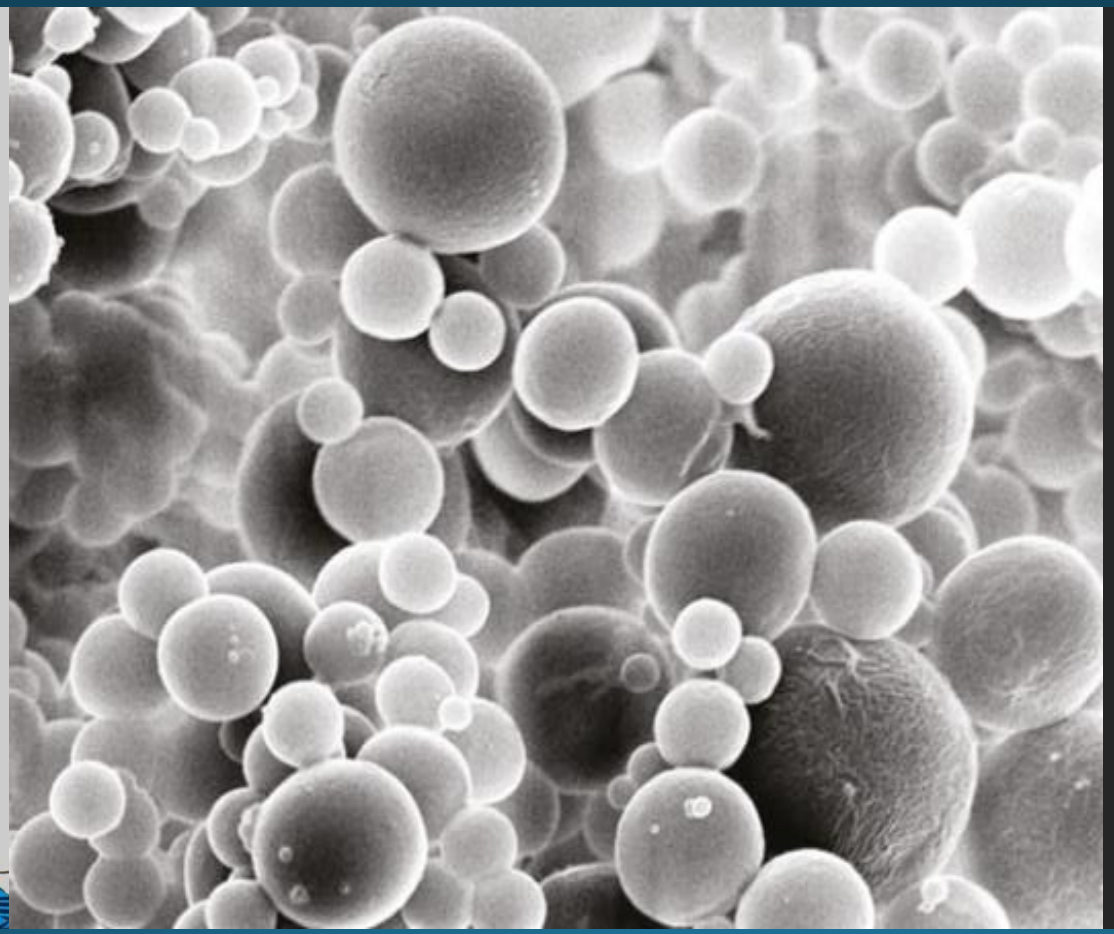
- Background
  - History of CEUS (what is it?)
  - Definity (how does it work?)
  - Indications (when is it suitable?)
- Technique
- Renal Applications
  - Normal enhancement patterns
  - Pseudo-lesions
  - Solid and cystic lesions
- Case studies
- Breaking out of the bubble in Australia

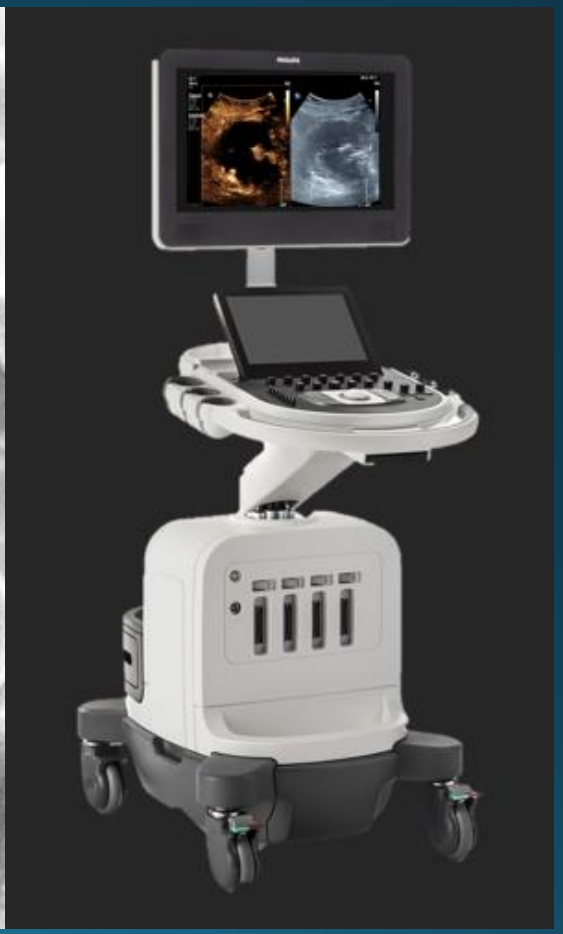


CEUS … ZEUS … SEUSS

BACKGROUND

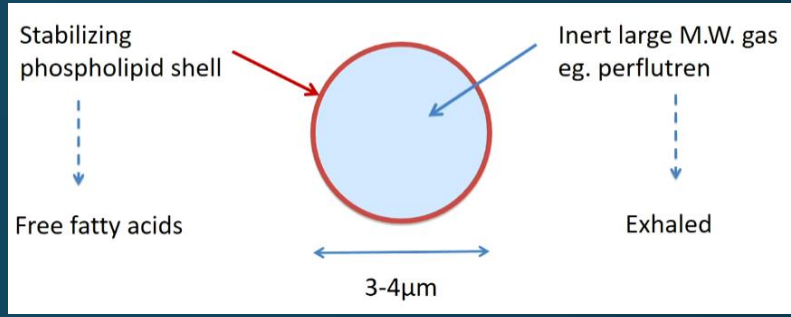






Contrast Enhanced Ultrasound -What is it?

- Definition
  - Administration of IV contrast agents containing gas microbubbles
  - Live/dynamic assessment
  - Enhancement patterns roughly equivalent to CT / MRI
  - Can interpret CEUS imaging based on our pre-existing knowledge of these patterns

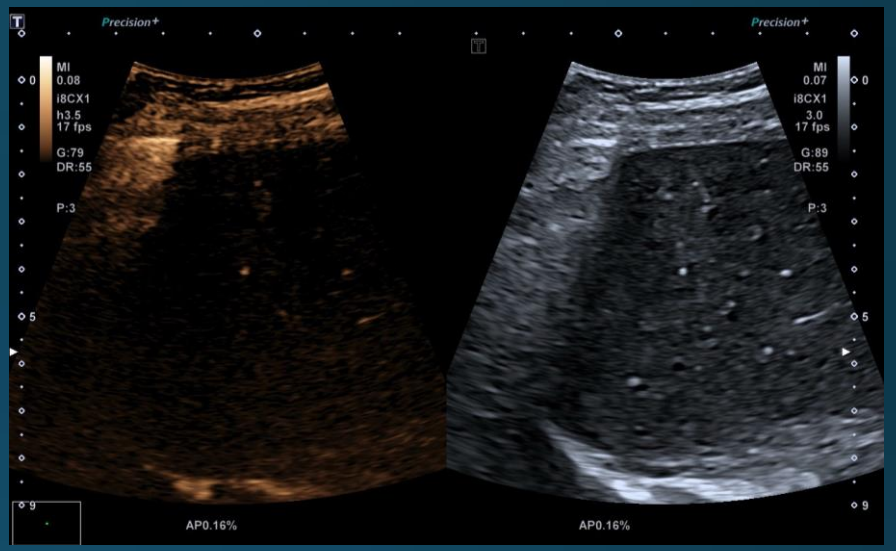


AGENT	GAS	STABILIZATION	COMPANY
SONOVUE	Sulfur Hexafluoride	Phospholipids	Bracco
DEFINITY	Perfluoropropane	Phospholipids	Lantheus
OPTISON	Perfluoropropane	Albumen	GE
SONAZOID *	Perfluorocarbon	?	GE

- Definity (Perflutren)
  - Perfluropropane (perflutren) gas encapsulated in phospholipid shell
  - Requires activation via agitator (Vialmix)
  - Injected IV tiny volume (0.2 – 1 mL)
  - Circulates 5-10 minutes before bubbles naturally burst
  - Tiny volume of microbubble gas breathed out in normal expiration
  - Tiny amount of phospholipid is metabolised or taken up by immune cells

CEUS – How does it work?

- Microbubbles
  - Smaller than RBC
  - Travels through capillary beds
  - Microbubbles are extremely strong signal enhancers (>> CT or MRI)
  - 10,000 x soft tissue echo intensity
  - Trick is to maximise the display of the echo signal of the bubbles (harmonic frequency) while suppressing the fundamental echoes
  - Different methods (pulse inversion and/or amplitude modulation)



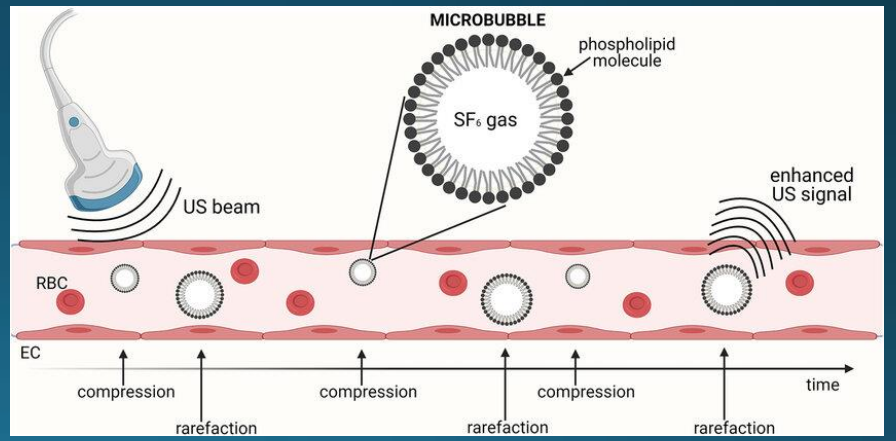


Image-guided surgery and novel intraoperative devices for enhanced visualisation in general and paediatric surgery: A review - Scientific Figure on ResearchGate

CEUS – Definity – Is it safe?

- TGA Approved:
  - "…for use in patients … to improve the characterization of focal lesions of the liver and kidney"
- Contraindications
  - Known allergy to perflutren, polyethylene glycol or other ingredients
  - Known (or highly suspected) right to left shunts
- Adverse reactions
  - Uncommon and mild
  - Headache (2%), flushing (1%), back pain (<1%)
  - Used to be a longer list but have been removed by FDA/TGA
  - Anaphylaxis = much lower than CT contrast (<0.002%)
- Other
  - No nephrotoxicity

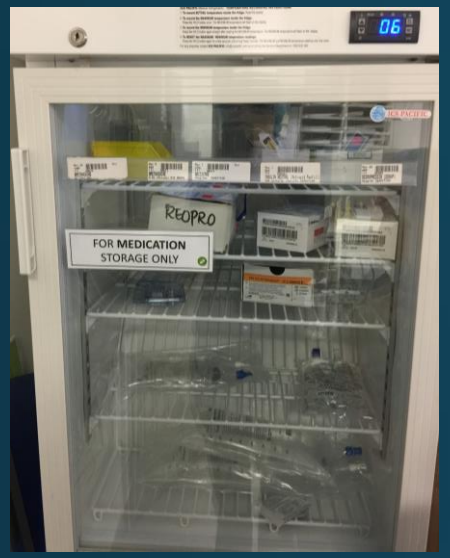
Preferred Term	All AEs		Treatment- Related AEs	
Total Subjects Treated	2526		2526	
Total Subjects with AEs	646	(25.6%)	193	(7.6%)
Fatigue	150	(5.9%)	4	(0.2%)
Headache	88	(3.5%)	50	(2.0%)
Dyspnoea	81	(3.2%)	3	(0.1%)
Chest pain	61	(2.4%)	8	(0.3%)
Flushing	41	(1.6%)	25	(1.0%)
Back pain	35	(1.4%)	23	(0.9%)
Nausea	35	(1.4%)	19	(0.8%)
Dizziness	25	(1.0%)	12	(0.5%)
Dysgeusia	21	(0.8%)	21	(0.8%)
Chest discomfort	18	(0.7%)	2	(<0.1%)
Pain NOS	15	(0.6%)	3	(0.1%)
Abdominal pain NOS	14	(0.6%)	3	(0.1%)
Hypertension NOS	14	(0.6%)	2	(<0.1%)
Diarrhoea NOS	13	(0.5%)	4	(0.2%)
Hypotension NOS	13	(0.5%)	4	(0.2%)
Injection site pain	12	(0.5%)	9	(0.4%)

Throat irritation, Pruritus, Increased Sweating	Uncommon (≥ 1/1,000, <1/100
Paresthesia, Syncope, Periperal Coldness, Cough, Dry Throat, Respiratory Distress, Dyspepsia, Erythema, Erythematous Rash, Rash, Urticaria, Arthralgia, Flank Pain, Neck Pain, Muscle Cramp, Pyrexia, Rigors, Abnormal Electrocardiogram	Rare (≥1/1,000, <1,000

CEUS – Is it suitable?

- Indications
  - Cardiac
  - Characterising liver and renal lesions
  - Other off label uses = gallbladder, pancreas, ovarian, endoleak, tumour thrombus
- Advantage over CT/MRI in special cases
  - Renal dysfunction
  - Iodine/Gadolinium allergy or intolerance
  - Reduce radiation burden (frequent follow-up)
  - Dynamic assessment
  - US guided procedures

TECHNIQUE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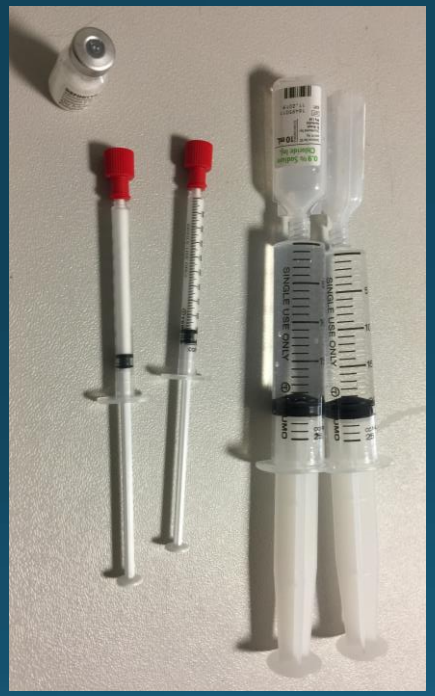
FOR MEDICATION
STORAGE ONLY


VIALMIX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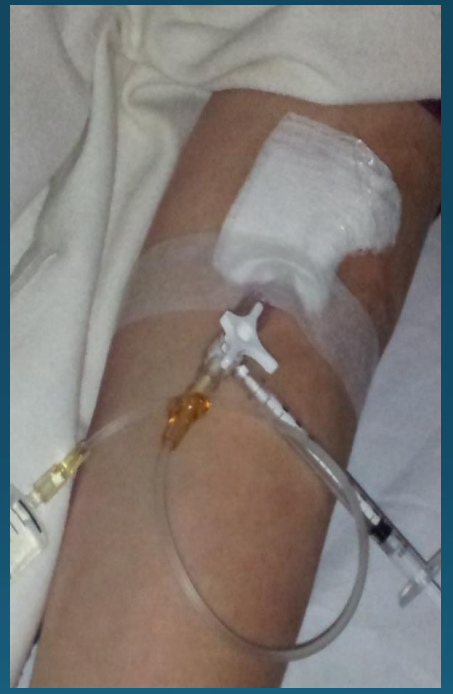
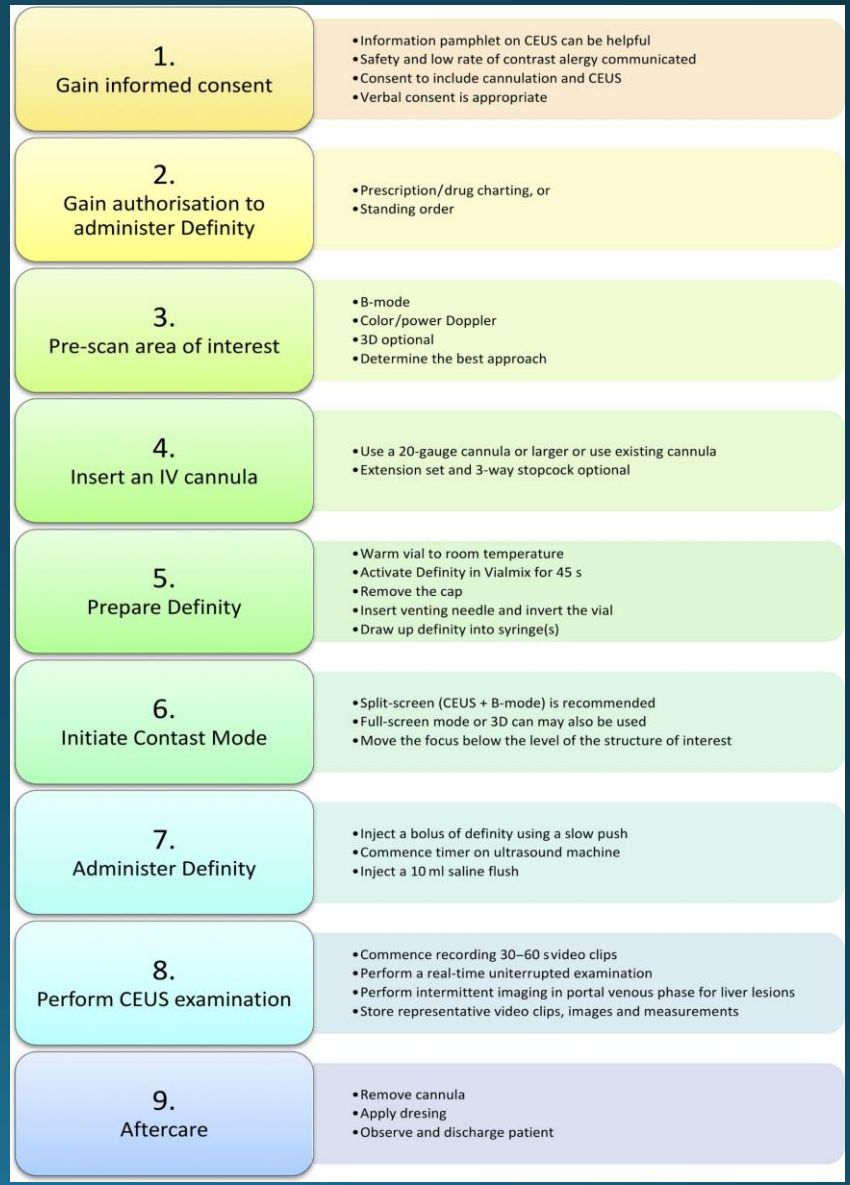



You can think a long time
about snuvs and their gloves.

CEUS – How do I do it?

- Radiologist / Sonographer Pre-Scan
  - Review imaging and referral
- Patient preparation
  - Consent, cannulation and expectations
- Contrast preparation and administration
  - Agitation, drawing-up and prescription
  - Each bolus 0.2-0.3mL with 15-20mL saline chaser
- Dynamic Assessment
  - Watch lesion live for phases
  - Pay attention to:
    - Morphology
    - Enhancement pattern
  - Use special techniques if applicable



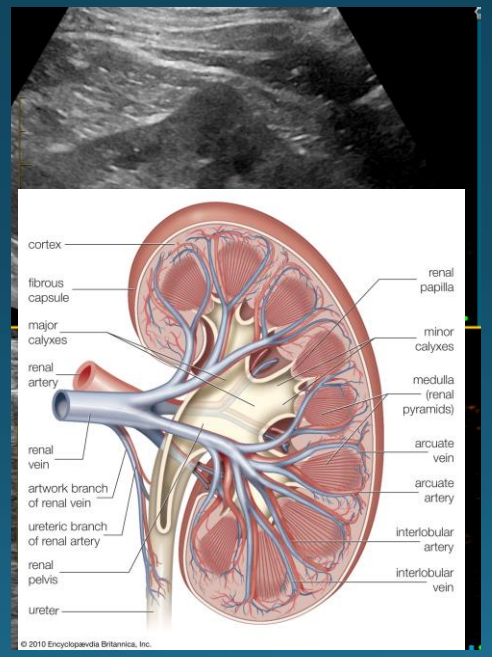
APPLICATIONS

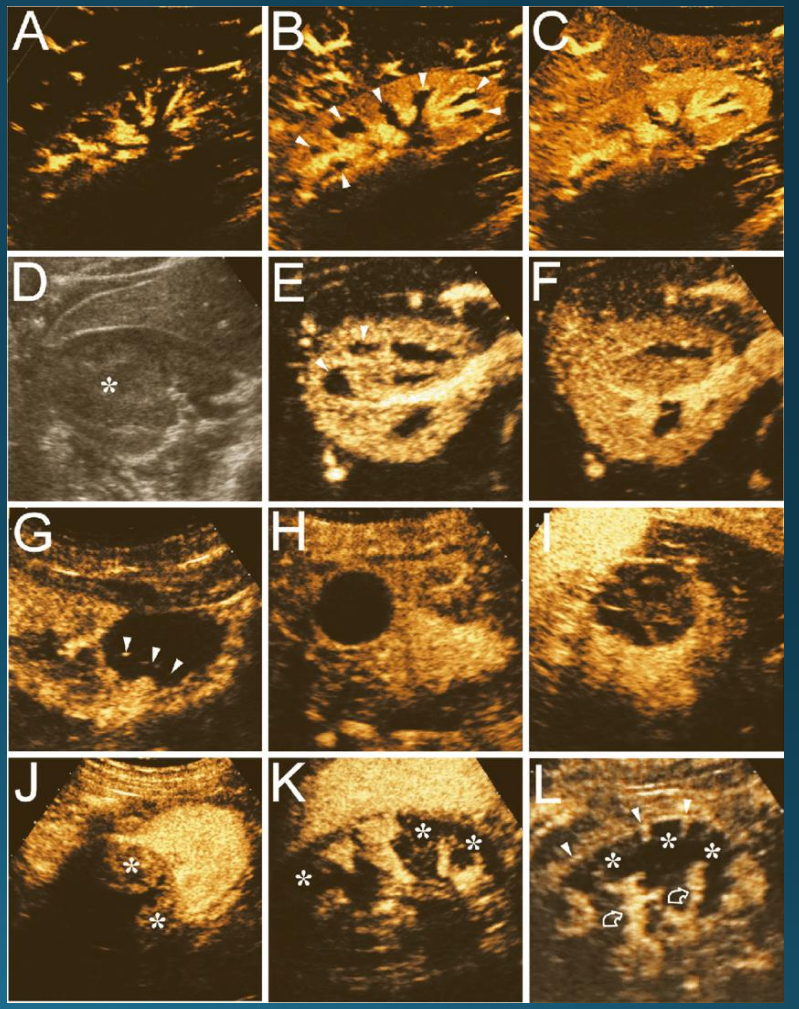
- Renal Applications
  - Normal enhancement patterns
  - Pseudo-lesions
  - Solid vs Cystic lesions
  - Classification of complex cysts lesions (CEUS-Bosniak)
  - Other
    - Pyelonephritis (nephronia vs abscess)
    - Intervention
    - Post-ablation monitoring

- Indications
  - Incidental Renal and Liver Lesion Characterisation
    - Targeted
      - Poor renal function
      - Contrast allergy
      - Problem solving
    - Opportunistic
      - Young
      - Point of care
      - Patient factors
  - Monitoring
    - Young
    - Requiring multiple studies
    - Treatment response
  - Guidance
    - Operative / IR planning
    - Live IR guidance

Renal – Normal Enhancement Patterns

- Phases
  - Hilar vessel phase
  - Cortical phase (10-15 seconds)
  - Medullary phase (45-120 seconds)
    - Outer medulla
    - Pyramids
  - No excretion to collecting system



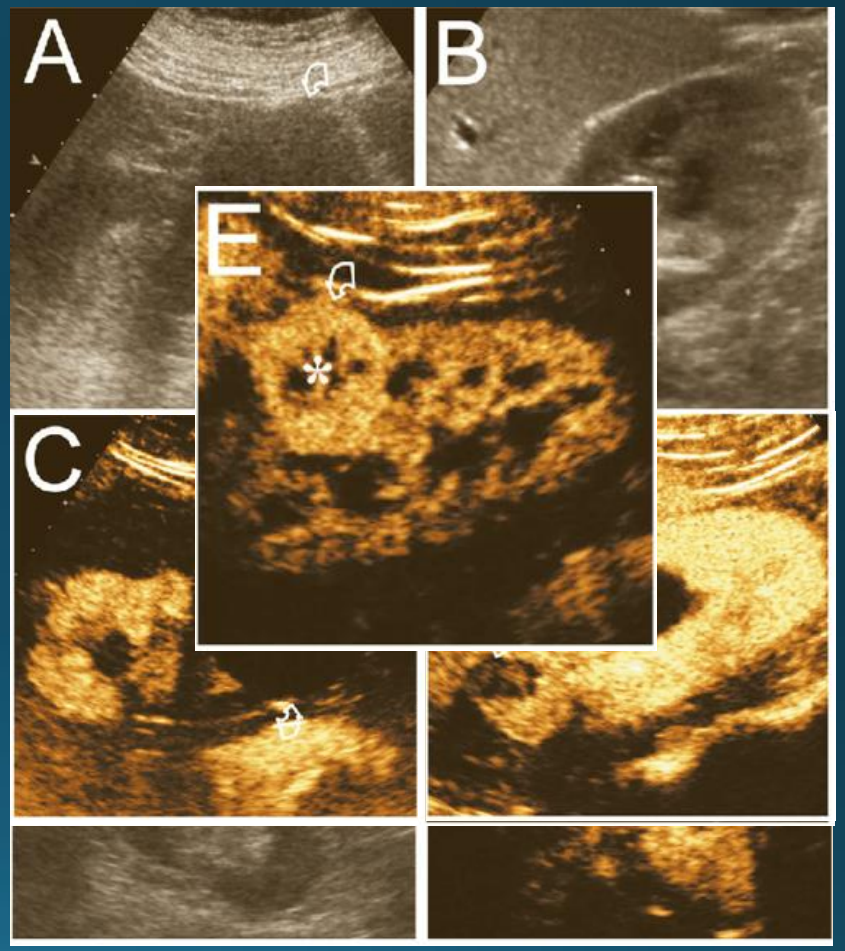


Contrast-enhanced ultrasound (CEUS) in nephrology: Has the time come for its widespread use? - ResearchGate.

Renal Pathology – Solid vs Cystic

- Standard Modalities
  - B-mode and Doppler US cannot reliably confirm/exclude a solid lesion
  - CT and MRI can be tricked out by complex cysts with debris, haemorrhage or minimally vascular components

- CEUS
  - Superior sensitivity (vs CT/MRI) for solid components
  - Some enhancement patterns are described for AML, oncocytoma, RCC (+ subtypes)
  - BUT cannot reliably differentiate between different renal tumours and RCC subtypes



Contrast-enhanced ultrasound (CEUS) in nephrology: Has the time come for its widespread use? - ResearchGate.

62 yo male

Previous left nephrectomy for RCC; very poor renal function.

CTs showing slow growing lesion right lower pole.

Cardiac implant incompatible with MRI.

Renal Pathology – Cystic Masses

- Complicated cystic lesions
  - CEUS more sensitive than CT in depicting cystic wall and septa vascularity
  - CEUS lower specificity but improved sensitivity and accuracy compared to MRI
- Bosniak
  - Malignancy risk stratification system
  - Classification originally CT, then later MRI and CEUS
  - CEUS has been shown to upgrade and downgrade compared to other techniques
  - In 2020, EFSUMB reviewed, redefined and standardised Bosniak-CEUS to take into account specifics of CEUS
- CEUS-Bosniak
  - Five classes of cysts

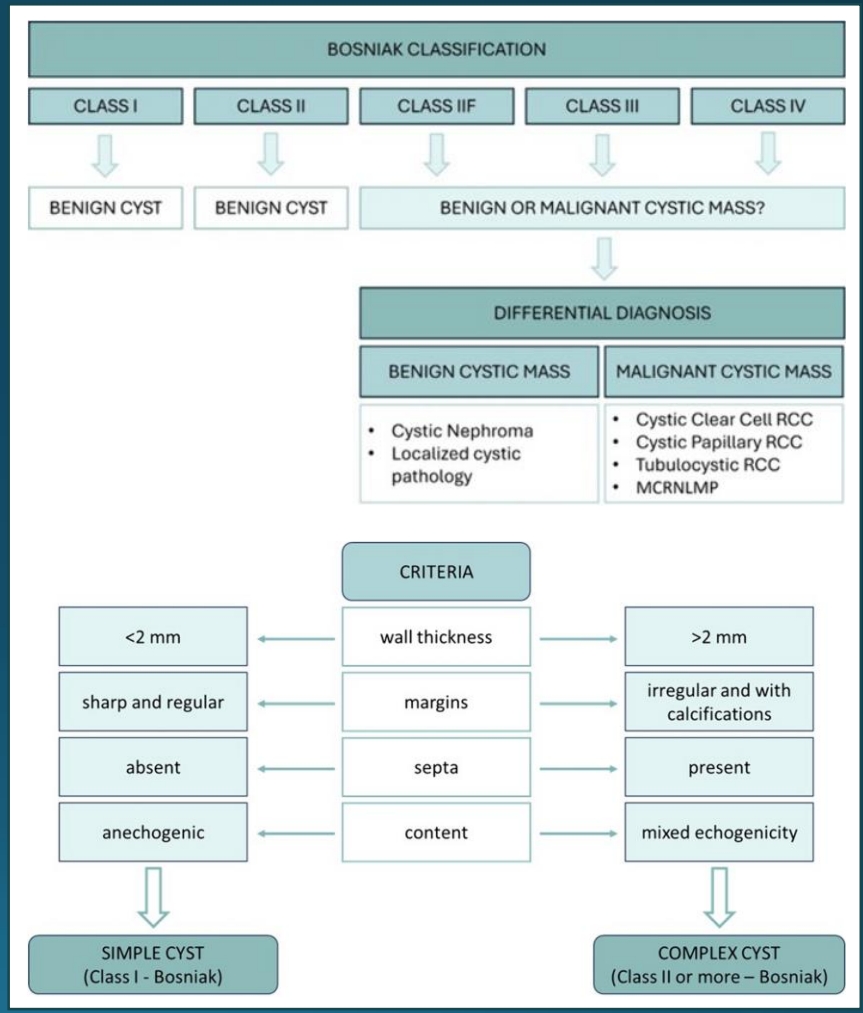


Image: Masino, JMU 2024 - CEUS in renal cystic lesions: an update

CEUS appearance	Bosniak score on multiparametric US
Thin wall without irregularities that show no enhancement on CEUS, or individual microbubbles running within tiny vessels in the wall	I
Thin wall and septa without irregularities showing no enhancement, or individual microbubbles running within tiny vessels in the wall and septa	II
Thin wall and septa without irregularities showing no enhancement, or individual microbubbles running within tiny vessels in the wall and septa	II
Multiple septa, thin or minimally thickened (2–3 mm). Smooth or minimally thickened wall	IIF
Thin septa without irregularities may be present, showing no enhancement, or individual microbubbles running within tiny vessels. Differentiation between non-enhancing and enhancing wall cannot be achieved	IIF
Enhancing smooth thick (≥ 4 mm) wall or septa, and/or enhancing irregular (> 3 mm) walls and/or septa. No nodules are seen	III
Enhancing smooth thick (≥ 4 mm) wall or septa, and/or enhancing irregular (> 3 mm) walls and/or septa. Enhancing soft-tissue protrusions, either nodules with obtuse margins (≥ 4 mm) or with acute margins of any size	IV

Image: EFSUMB 2020 Proposal for a Contrast-Enhanced Ultrasound-Adapted Bosniak Cyst Categorization

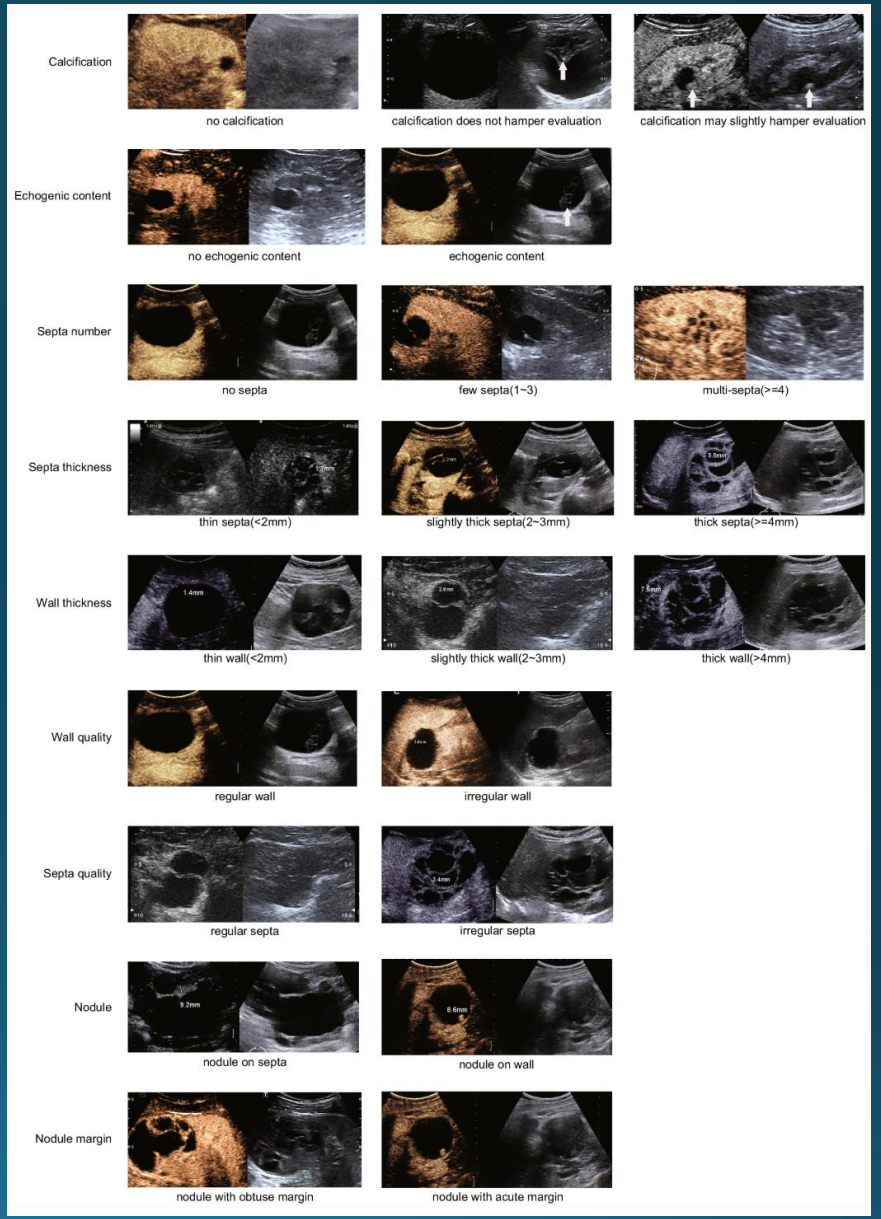


Image: Jin, Zhuang, Lin et al - CEUS Bosniak Classification: intra- and inter-rater agreement, confounding features, and diagnostic performance. Insights Imaging 2024

Active Surveillance of Renal Masses: The Role of Radiology

Nicola Schieda*, Satheesh Krishna*, Ivan Pedrosa, Samuel D. Kaffenberger, Matthew S. Davenport, Stuart G. Silverman

* N.S. and S.K. contributed equally to this work.

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Vol. 302, No. 1

Active surveillance versus initial surgery in the long-term management of Bosniak IIF–IV cystic renal masses

Lassi Luomala, Juhana Rautiola, Petrus Järvinen, Tuomas Mirtti & Harry Nisén

Scientific Reports **12**, Article number: 10184 (2022) | Cite this article

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Home / Vol 7 (December 30, 2022) / Active surveillance for complex renal cysts: is it time for III-F and IV-F?

Editorial Commentary: Surgery: Urological Surgery

Active surveillance for complex renal cysts: is it time for III-F and IV-F?

José Ignacio Nolazco[1,2^], Yuzhe Tang[1,3], Steven L. Chang[1,4]

[1]Division of Urological Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; [2]Servicio de Urología, Hospital Universitario Austral, Universidad Austral, Pilar, Argentina; [3]Urology Department, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing, China; [4]Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Boston, MA, USA

June 2019, Volume 212, Number 6

FOCUS ON: Genitourinary Imaging
Original Research

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Active Surveillance of Small (< 4 cm) Bosniak Category 2F, 3, and 4 Renal Lesions: What Happens on Imaging Follow-Up?

Hiram Shaish[1], Firas Ahmed[1], Jessica Schreiber[2] and Nicole M. Hindman[3]

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Citation: American Journal of Roentgenology. 2019;212: 1215-1222. 10.2214/AJR.18.20758

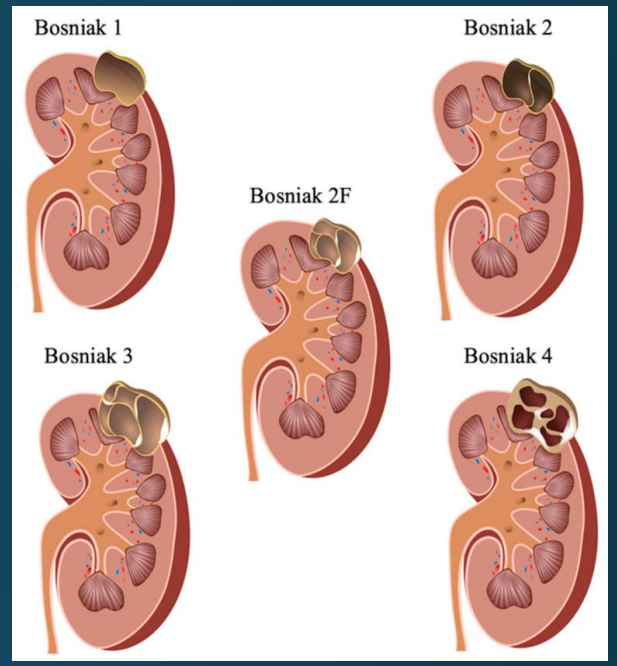


Image: Rubenthaler, Cancers (2020) - CEUS for Follow-up of Bosniak 2F Lesions

Bosniak 1 or 2	Bosniak 3	Bosniak 4

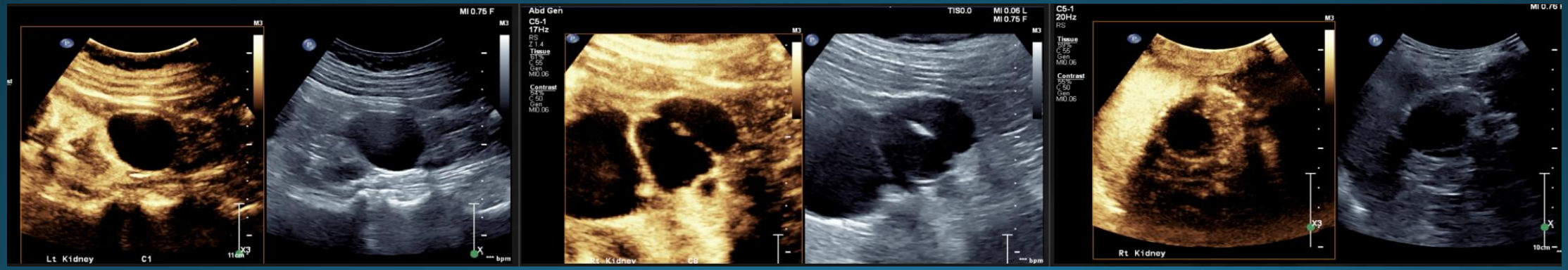
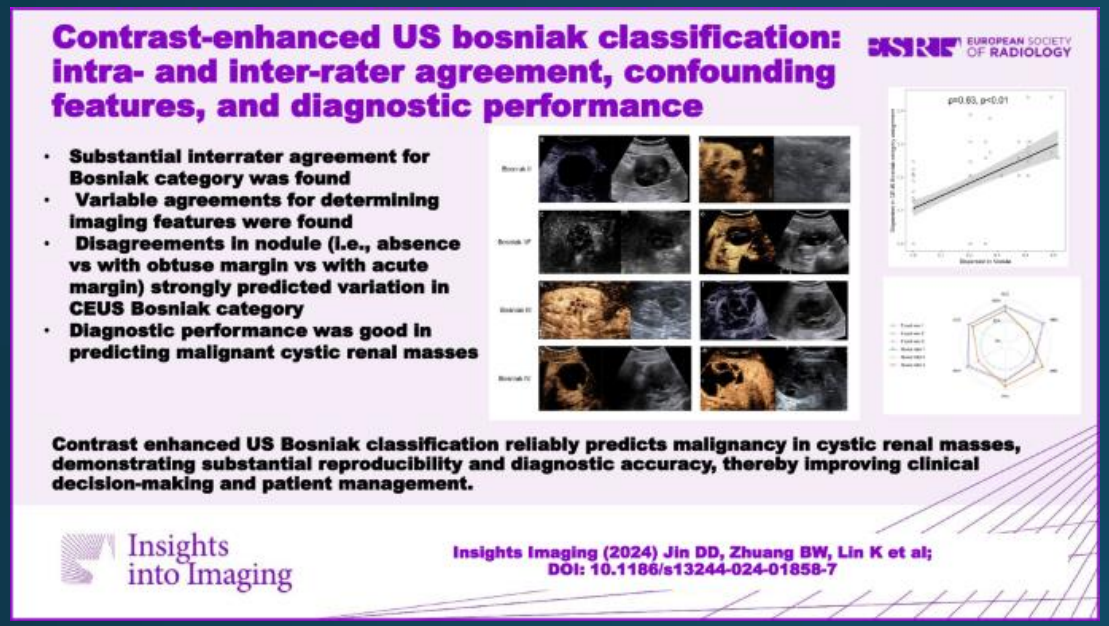
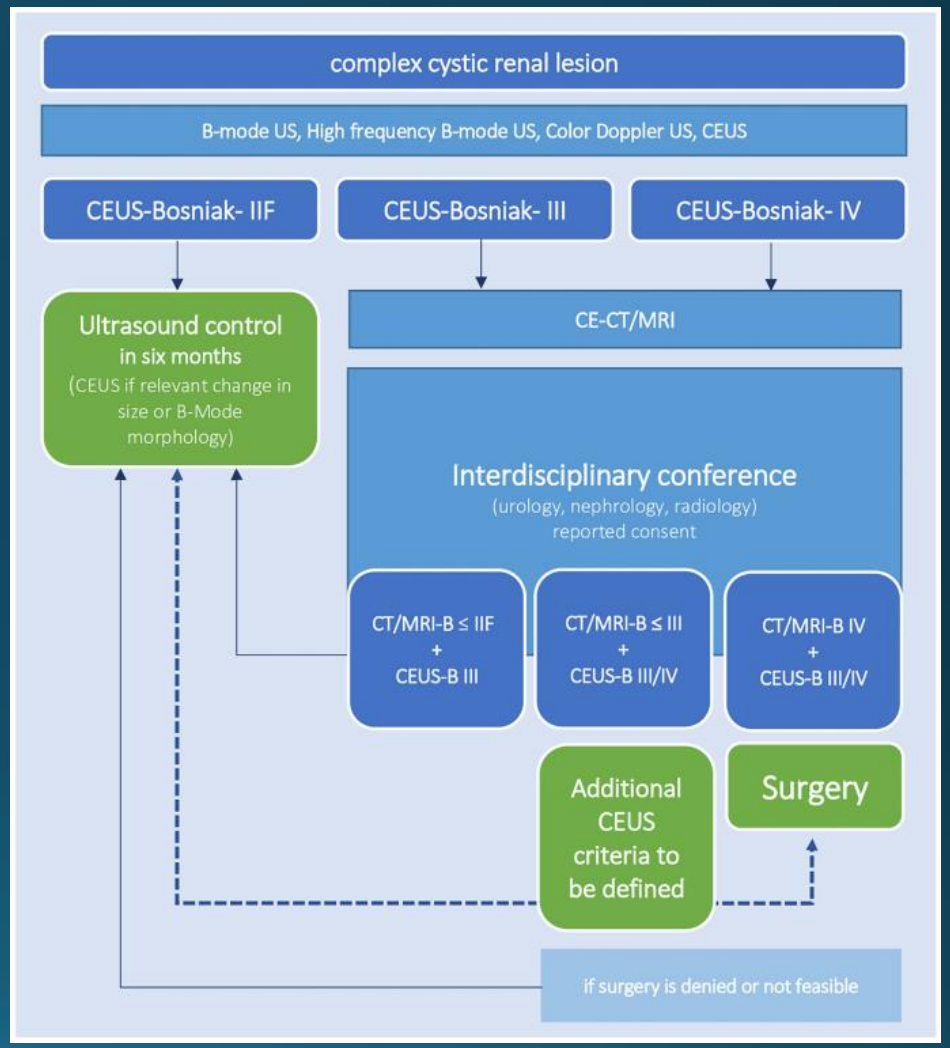
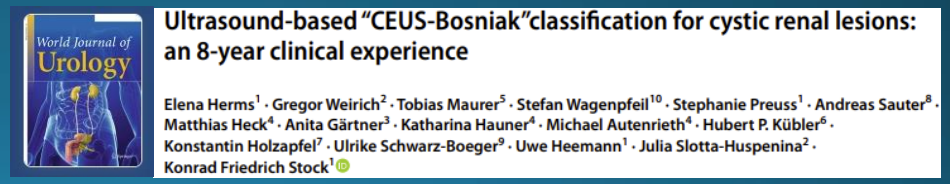


Image: Martin Necas, New Zealand



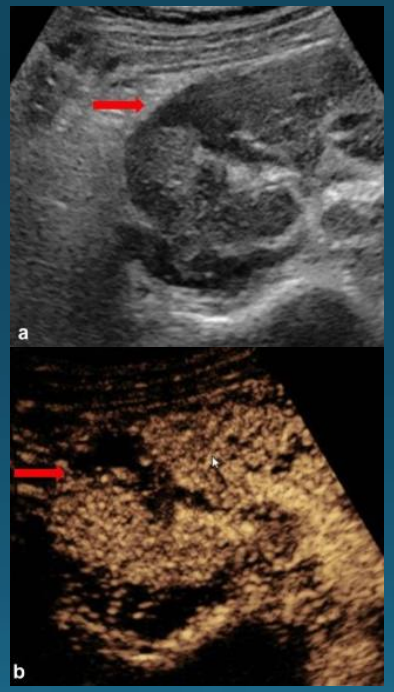


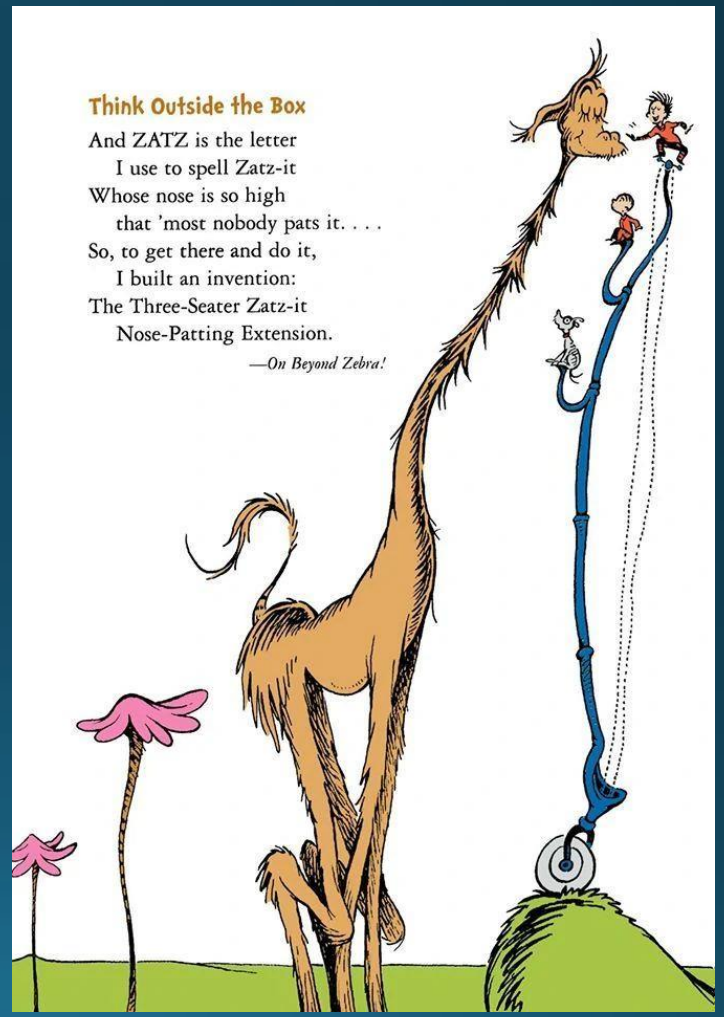
- CEUS-Cystic Renal Lesion Evidence
  - High sensitivity (many studies including *Cantisani et al 2017*)
  - Some studies showing superiority over CT (*Clevert et al 2020, Xu et al 2018*)
  - Strong CEUS-Bosniak histopath correlation (*Herms et al 2024*)
  - Long-term surveillance advantage due to access/no radiation; particularly Bosniak IIF, given long-term stability of these lesions (*Wei et al 2022*)



Renal Pathology – Other Uses

- Inflammatory
  - Pyelonephritis/lobar nephronia
  - Abscess
- Vascular
  - Renal ischaemia
    - hilar/branch vessel and cortical absent
    - segmental, unilateral
  - Cortical necrosis
    - preserved hilar/branch vessels
    - cortical perfusion absent
    - diffuse, bilateral
- Renal Transplant Evaluation
- Intervention
  - Guiding / targeting therapy
  - Post-ablation follow-up





Summary – How do I interpret my findings?

- Known normal enhancement pattern
- Identify normal variants and pseudolesions
  - Column of Bertin, dromedary hump
  - Scarring
- Cystic lesions
  - Differentiate from solid
  - Use Bosniak concepts
- Solid lesions
  - Angiomyolipoma
  - Oncocytoma, RCC, Lymphoma
  - Identify regions of necrosis
- Other
  - Lobar nephronia vs abscess
  - Hypoperfusion, ischaemia/infarct

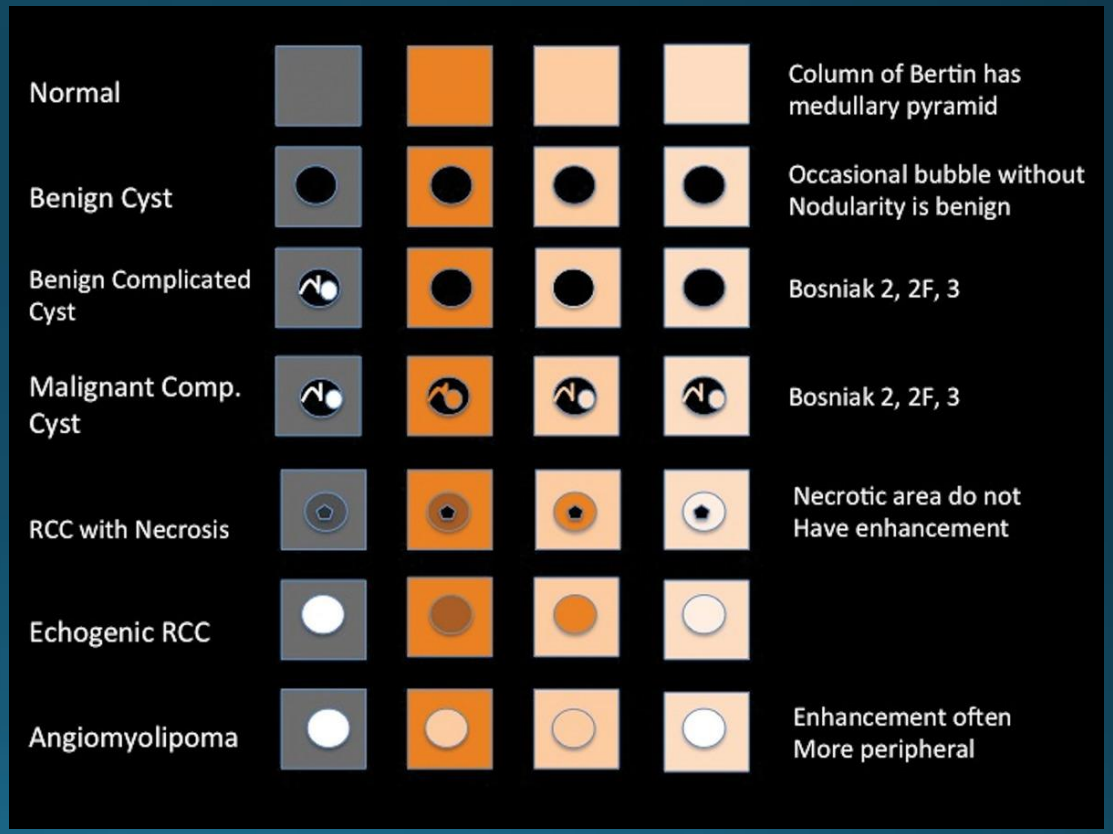
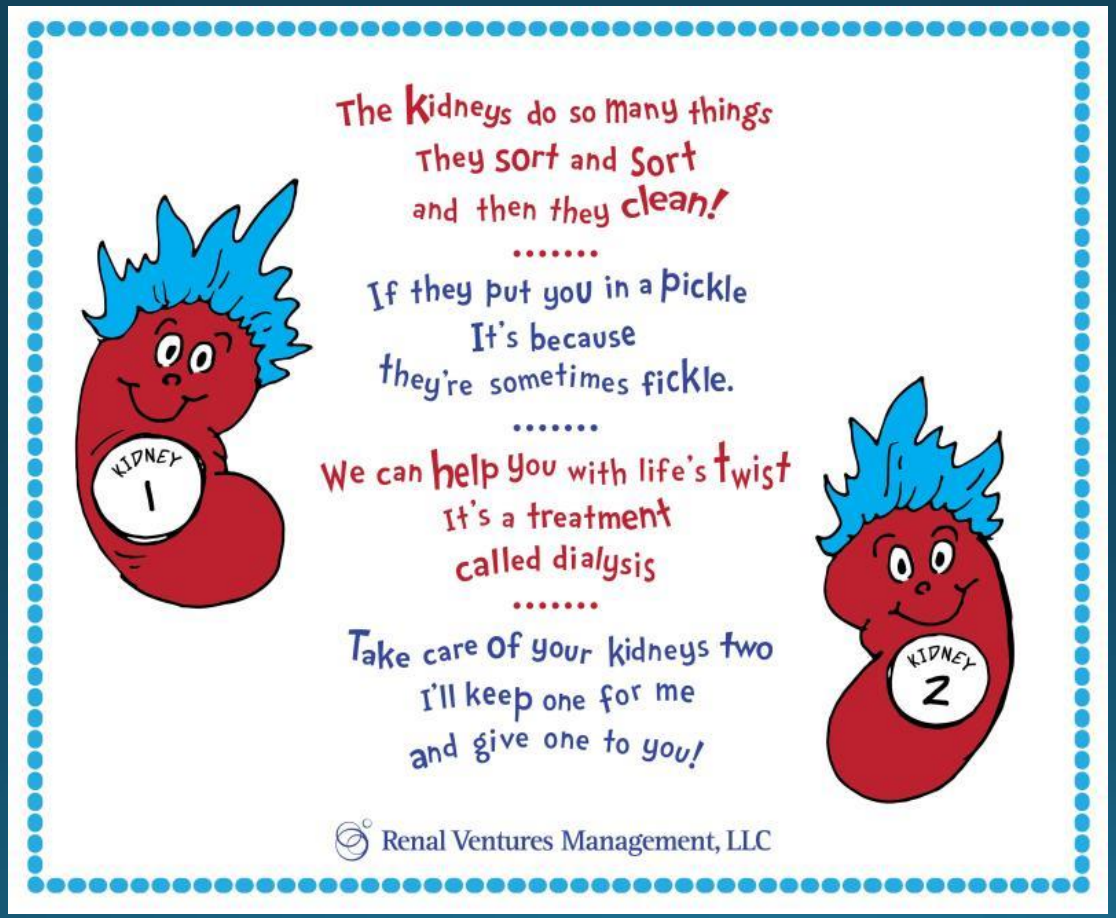


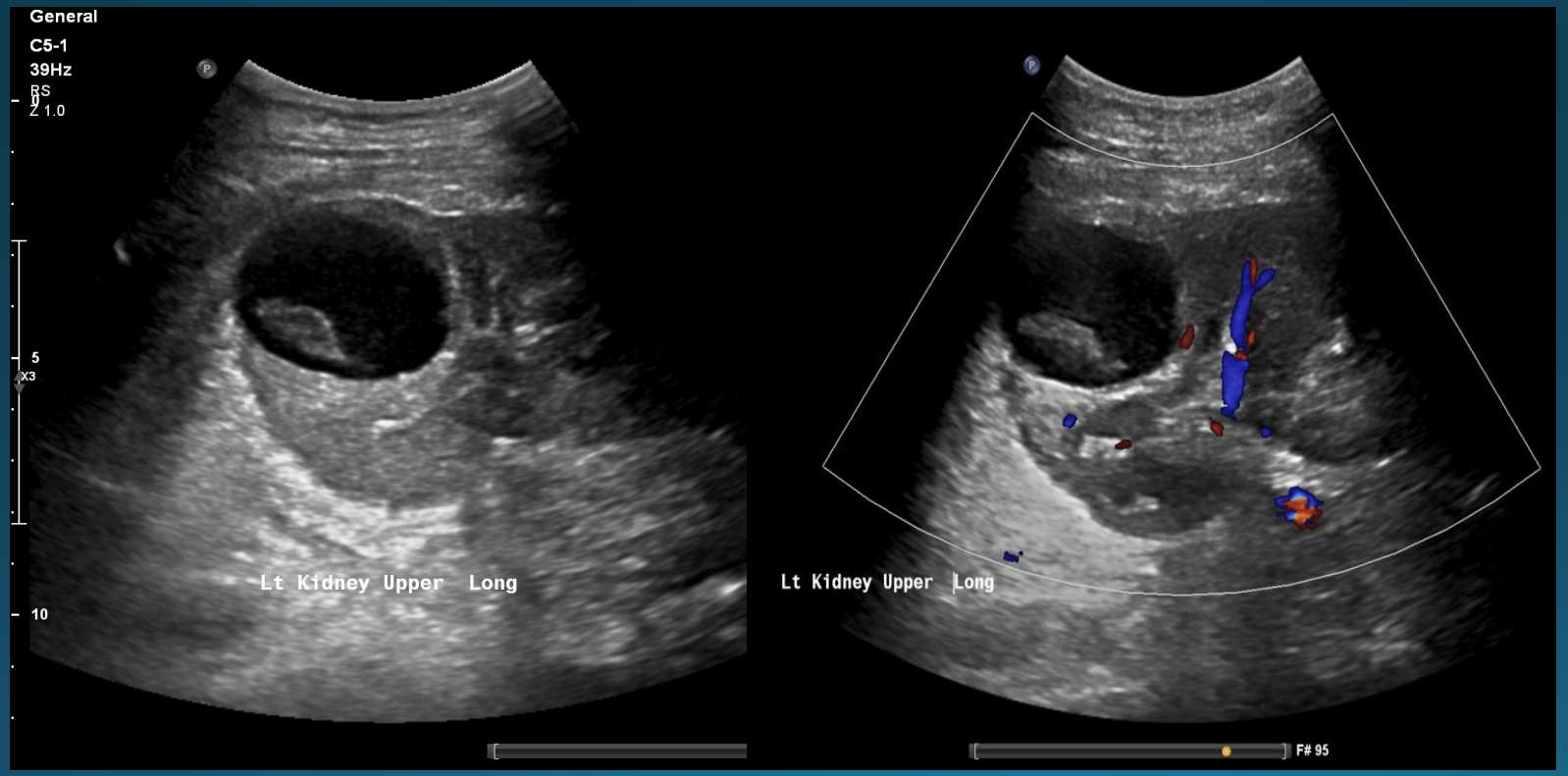
Image: Richard G Barr Northeast Ohio Medical University

ADDITIONAL CASES



Case 1 – ZF

- 23yo Female
- Fever, dysuria, routine US performed for ?pyelonephritis

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DOB: 07/04/1997
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TIS0.2
MI 1.1
Lt Kidney Upper Long
M4
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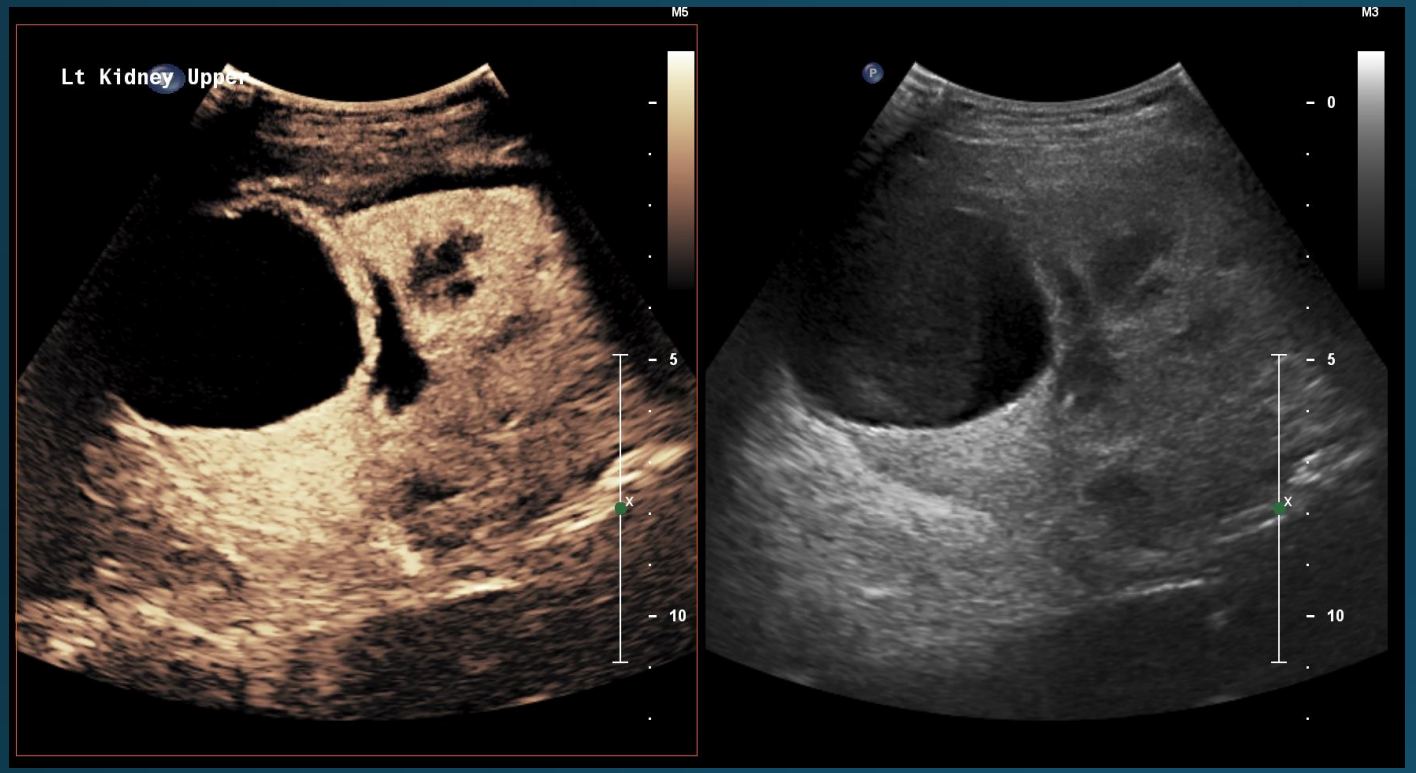
5
10
X4
F#327



Dx = complicated cyst (CEUS-equivalent Bosniak II-F)

CEUS appearance	Bosniak score on multiparametric US
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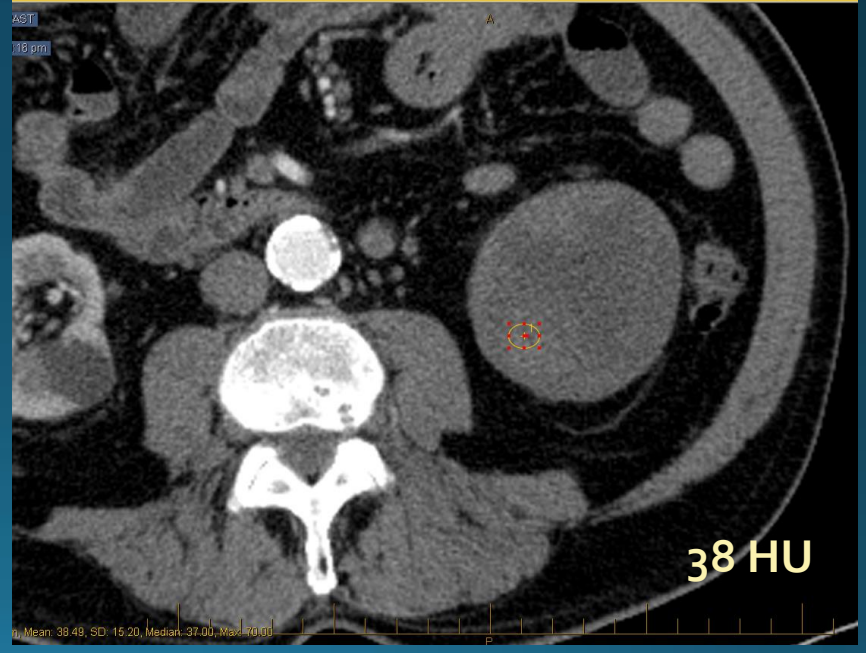
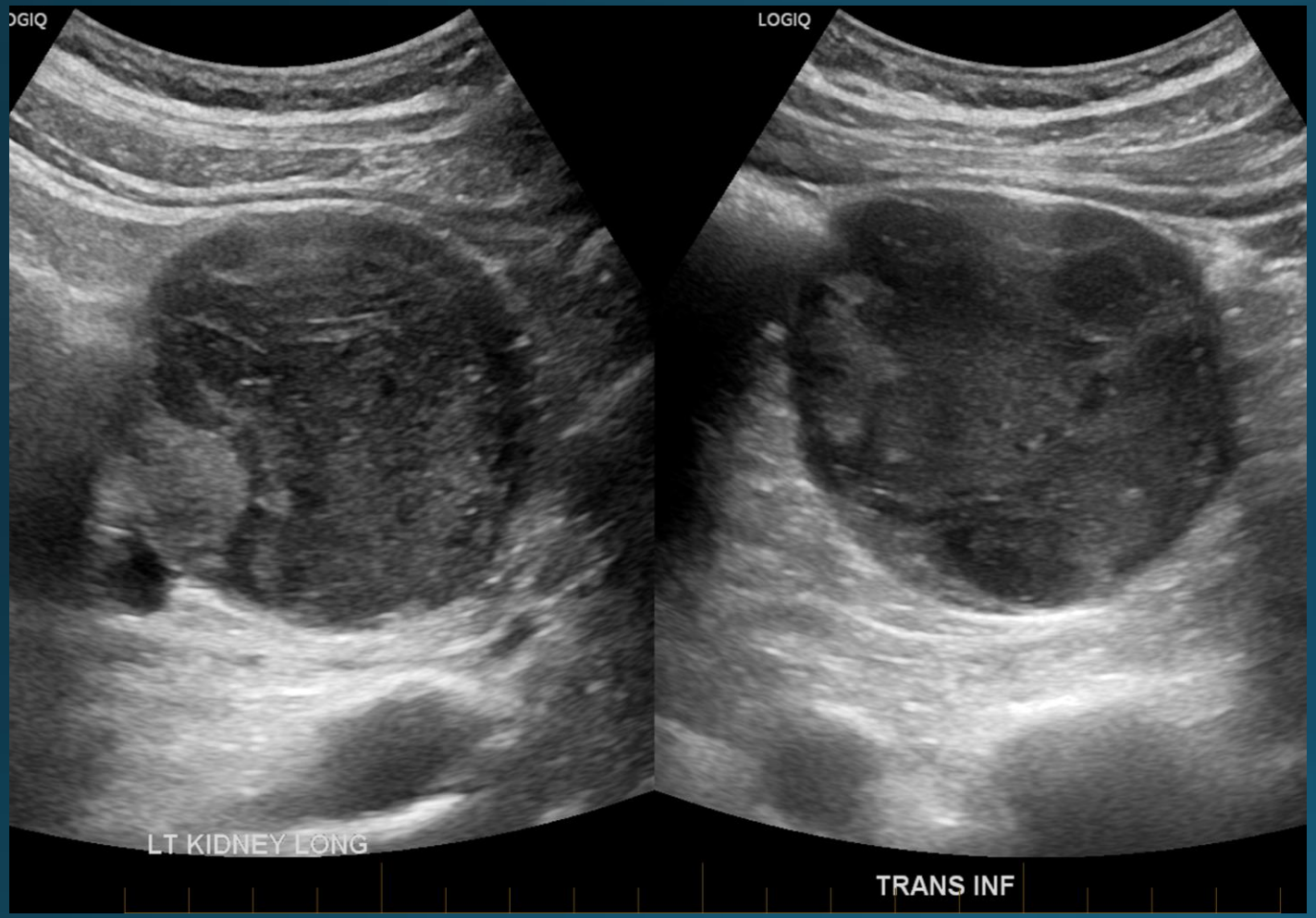
Enhancing smooth thick (≥ 4 mm) wall or septa, and/or enhancing irregular (> 3 mm) walls and/or septa. Enhancing soft-tissue protrusions, either nodules with obtuse margins (≥ 4 mm) or with acute margins of any size	IV

Case 2 – JR

- 70yo Male
- Previous right partial nephrectomy for renal tumour. New lesion seen on CT but indeterminate.

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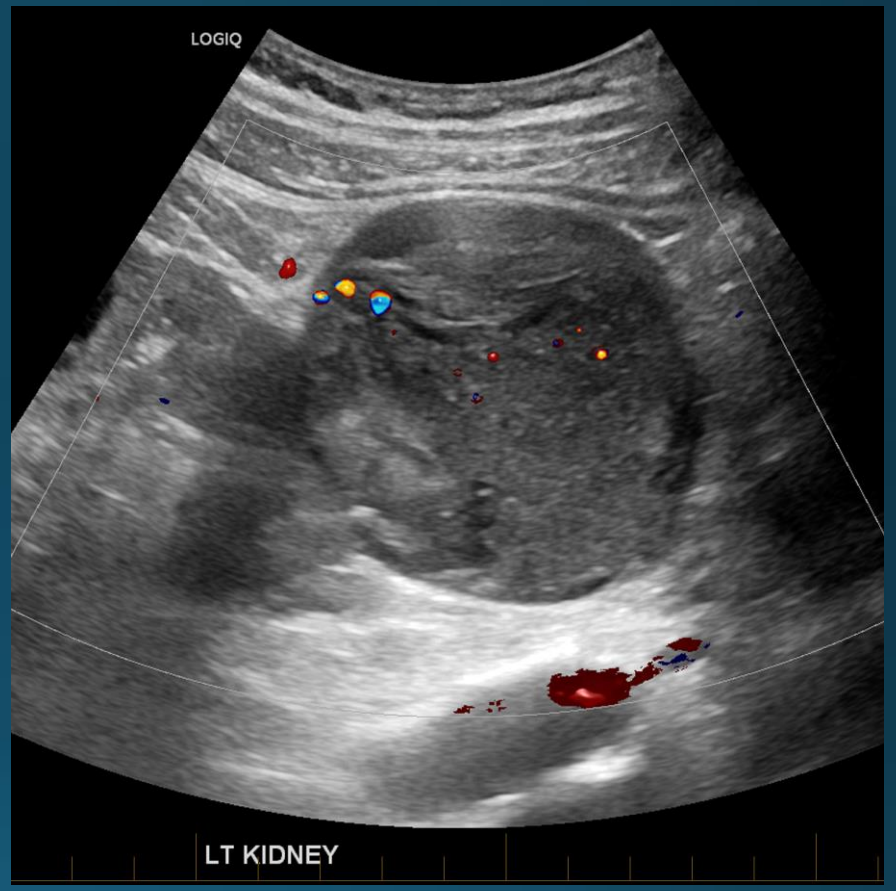
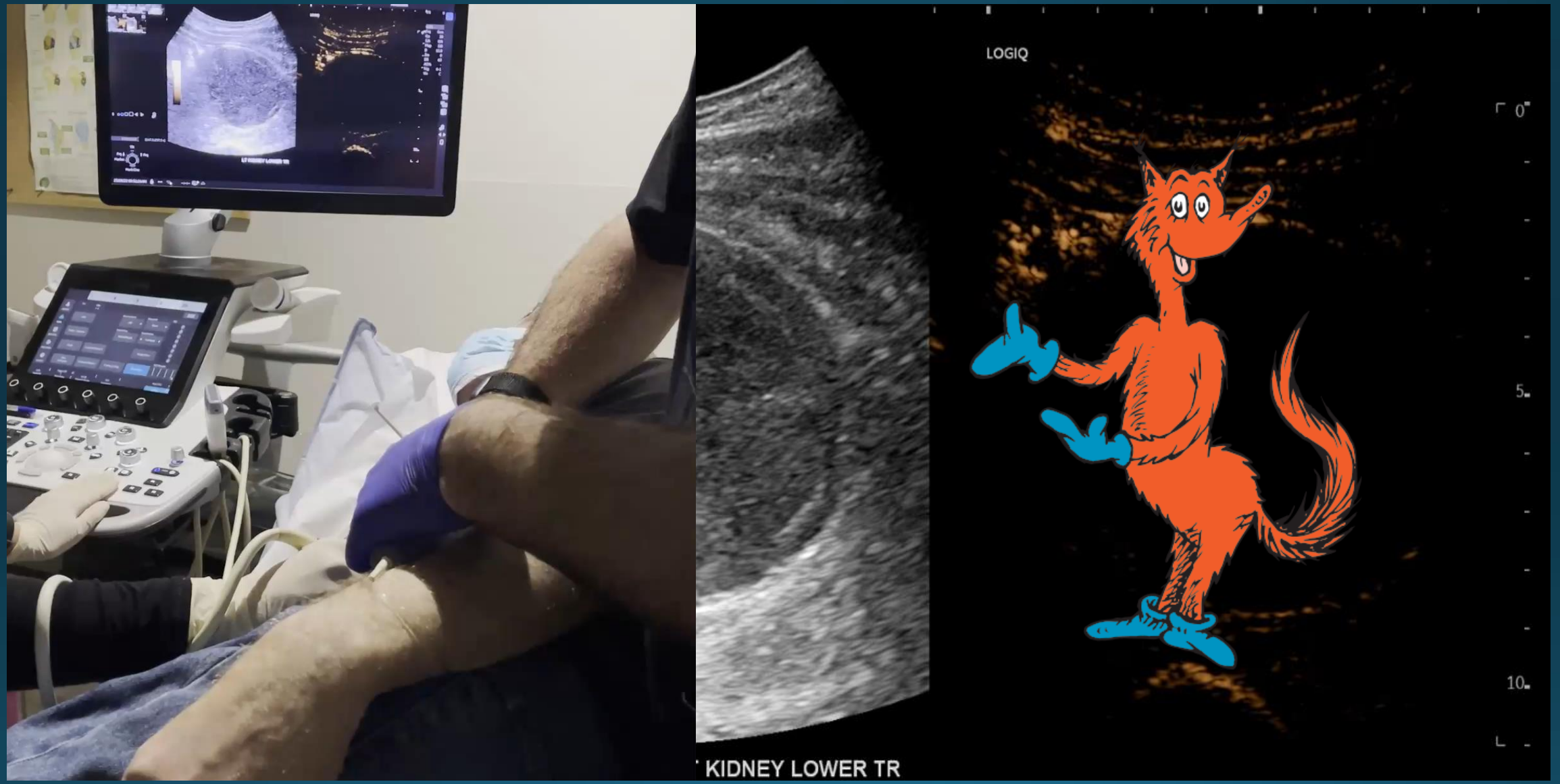

LOGIQ
LT KIDNEY



Dx = Bosniak IV lesion, highly likely tumour

CEUS – Breaking through the Bubble

- Advantages of CEUS
  - Safety = no radiation, not nephrotoxic, low risk
  - Indications = patients with renal dysfunction, unable to lie flat or keep still, portable, point of care
  - Realtime, multiple passes, guide intervention
  - Cost effective = cheaper than CT/MR
  - Diagnostic accuracy
- What Do You Need Next?
  - Machine capable of CEUS
  - Radiologists and Sonographers trained to perform
  - Vendors and Definity will help set up and train
  - 5-10min Radiologist time, 30min bookings

Ultrasound machine:
- Non-linear contrast imaging mode
- 30–60 s video clips
- Optional = 3D capability, fusion capability

Equipment:
- 20-gauge cannula
- Needle-free valve
- 20-ml saline flush
- 18-gauge blunt needles (no filter)
- 1-ml syringes
- Extension set
- 3-way Stopcock

Stock of Definity® contrast agent:
- Refrigerator
- Definity®
- Vialmix activator

Resuscitation equipment

CEUS – References and Reading

- *How to set-up and perform contrast-enhanced ultrasound* - Necas 2019 - Australasian Journal of Ultrasound in Medicine - Wiley Online Library
- *How to perform Contrast-Enhanced Ultrasound* - Dietrich 2018 - Ultrasound International Open
- *How to Develop a Contrast-Enhanced Ultrasound Program* - Barr 2017 - Journal of Ultrasound Medicine
- *Contrast-enhanced US for the Interventional Radiologist: Current and Emerging Applications* – Malone 2020 – Radiographics
- EFSUMB 2020 Proposal for a Contrast-Enhanced Ultrasound-Adapted Bosniak Cyst Categorization
- CEUS LI-RADS v2017
- Radiopaedia: Contrast-enhanced ultrasound
- StatDx: Contrast-enhanced ultrasound