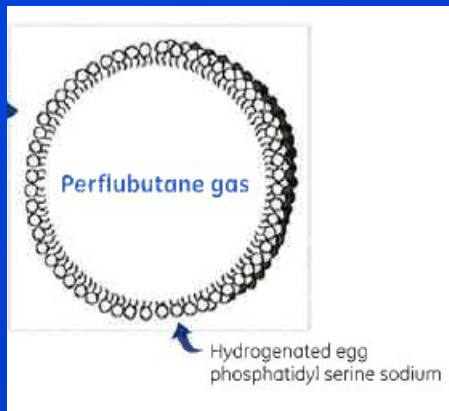




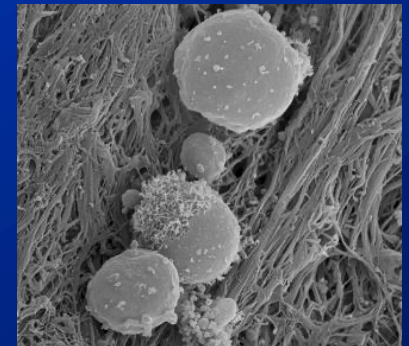
# Nasjonalt Senter for Gastroenterologisk Ultrasonografi

National Centre for Ultrasound in Gastroenterology  
Haukeland University Hospital, Bergen, Norway

## Contrast-Enhanced Ultrasound CEUS



Odd Helge Gilja  
Professor, MD, PhD  
Department of Clinical Medicine  
University of Bergen





# The Ultrasound Tool-box

- Ultrasound of liver

- B mode

- B-Flow

- Doppler

- Color Doppler

- Pulsed Doppler

- Elastography

- Strain imaging

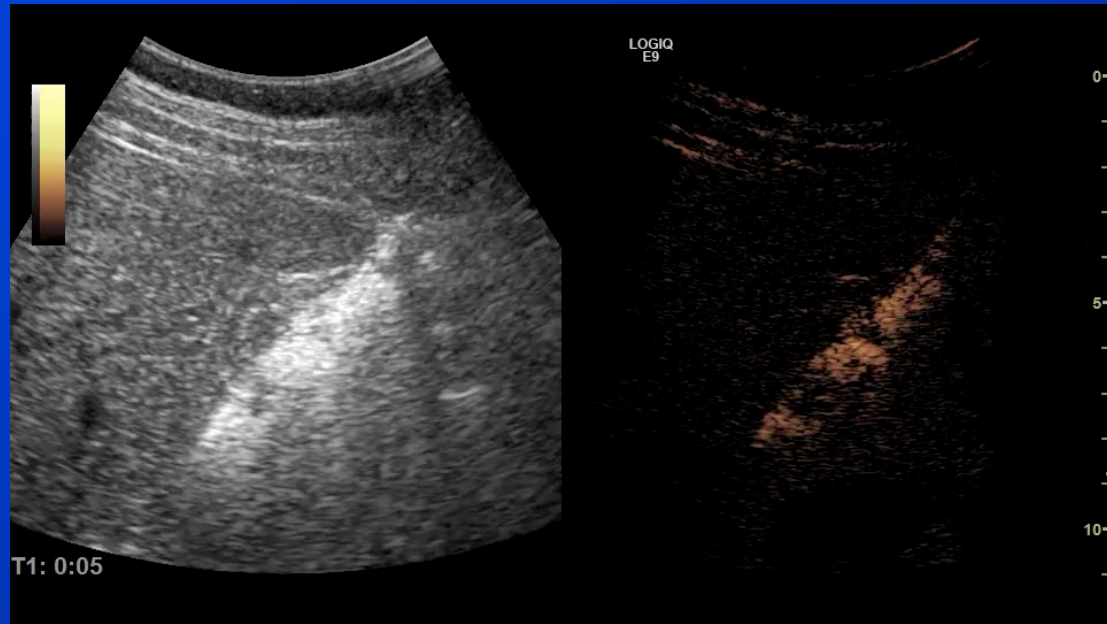
- Shear wave

- **Contrast-US (CEUS)**

- US-guided liver biopsy (Menghini and Pistol)

- US-guided ablation techniques

- Sonoporation therapy

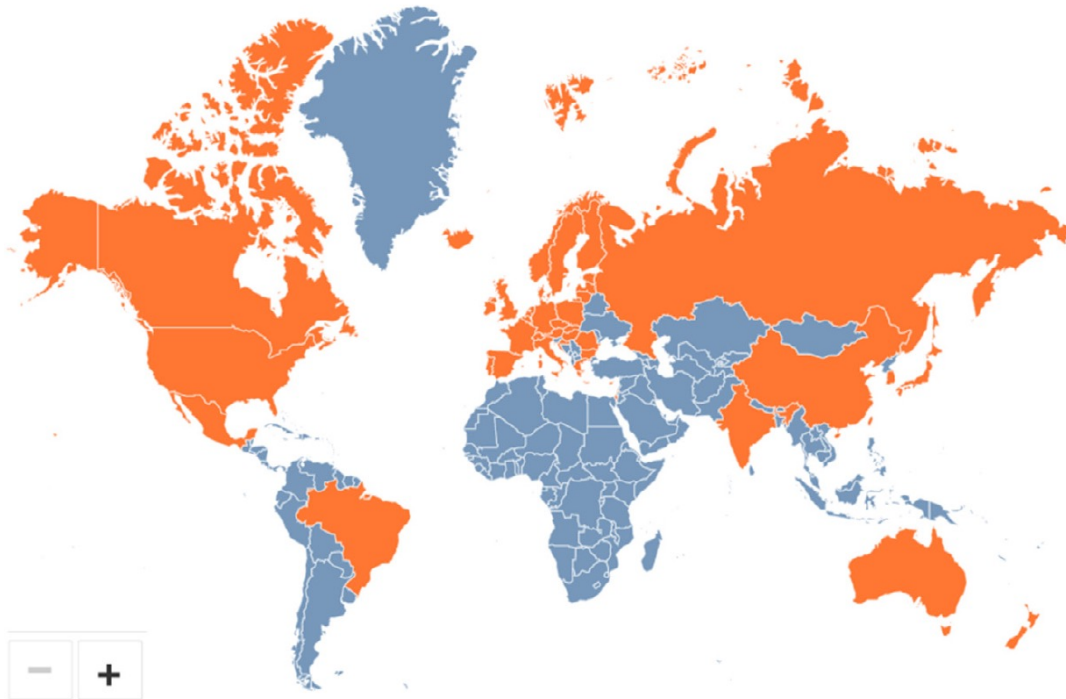






# World map of CEUS

## Global Contrast-Enhanced Ultrasound (CEUS)

*Click on any country shaded in orange to see the commercially available agent(s).*



-  (Agent(s) commercially available)
-  (No agent commercially available at this time)



# Available agents for liver CEUS

- Definity/Luminality (Lantheus Medical Imaging, Inc., North Billerica, MA, USA)
- SonoVue/Lumason (Bracco Suisse SA, Geneva, Switzerland)
- Optison (GE Healthcare AS, Oslo, Norway)
- Sonazoid (GE Healthcare AS, Oslo, Norway)



# New CEUS guidelines 2020



ELSEVIER



Ultrasound in Med. & Biol., Vol. 46, No. 10, pp. 2579–2604, 2020  
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0301-5629/\$ - see front matter

<https://doi.org/10.1016/j.ultrasmedbio.2020.04.030>

## ● Review Article

### GUIDELINES AND GOOD CLINICAL PRACTICE RECOMMENDATIONS FOR CONTRAST-ENHANCED ULTRASOUND (CEUS) IN THE LIVER—UPDATE 2020 WFUMB IN COOPERATION WITH EFSUMB, AFSUMB, AIUM, AND FLAUS

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XIAOYAN XIE,<sup>¶¶¶¶¶¶</sup> and RONGQIN ZHENG<sup>|||</sup>



# World-wide team-work

- **38 authors !**
  - 19 were from 9 European countries representing EFSUMB
  - 13 from China, Japan, Korea and India representing AFSUMB
  - 5 from the USA representing AIUM
  - 1 from MASU
  - 1 from FLAUS
- **38 recommendations were voted upon**



# Is CEUS safe?

## **RECOMMENDATION 1**

Intravenous use of UCAs in adult populations is safe (LoE 2) (Pro 28, Abs 0, Against 0).

## **RECOMMENDATION 2**

Intravenous use of UCAs in pediatric populations is safe (LoE 3) (Pro 28, Abs 0, Against 0).

## **RECOMMENDATION 3**

Intracavitary use of UCAs is safe (LoE 2) (Pro 27, Abs 1, Against 0).



# Before you inject...

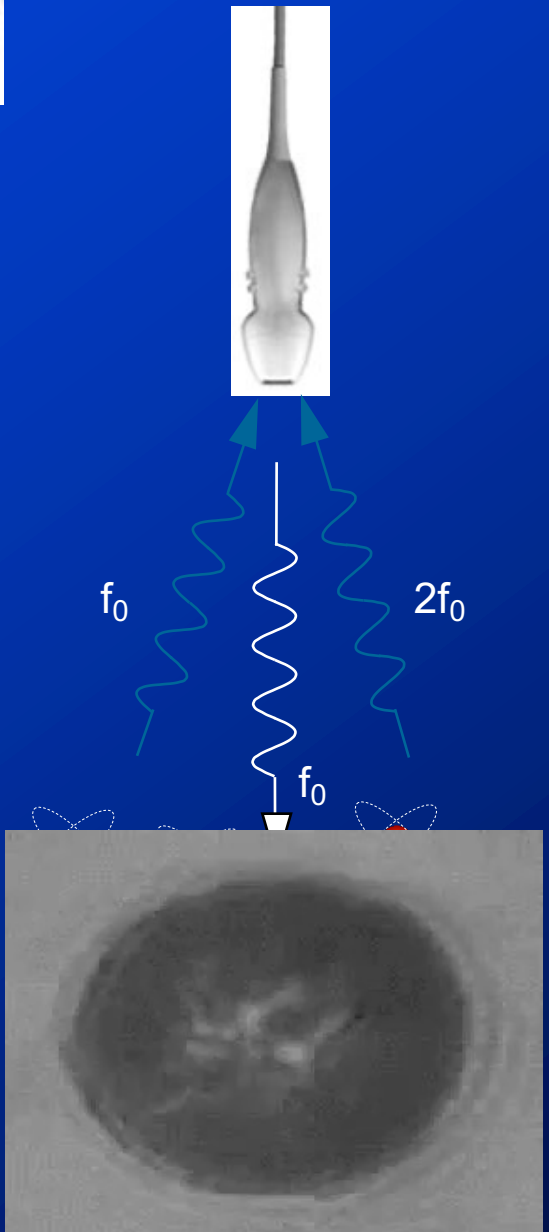
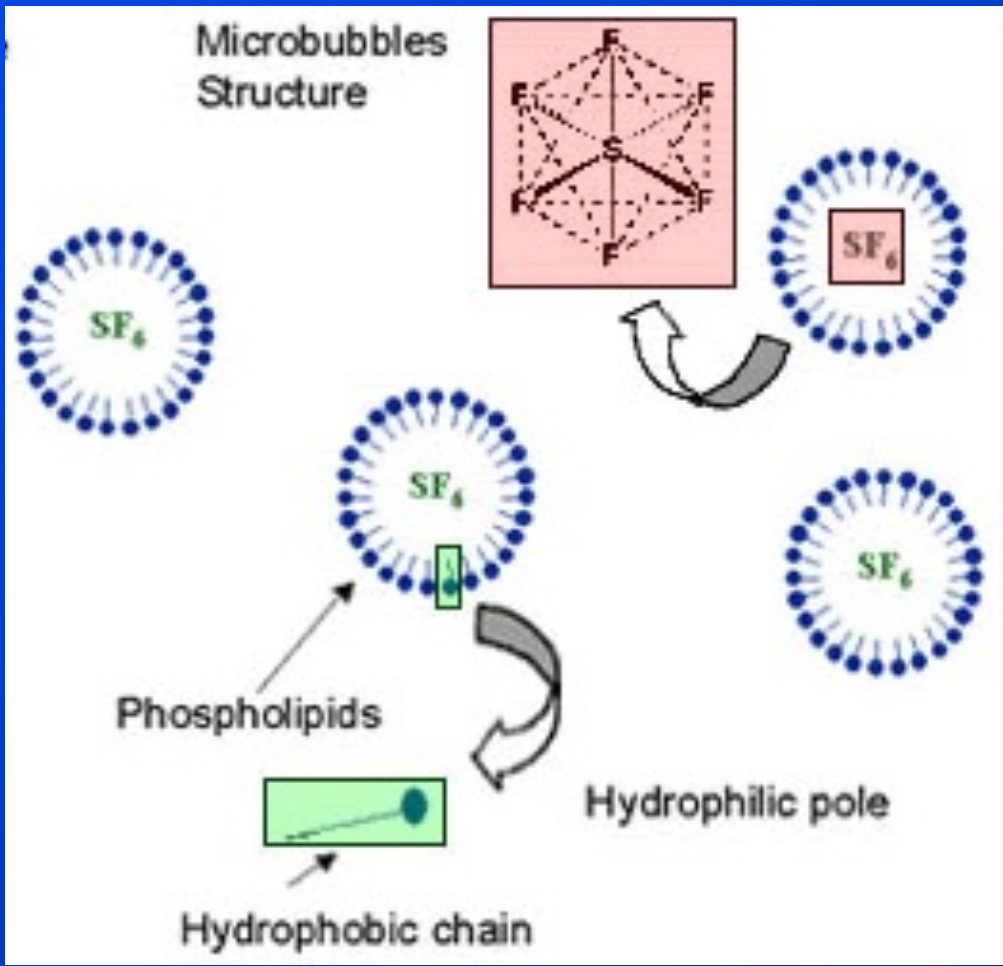
## RECOMMENDATION 37

Appropriate dose of contrast agent based on lesion location, patient factors and sensitivity of US scanner as well as imaging with appropriate low mechanical index should be used to produce high quality CEUS images (LoE 5, strong recommendation) (Pro 26, Abs 2, Against 0).

### Dosing of SonoVue:

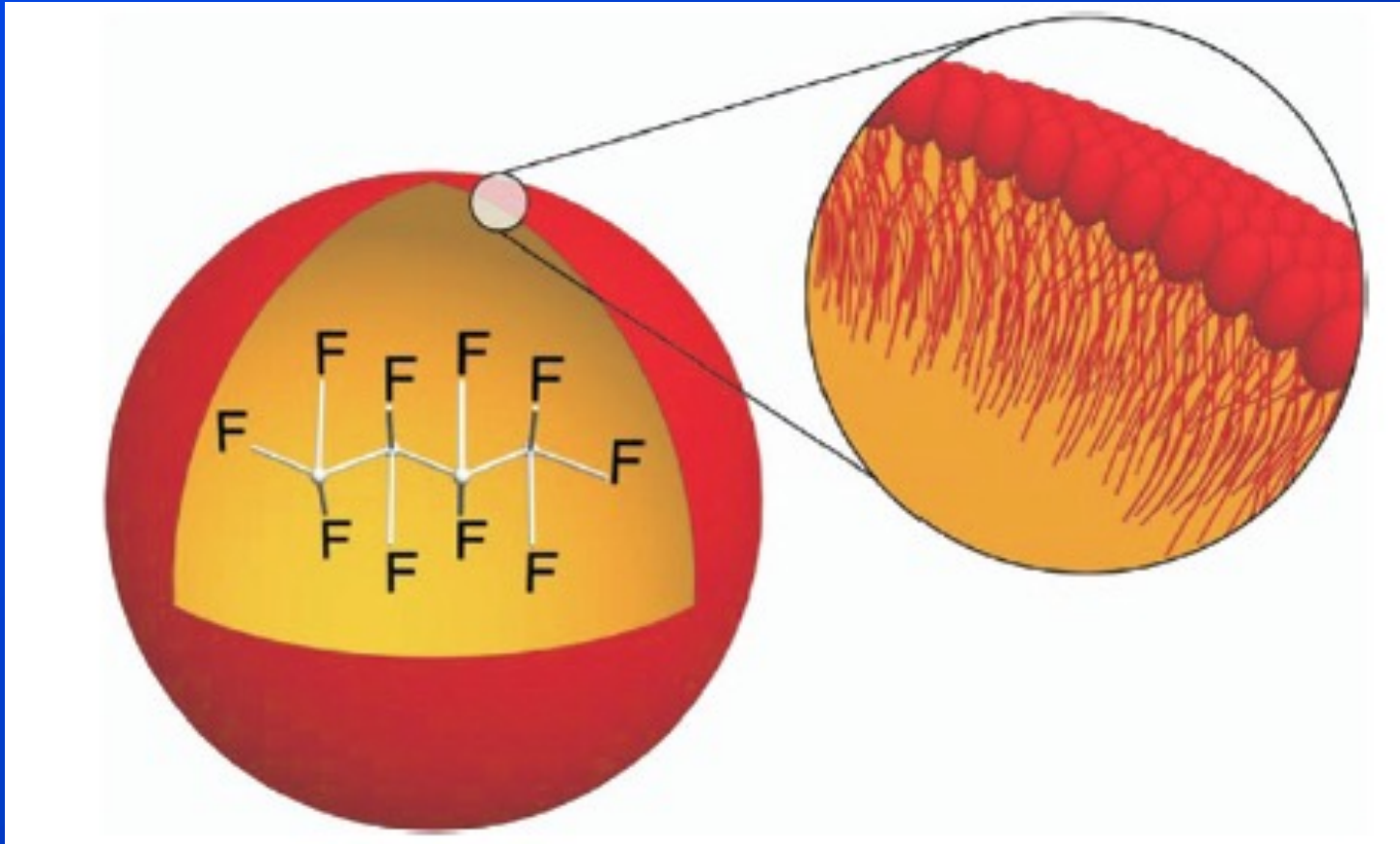
- Liver 2,4 ml
- Pancreas, kidneys, spleen 1,2 ml
- Intestine (high-f.) 4,8 ml
- Intra-cavitary 1-3 drops in 20 ml 0,9 %saline







# Sonazoid



- Membrane is hydrogenated egg phosphatidylserine sodium (HEPSNa)
- The gas is perfluorobutane (PFB)



# Fine tuning the Instrument by adjusting the MI



- Non-linear response from microbubbles is based on two different mechanisms:
- non-linear response from microbubble oscillations at low acoustic pressure, chosen to minimize disruption of the microbubbles. "Low MI" Imaging.
  - high MI (energy) broadband non-linear response arising from microbubble disruption.



# 3 Phases of Liver Perfusion

- Arterial phase
  - 0-30 sec.
- Portal phase
  - 30-120 sec.
- Sinusoidal phase (Parenchymal)
  - 2-4(5) min
- Postvascular phase
  - 6-30 min



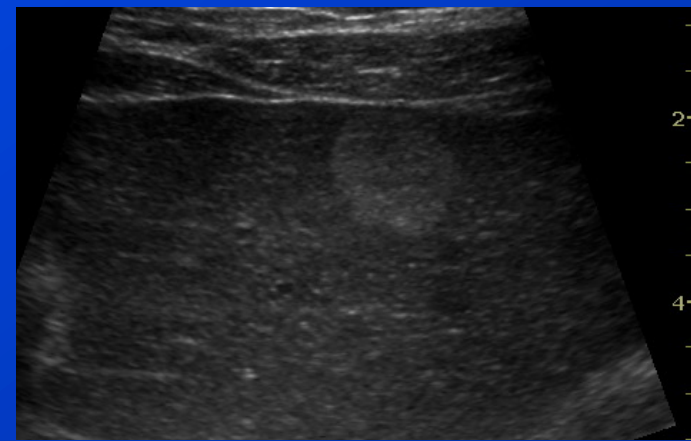


# Indications - Liver

- Detection of focal lesions
  - metastasis
- Characterisation of benign focal lesions
  - FNH, haemangioma, adenoma
- In cirrhosis: Characterize nodules / HCC
- Guiding of biopsies
- Guiding of intervention,- eg. ablation



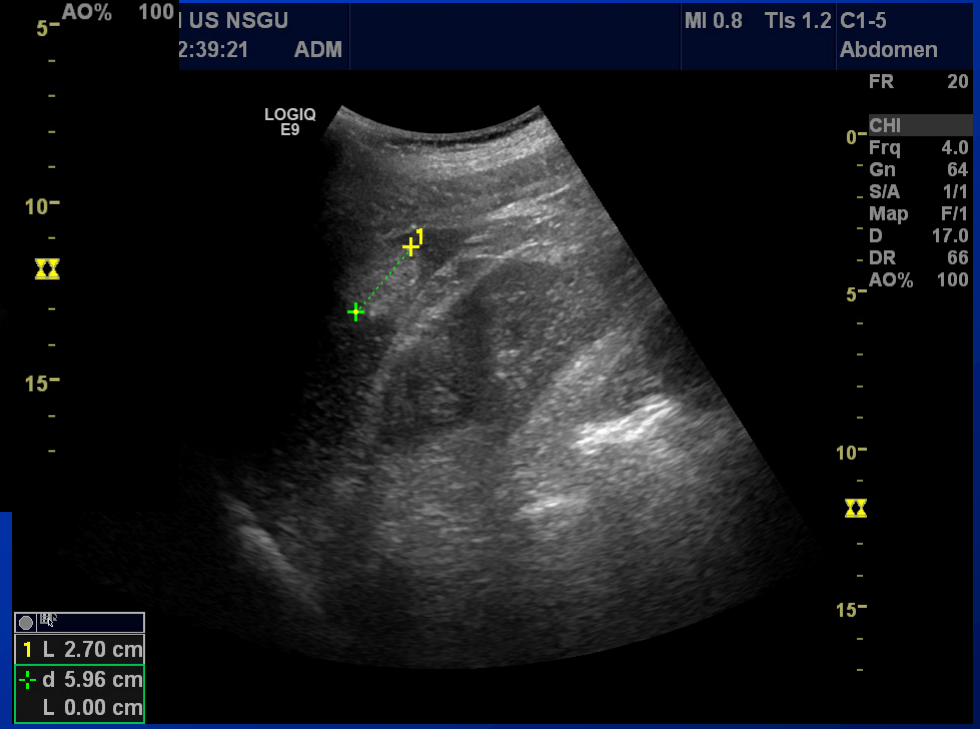
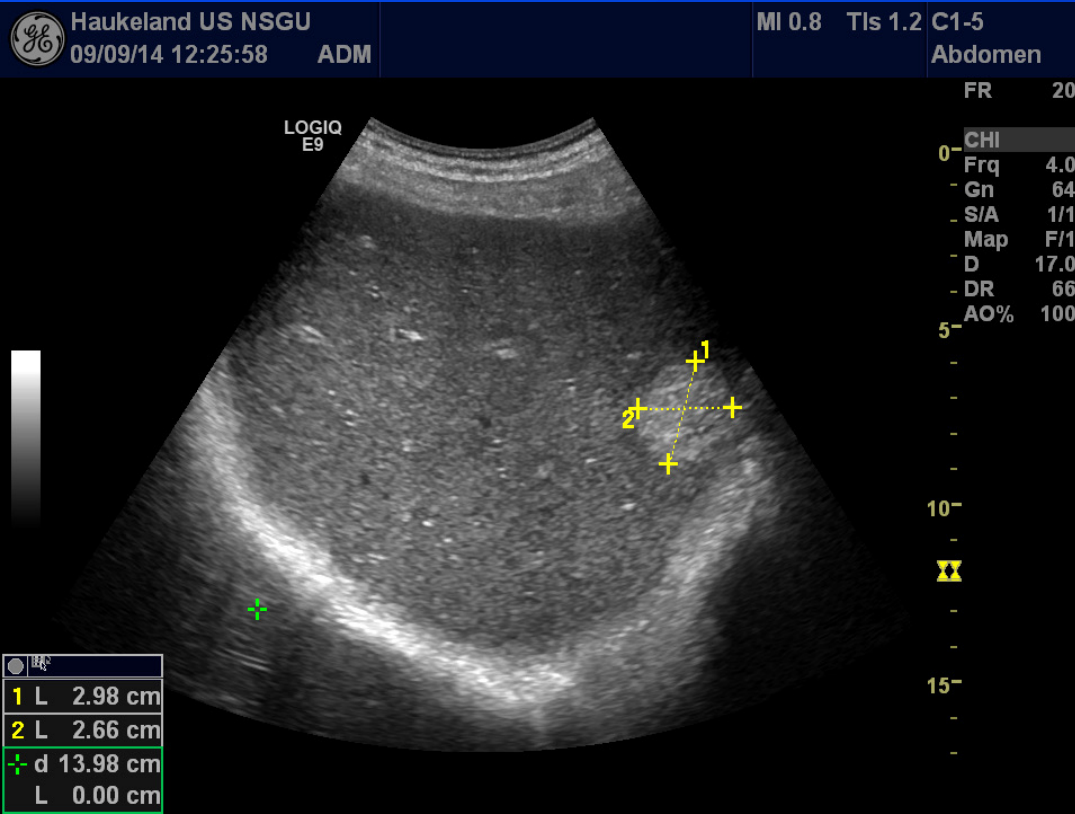
# Haemangioma



- Peripheral globular contrast pooling in arterial phase
- Globular enlargement and centripetal fill-in
- Nicolau (2004):
  - 19 of 22 hemangiomas could be correctly identified in the late phase (86.4%) and 18 in the vascular phase (81.8%).
- Ding (2005):
  - sensitivity of 96.3% and specificity of 97.5% when centripetal fill-in enhancement was regarded as a positive finding of hemangioma.

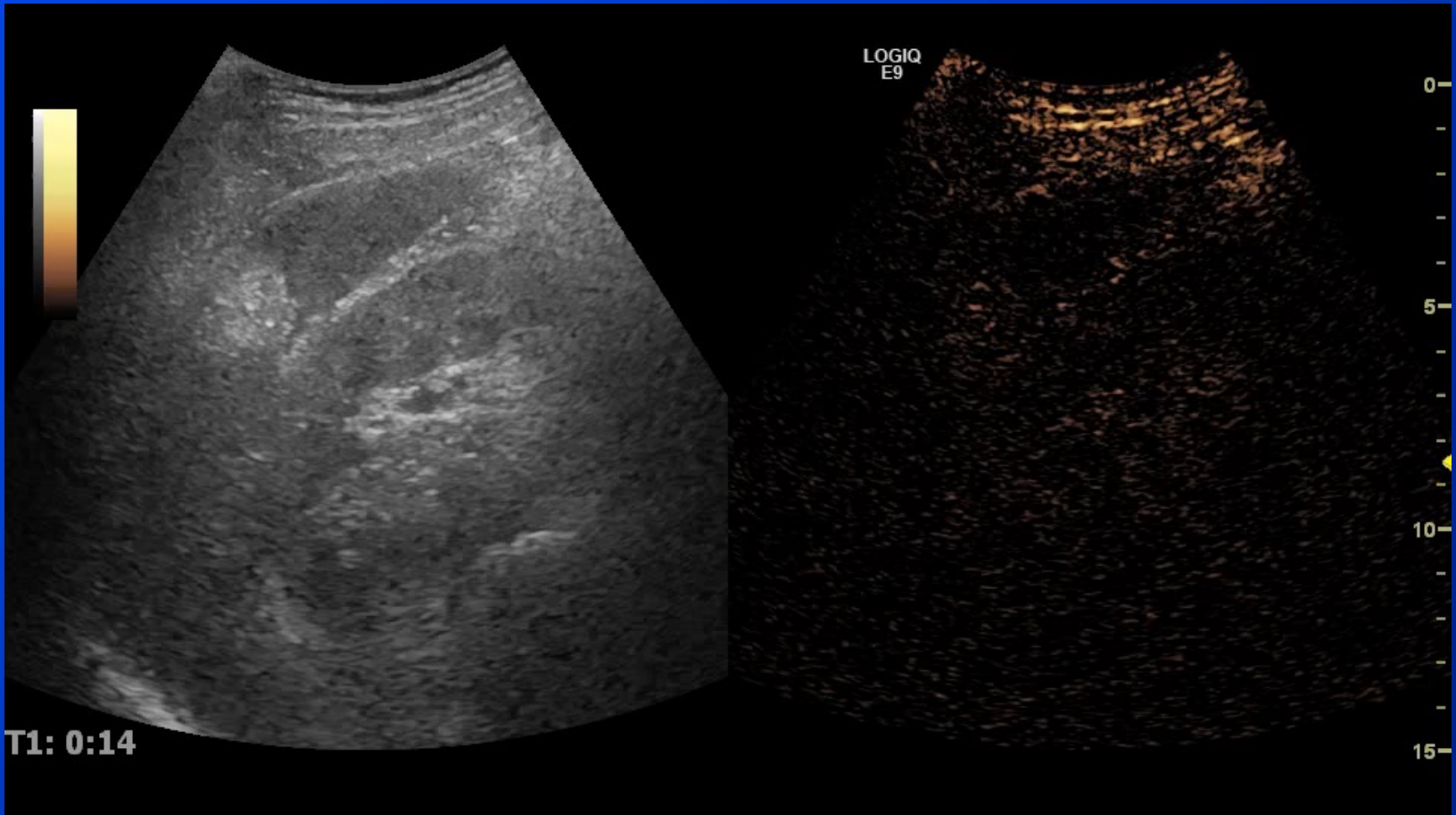


# Lesion in Liver – S7





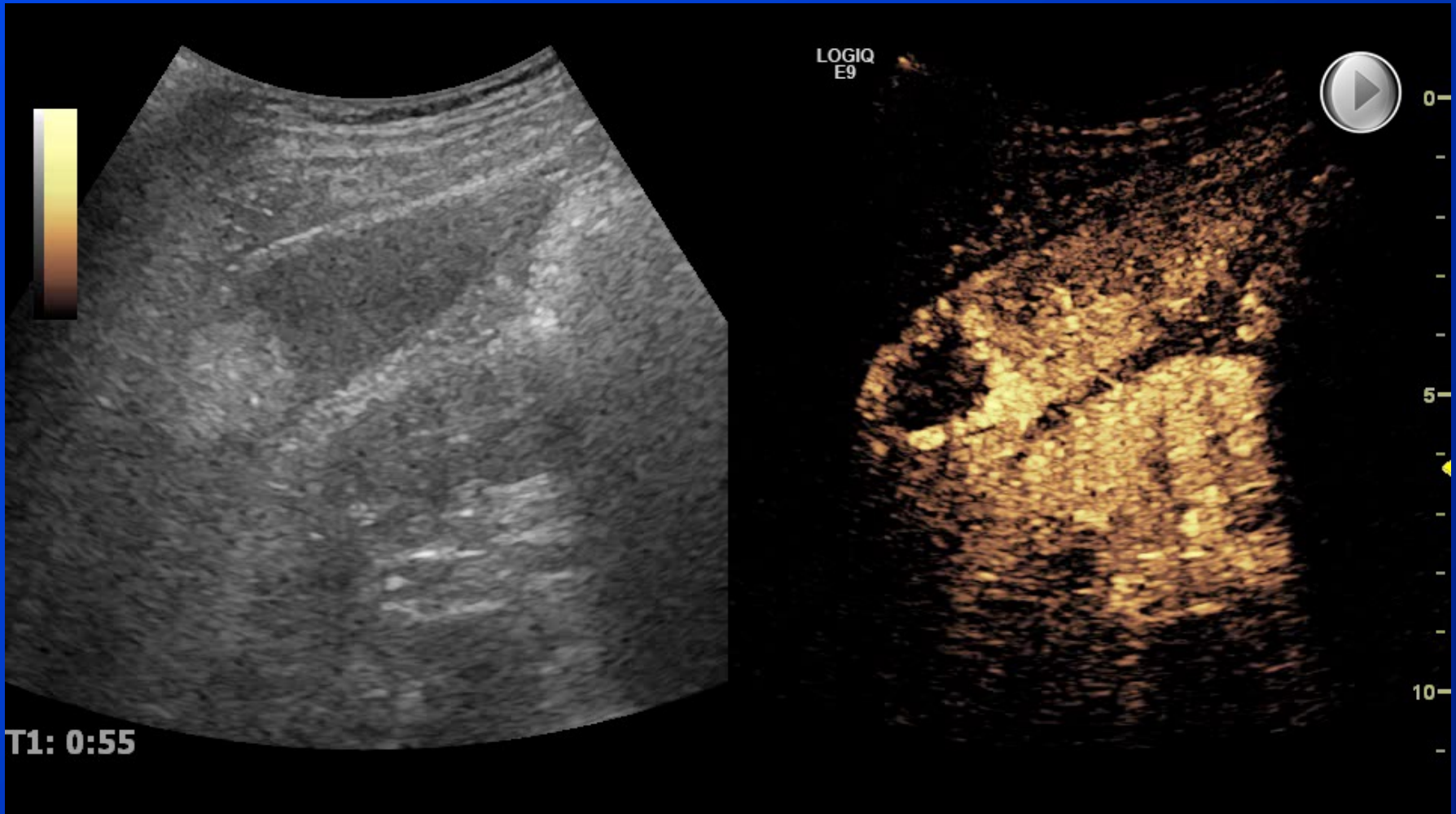
# Haemangioma – High Res







# Portal Phase - Sonazoid



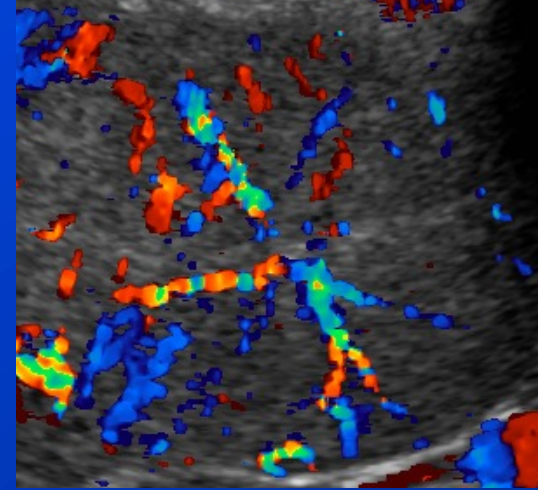


# In Haemangiomas, be aware...

- ...not to use too high MI
- ...not to focus on one lesion in all phases
- ...to scan longer than 5 min.
- ...some h. never totally fill in, but it is still benign
- ...big h. may behave atypically (thrombosis)



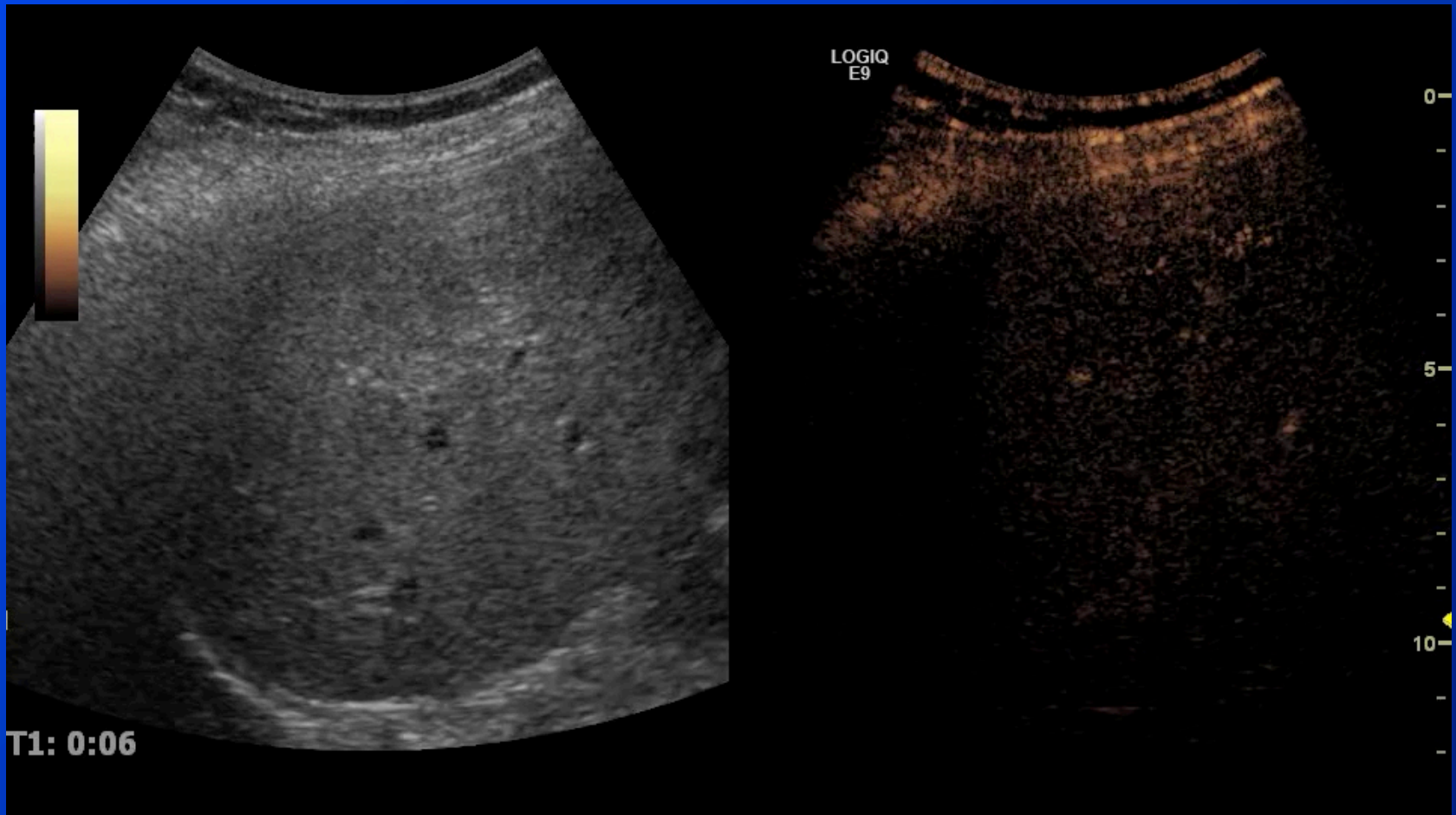
# Focal Nodular Hyperplasia - FNH



- FNH- a centrifugal stellate branching in early arterial phase
- Spoke wheel pattern in approx 40%
- Intense homogenous uptake
- Iso- or hyperechoic lesion is seen in portal venous phase.
- With these characteristic features:
  - sensitivity and specificity of contrast-enhanced low MI real-time US are 87.6% and 94.5%, respectively
  - Di Stasi 1996

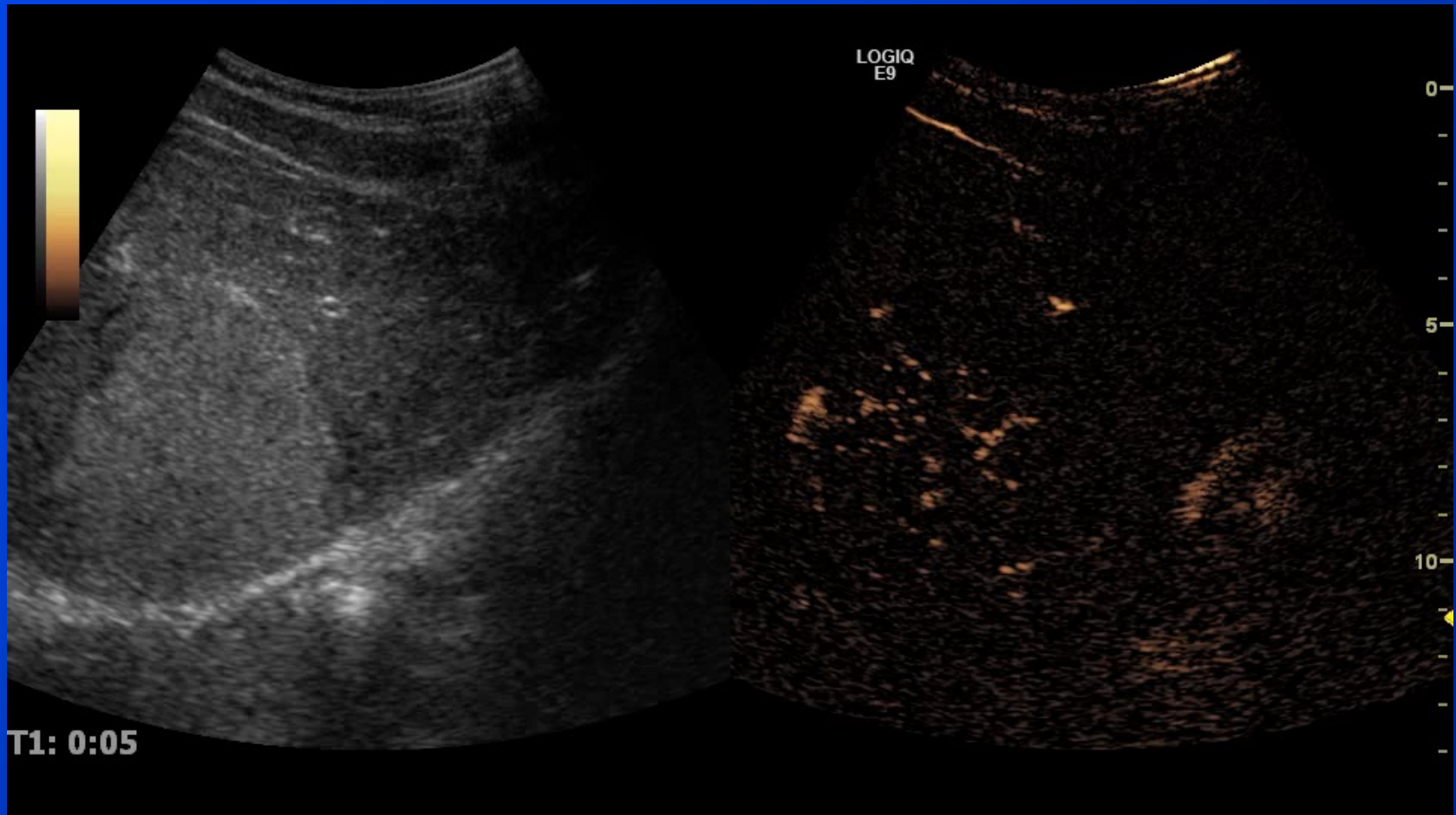


# FNH - CEUS



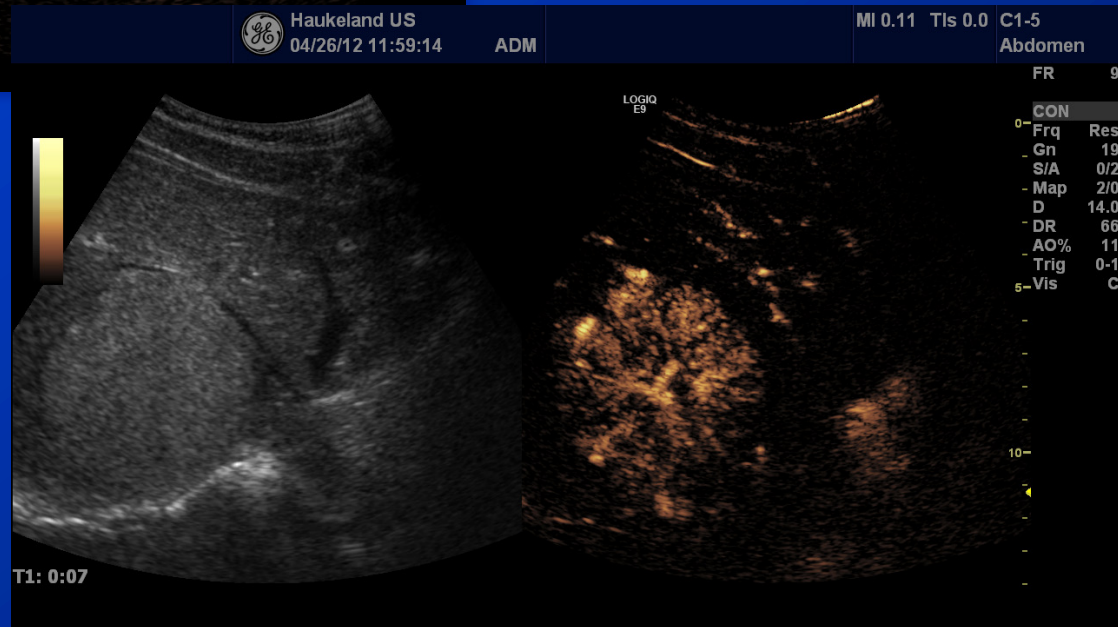
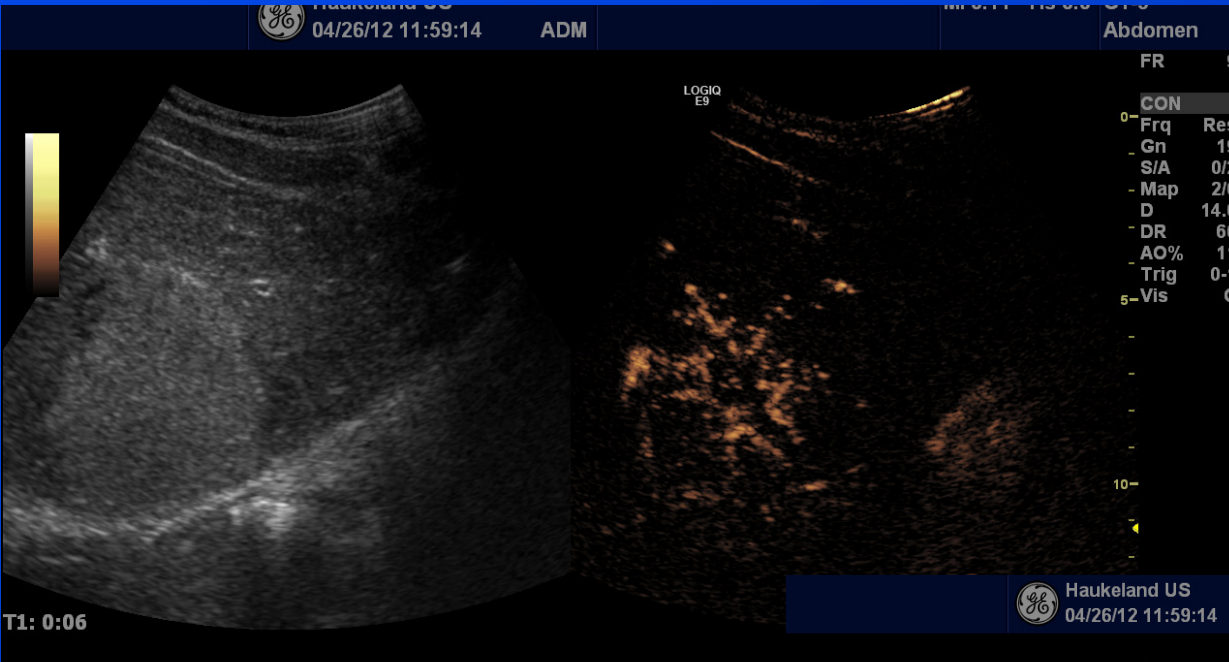


# FNH- Arterial Phase



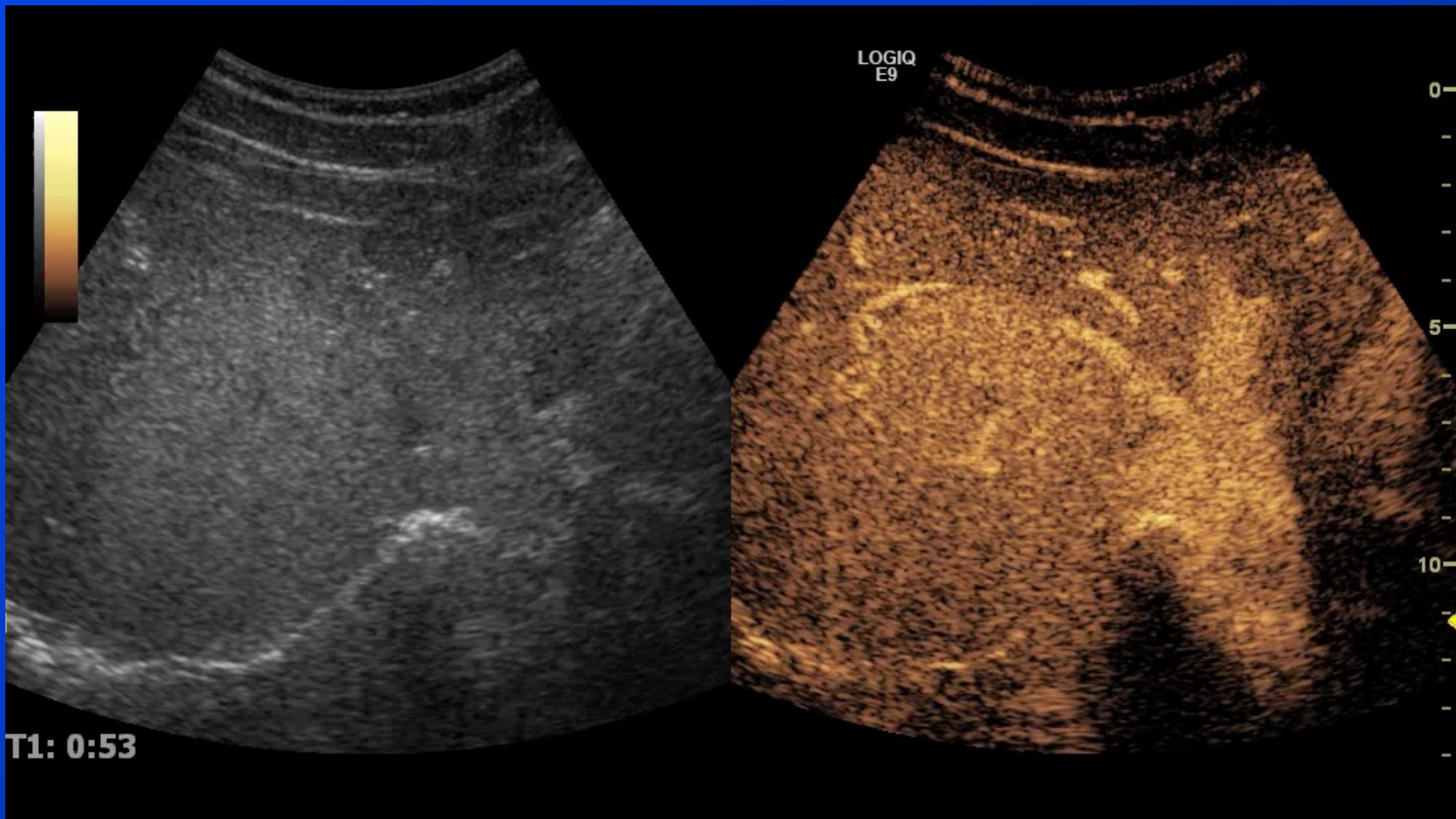


# FNH



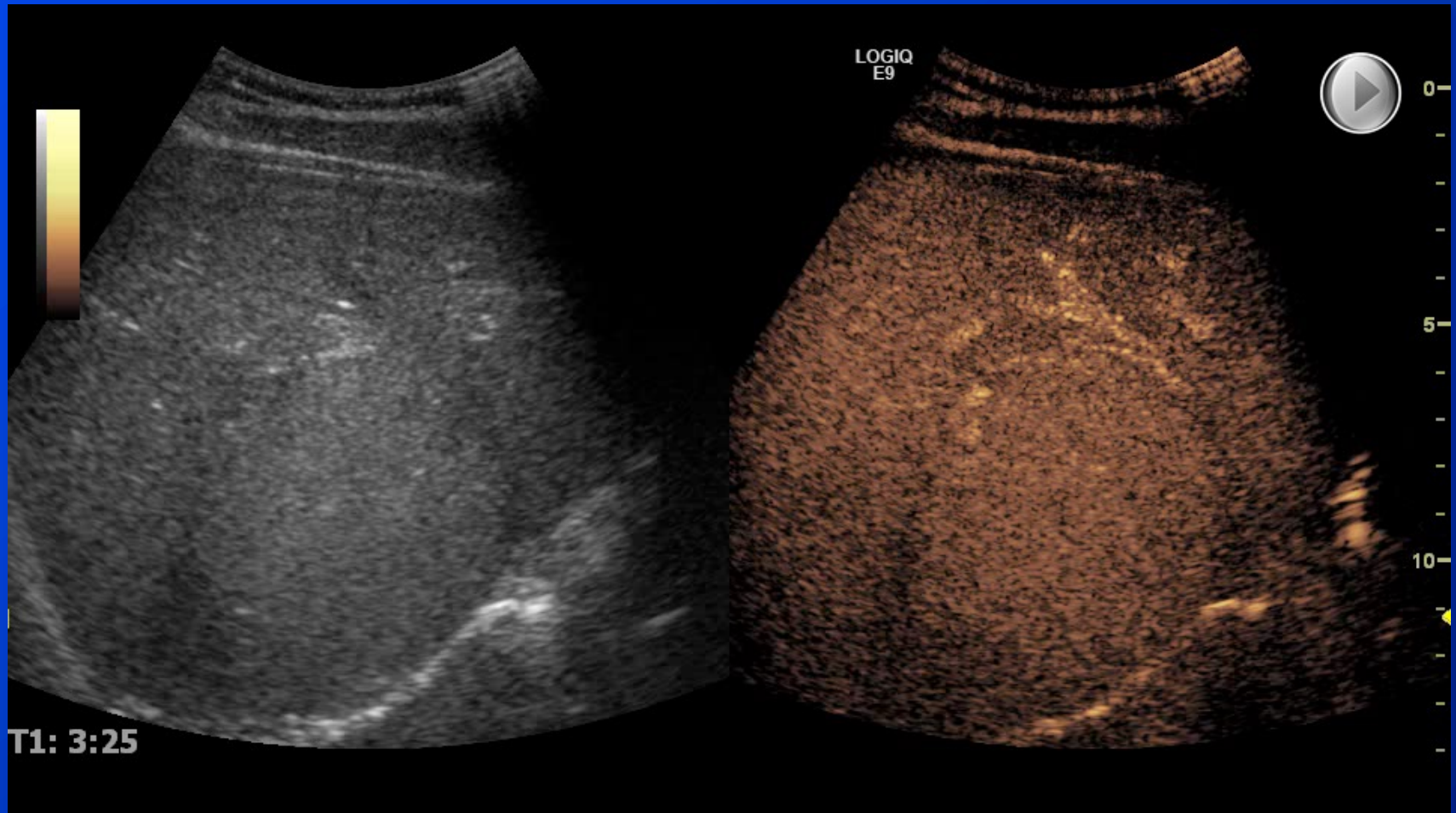


# Trick: Destroy the MB by increasing the MI (Flash)





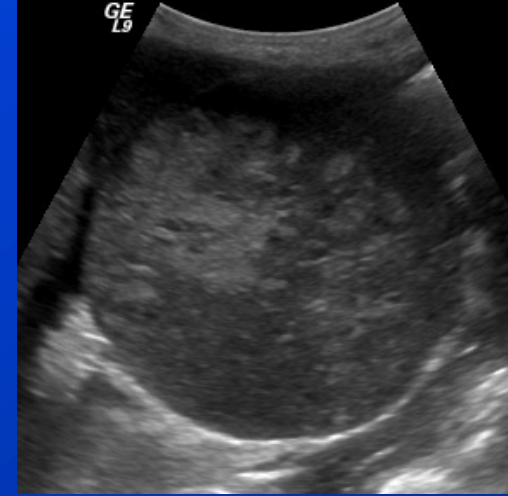
# FNH – Late Phase (Sinosoidal)







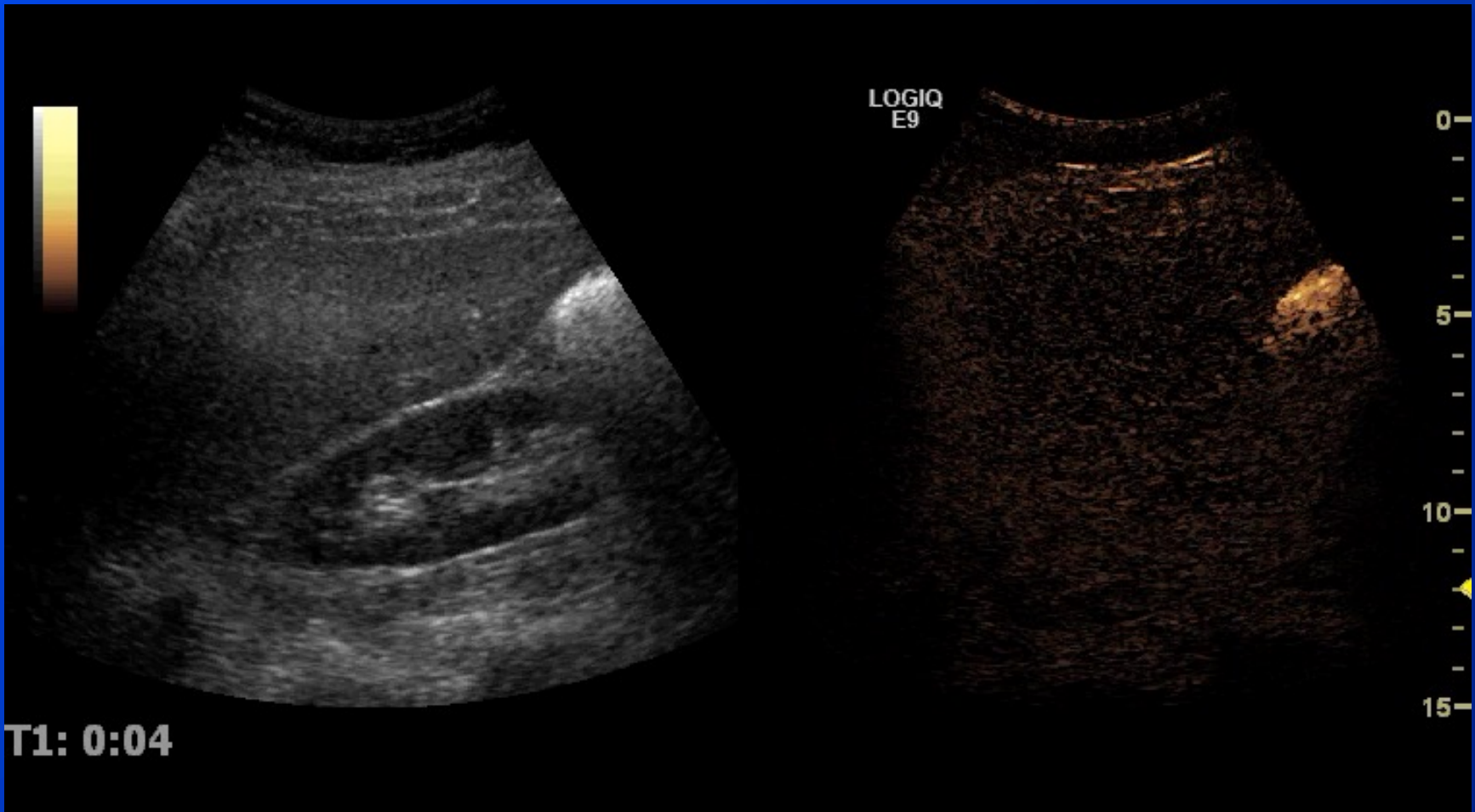
# Liver cell adenoma



- Liver cell adenoma (LCA) is a rare primary benign neoplasm found mainly in young women with a history of oral contraceptive use
- The hypervascularity of adenomas can be demonstrated on Doppler,- sentripetal
- CEUS identification of the early and homogeneous hyperechoic enhancement in the periphery of the tumor, reflecting the presence of the subcapsular feeding arteries.
- The enhancement of LCA in the portal and late phases is nearly comparable with that of liver parenchyma, but LCA can remain slightly hypoechoic in relation to the adjacent liver

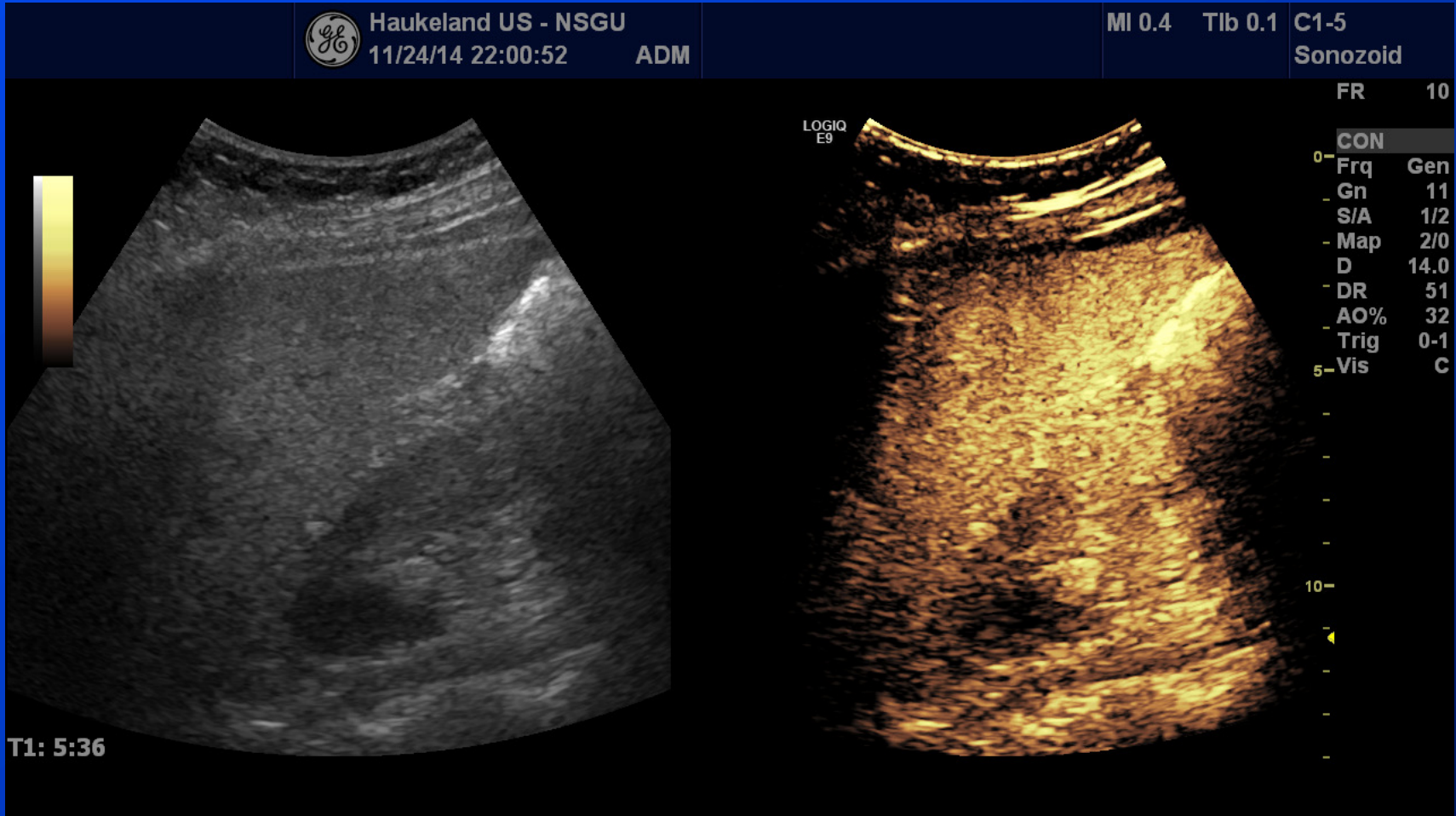


# Hepatic Adenoma





# Sinusiodal Phase





# Liver Metastasis ?

Before contrast injection





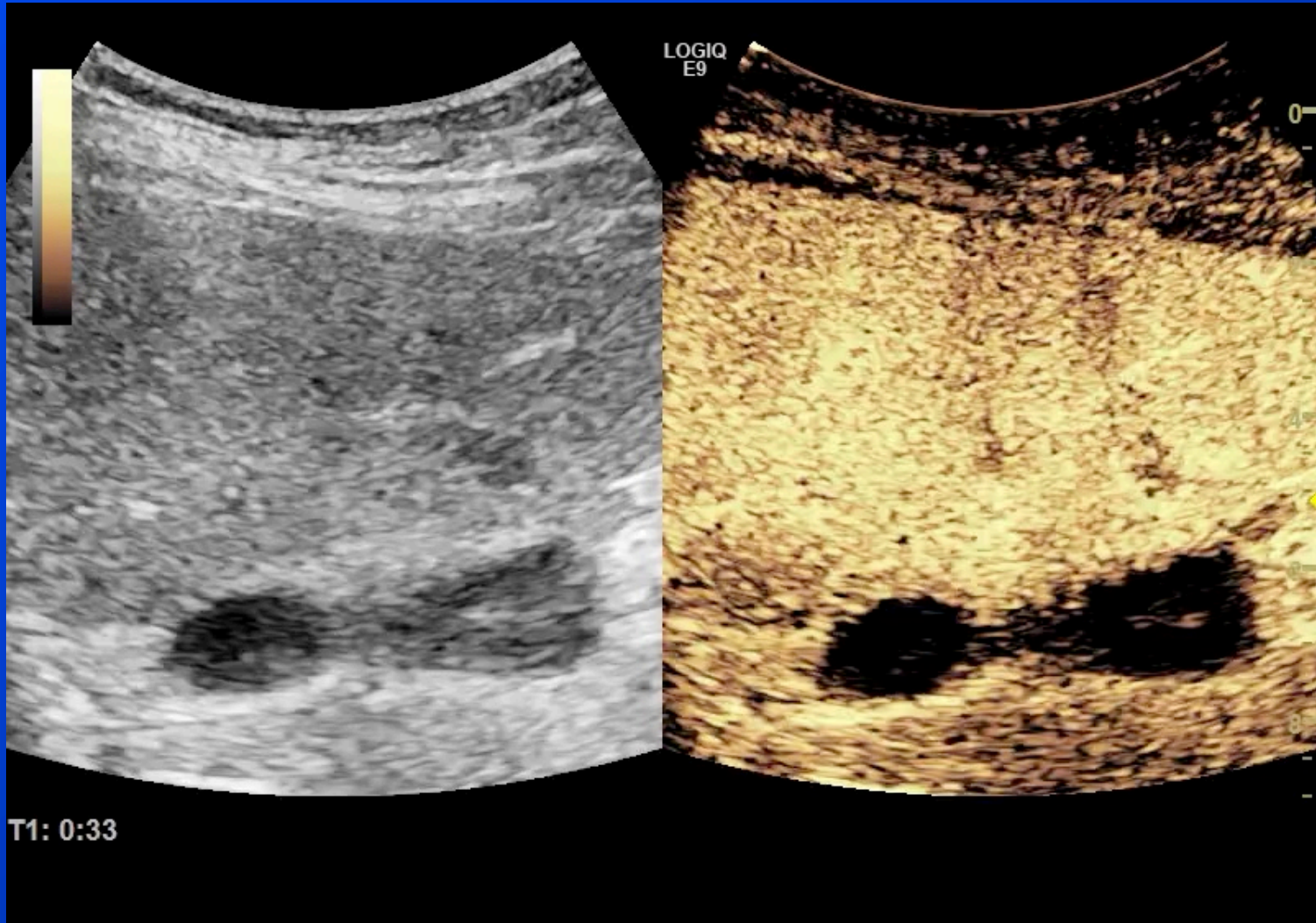
# Liver Metastasis ?

After contrast injection in late phase





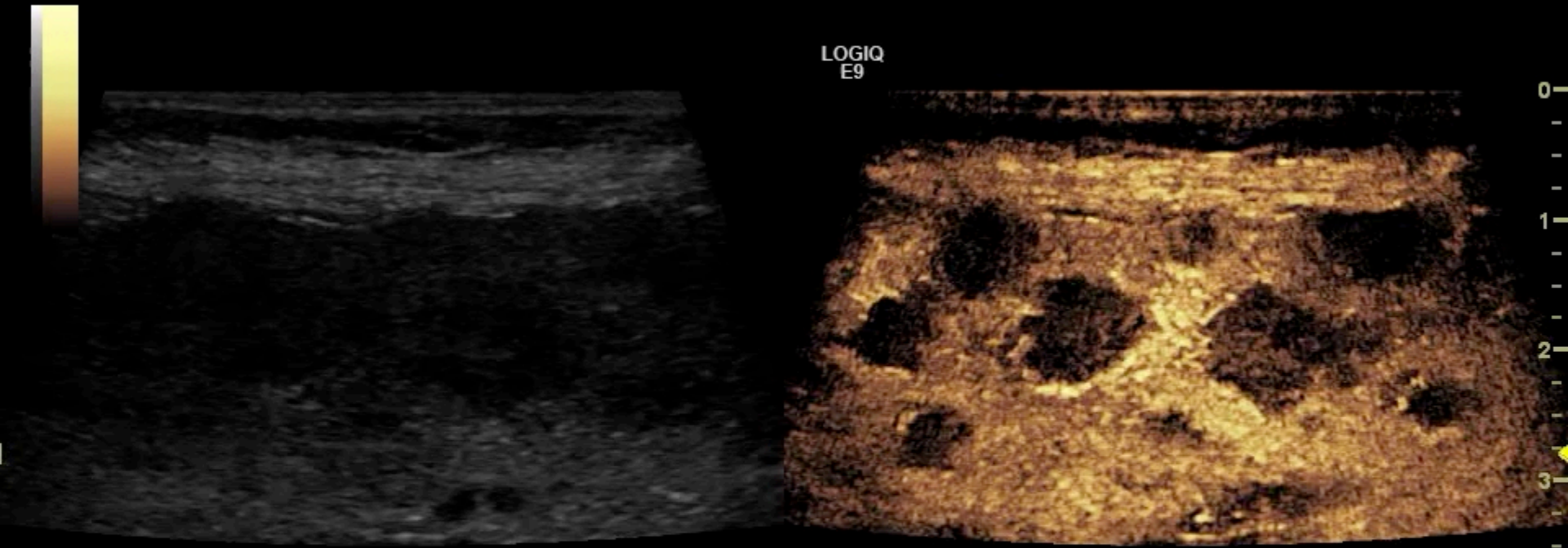
# Early wash-out typical for mets



Not easily observed on CT and MRI



# High-Frequency 9 MHz LA probe Post-vascular phase (Kupffer)



T1: 11:02



# The role of CEUS in HCC

## RECOMMENDATION 7

Routine use of CEUS for the surveillance of patients at risk for HCC is not recommended (LoE 4, strong recommendation) (Pro 29, Against 2, Abs 0).

## RECOMMENDATION 8

Routine use of CEUS for staging of HCC is not recommended (LoE 2, strong recommendation), (Pro 31, Against 0, Abs 0).





# CEUS in HCC

## RECOMMENDATION 16

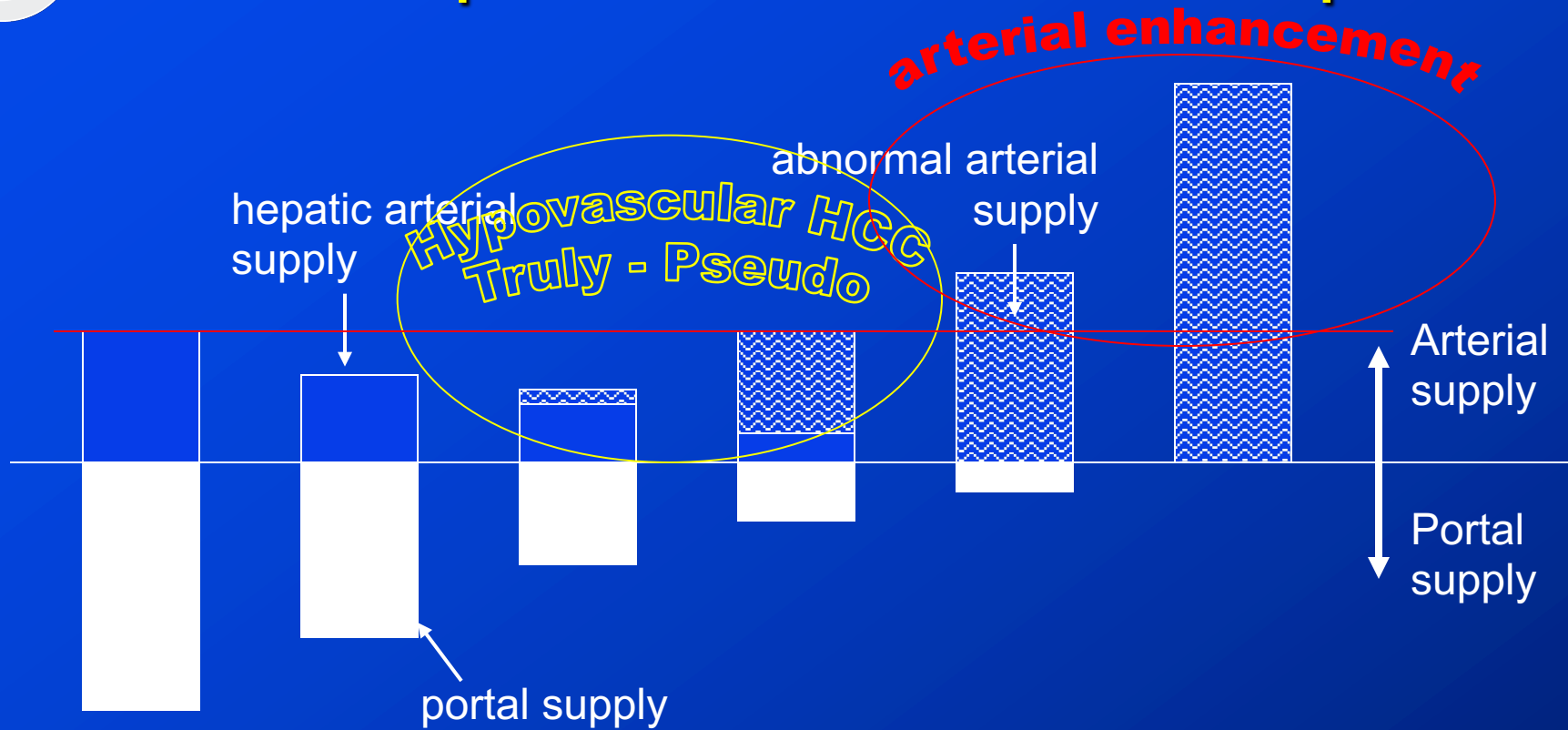
CEUS can be utilized in first line to characterize FLL found in patients with liver cirrhosis to establish a diagnosis of malignancy (CEUS LR-M) or specifically of HCC (CEUS LR-5), but CT or MR imaging remain required for accurate staging unless contraindicated (LoE2, weak recommendation) (Pro 29, Abs 0, Against 0).

## RECOMMENDATION 17

CEUS can be utilized when CT or MR imaging is inconclusive, especially in FLL in cirrhotic liver not suitable for biopsy, to assess the probability of a lesion to be an HCC (LoE3, weak recommendation) (Pro 29, Abs 0, Against 0).



# The Sequence of HCC Development



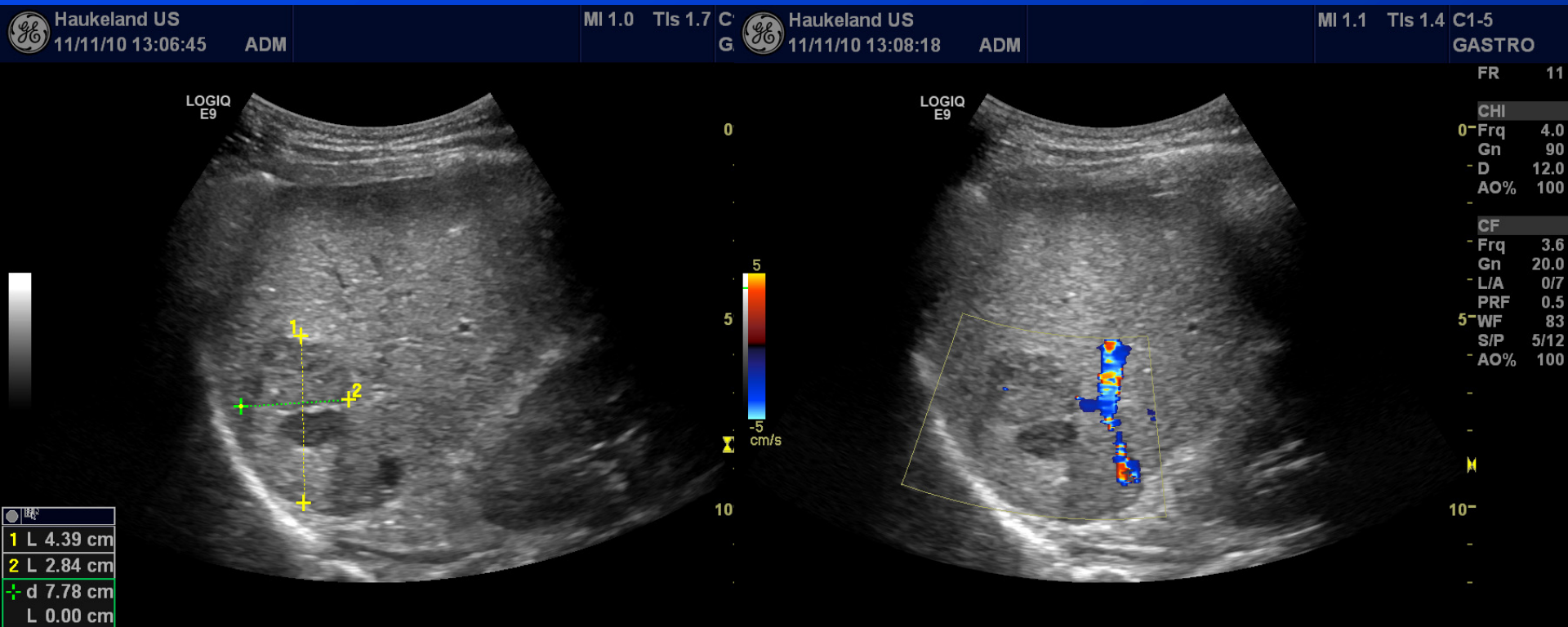
LRN ~ LGDN ~ HGDN ~ e-HCC ~ wdHCC ~ classical HCC

early HCC

*from: Matsui, Clin Hep Gastro, 2005.  
(based on CT-arteriportal-angiography)*

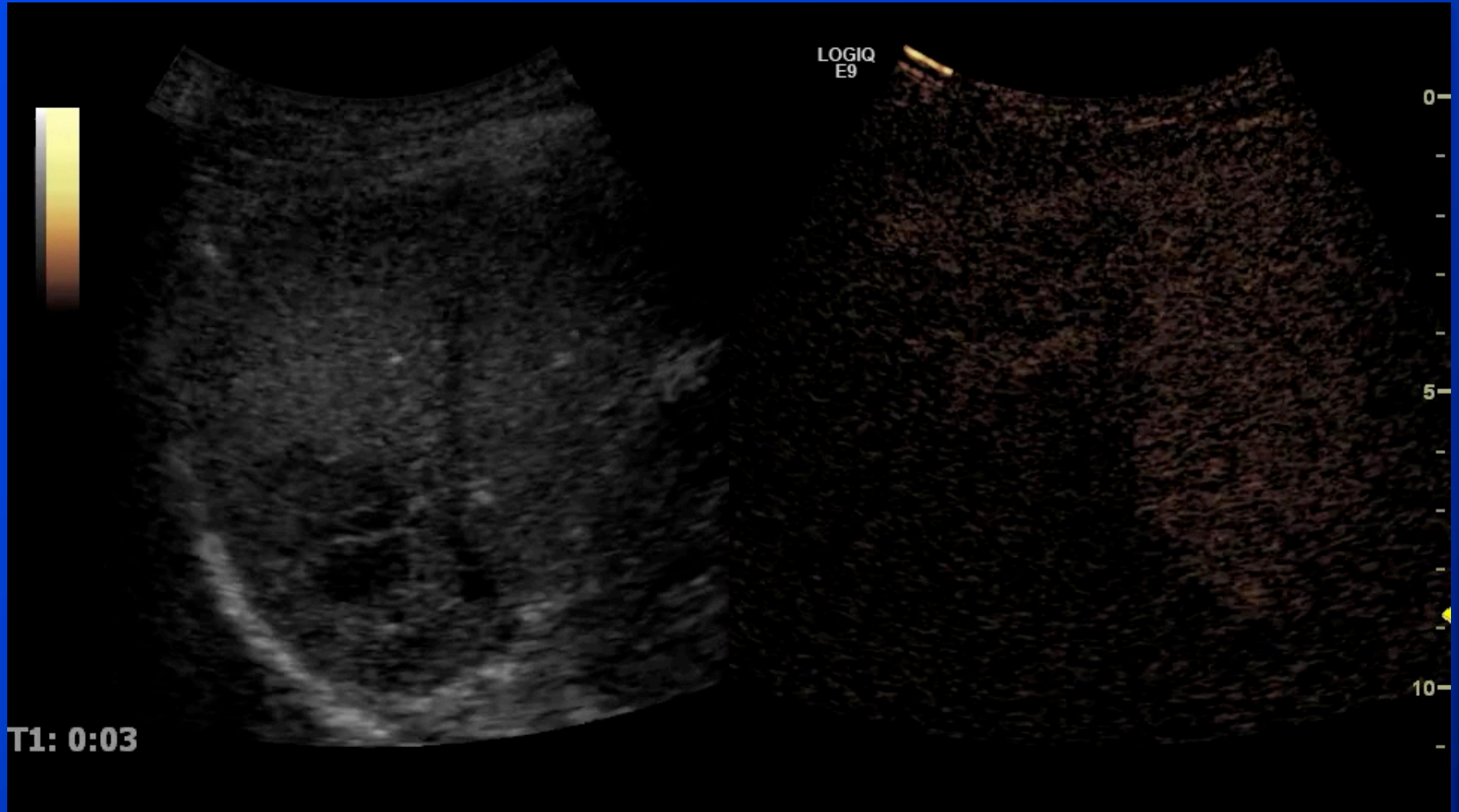


# CEUS in cirrhosis (AIH) – HCC?





# SonoVue in AIH – HCC?





# Probability of HCC in Cirrhosis

Which nature is expected to have a focal liver lesion newly detected in a cirrhotic liver?

From a likelihood approach:

65% HCC if 1-2cm,

85% HCC if 2-3cm,

>90-95% if >3 cm

If not an HCC, consider:

1. Regenerative dysplastic nodule
2. Hemangioma
3. Cholangiocellular carcinoma
4. Lymphoma



# FNH versus HCC



**FNH**



**HCC**



# New European Guidelines on CEUS

Paul S. Sidhu, Vito Cantisani, Christoph F. Dietrich,  
Odd Helge Gilja, Adrian Saftoiu, Eva Bartels,  
Michele Bertolotto, Fabrizio Calliada, Dirk-André Clevert,  
David Cosgrove, et al.

With compliments of Georg Thieme Verlag

[www.thieme.de](http://www.thieme.de)

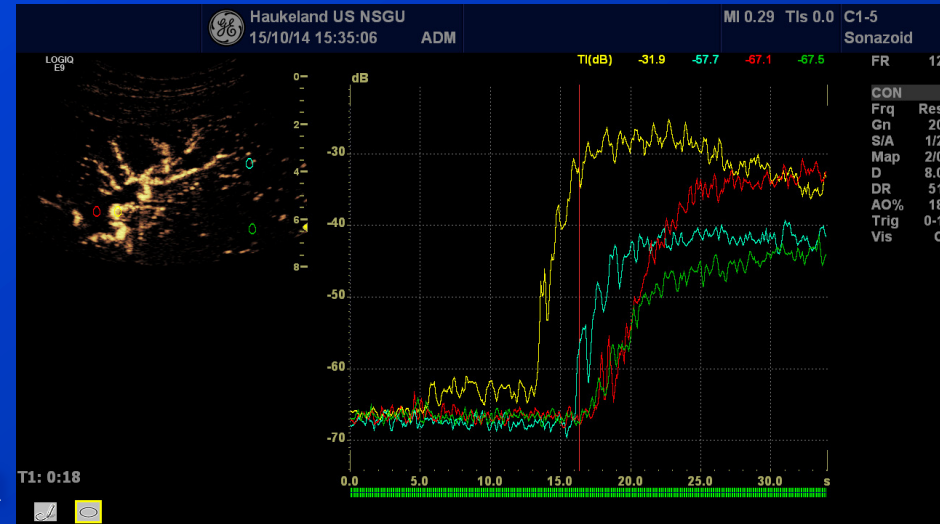
The EFSUMB Guidelines and  
Recommendations for the  
Clinical Practice of Contrast-  
Enhanced Ultrasound (CEUS) in  
Non-Hepatic Applications:  
Update 2017 (Long Version)

Includes 74 recommendations



# Non-liver CEUS Applications

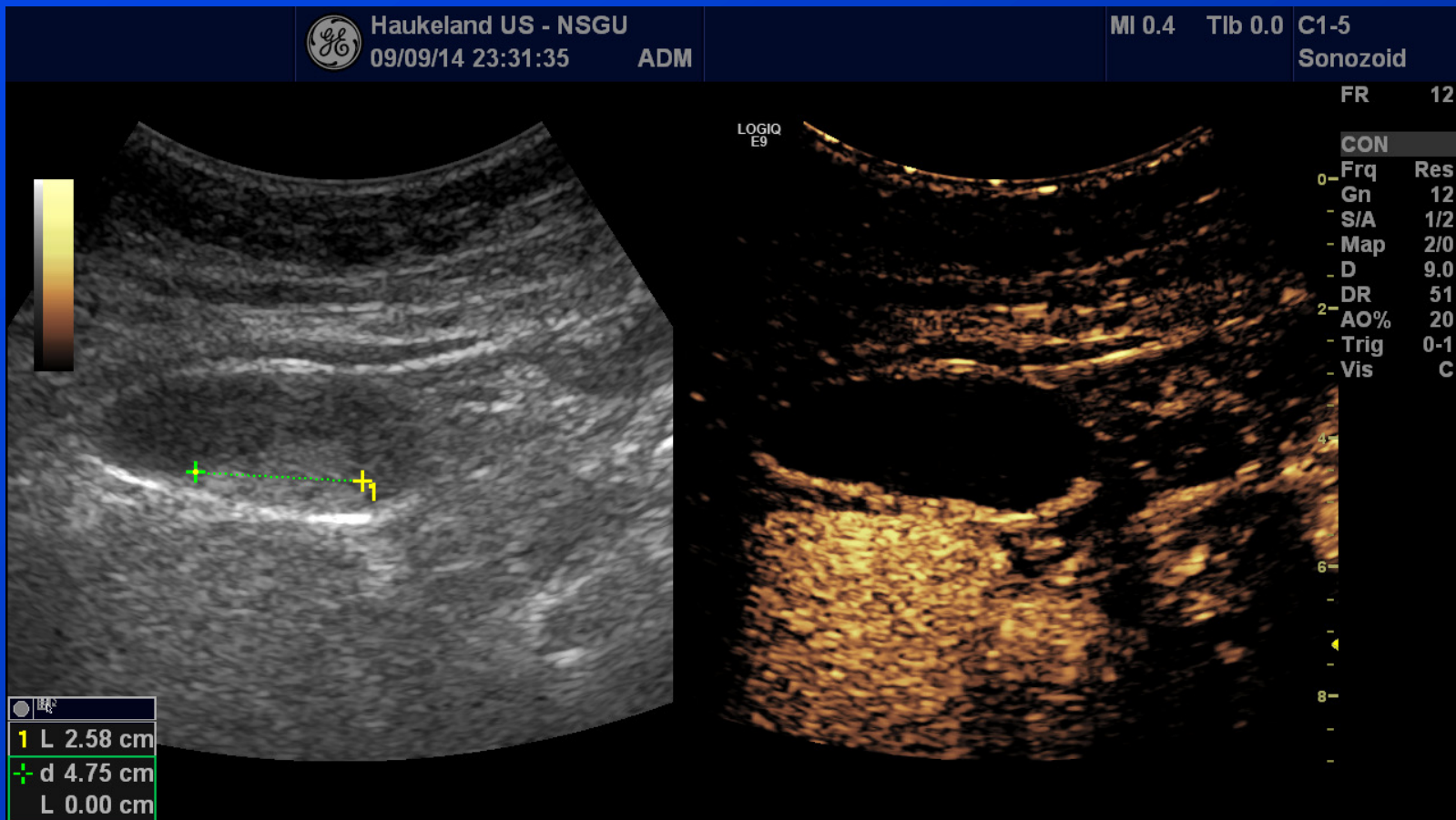
- Gallbladder tumors
- Kidney scanning
- Pancreas
- Bladder reflux
- Blaunt abdominal trauma
- Transcranial scanning
- Spleen
- Intestines
- ...>30 clinical applications of CEUS







# Gallbladder Tumor? or Sludge?





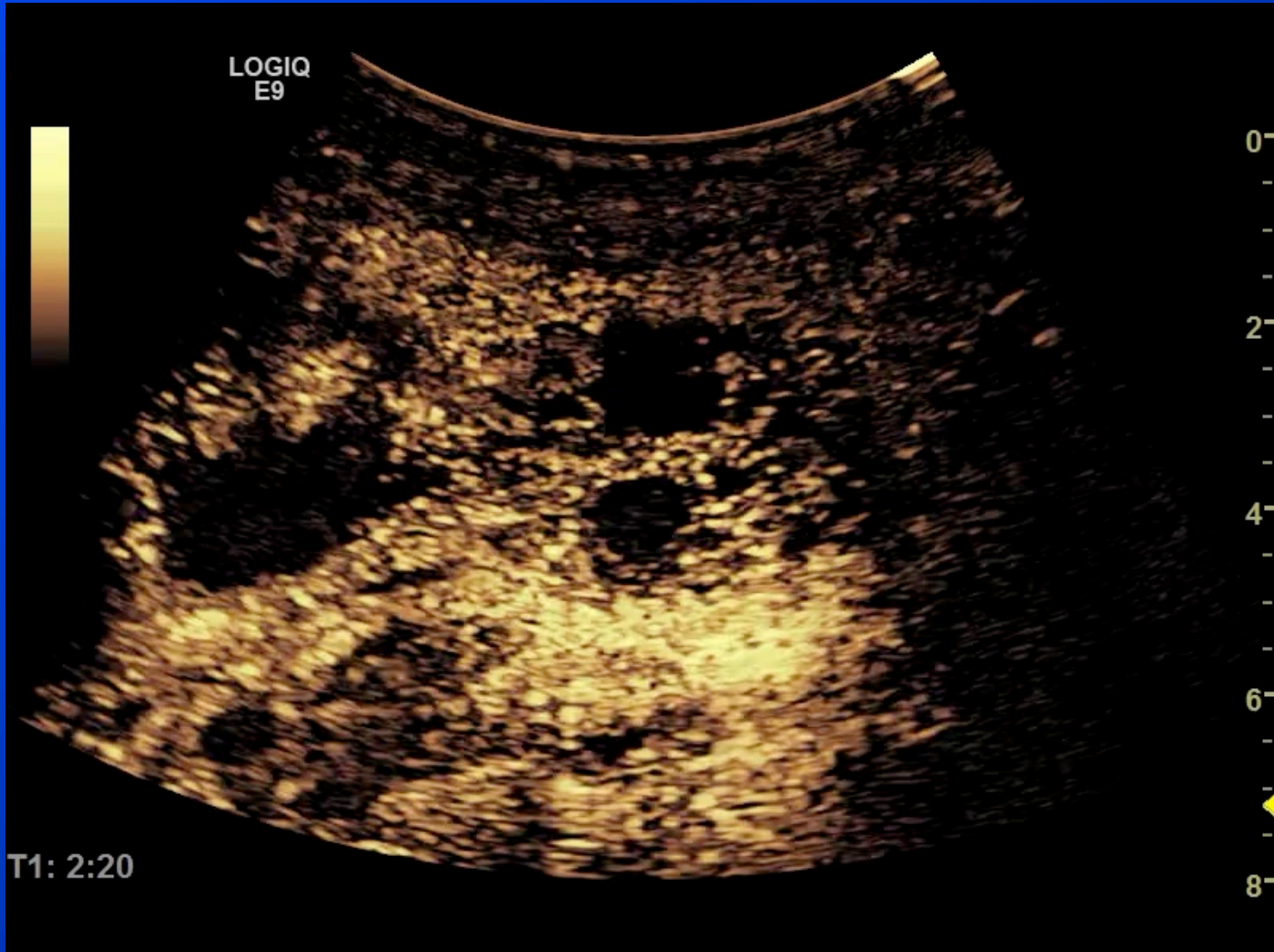
# Female-65 years

## Chronic subcostal pain





# CEUS of gallbladder





# Pancreas: PDAC vs. NET

## RECOMMENDATION 25

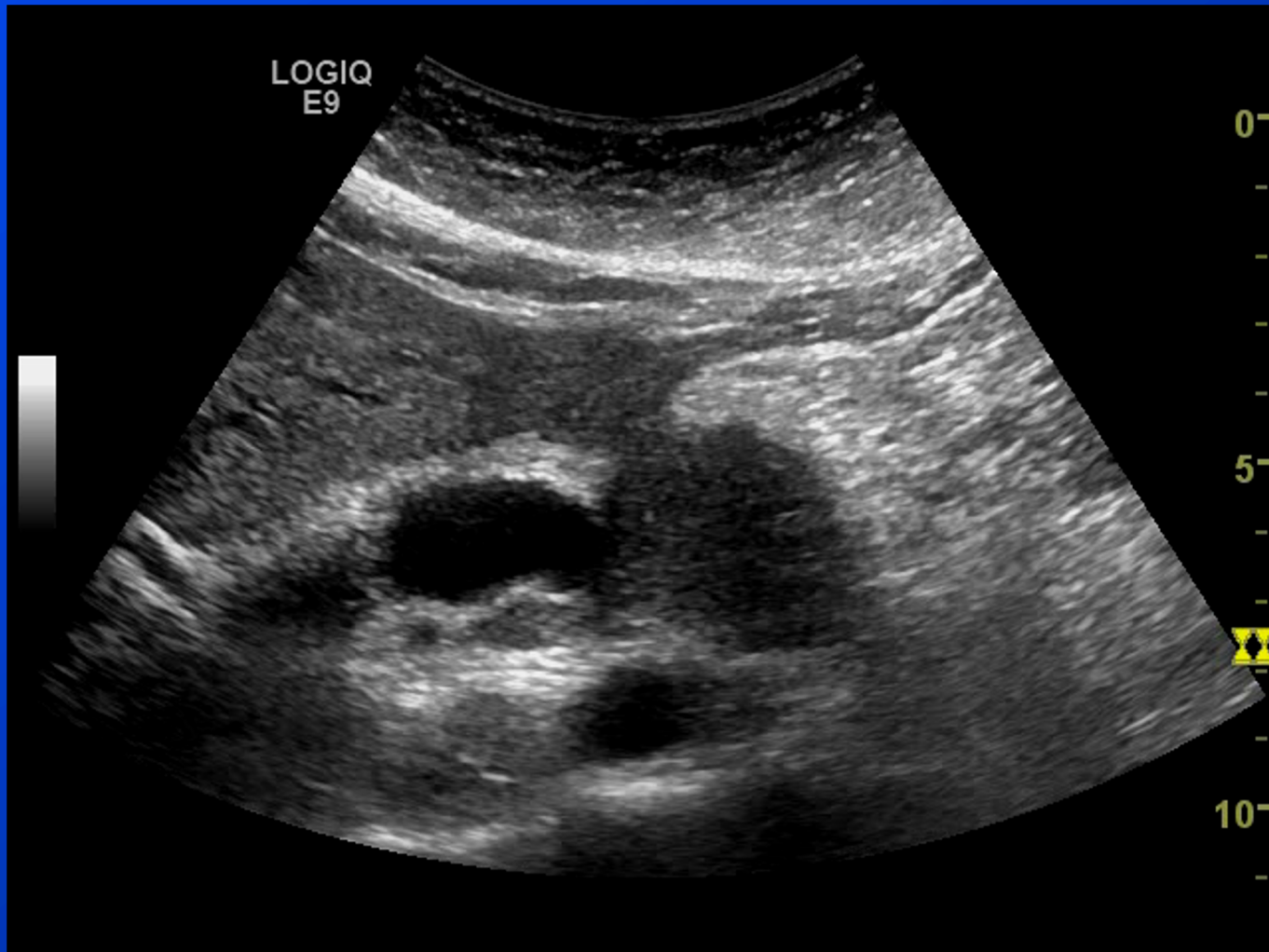
In solid pancreatic lesions detected on ultrasound, CEUS can be used to reliably characterize ductal adenocarcinoma (LoE 1a, GoR A). Broad consensus (18/0/2, 90 %)

## RECOMMENDATION 26

CEUS can be used to distinguish between pancreatic ductal adenocarcinoma and neuroendocrine tumors (LoE 1a, GoR A). Strong consensus (20/0/0, 100 %)

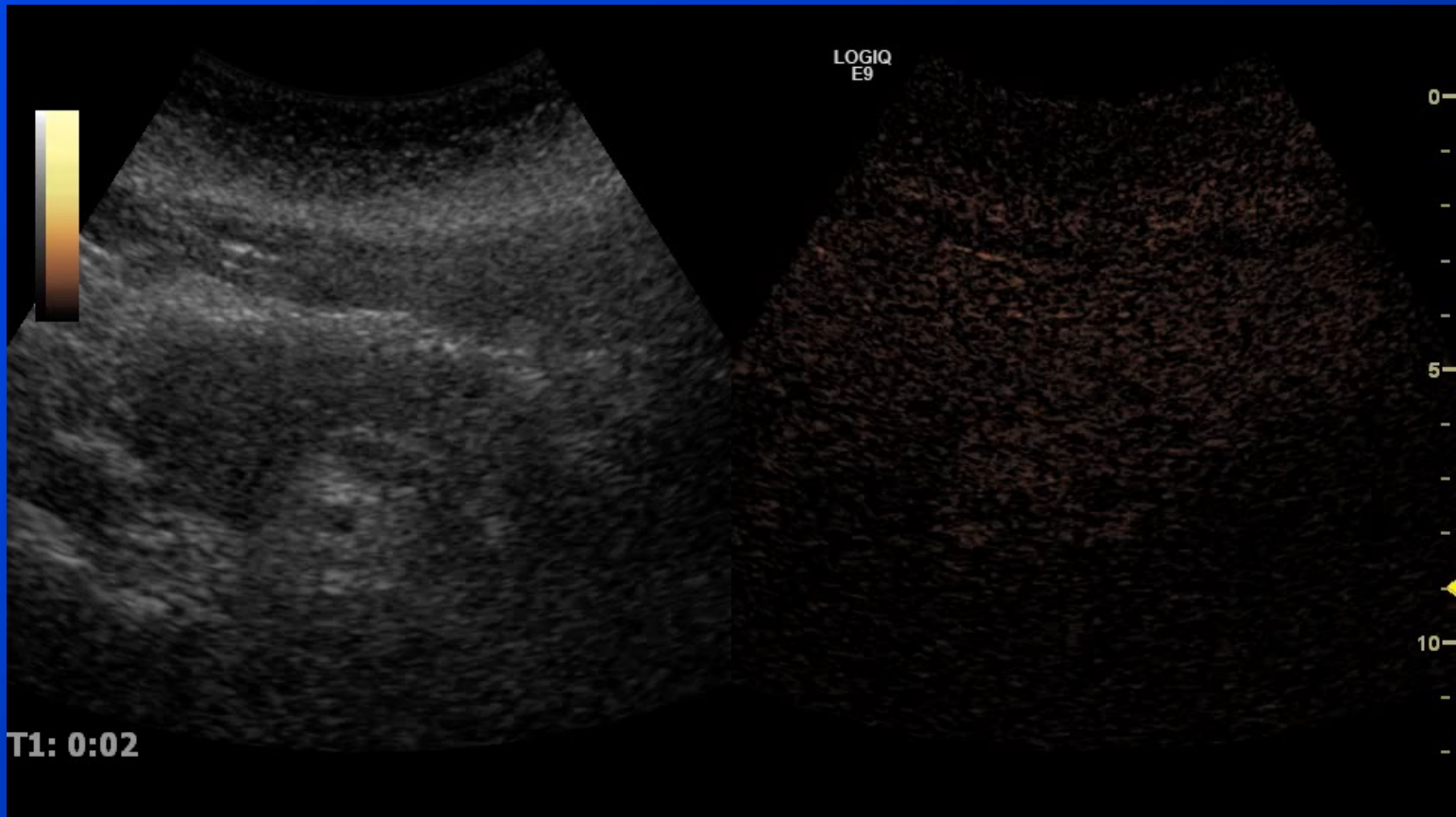


# Pancreatic Cancer



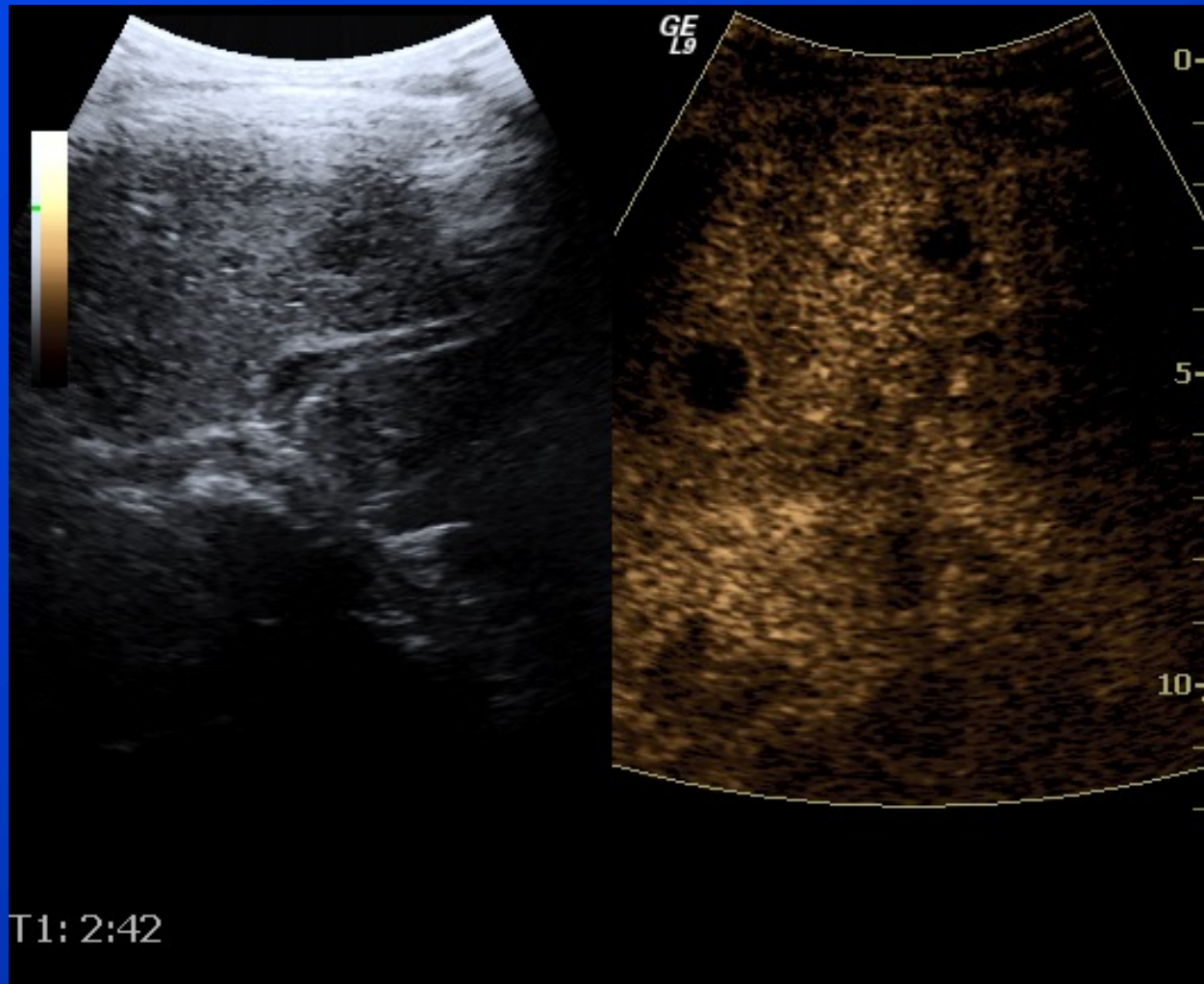


# CEUS of Arterial Phase





# Liver scanning in late phase





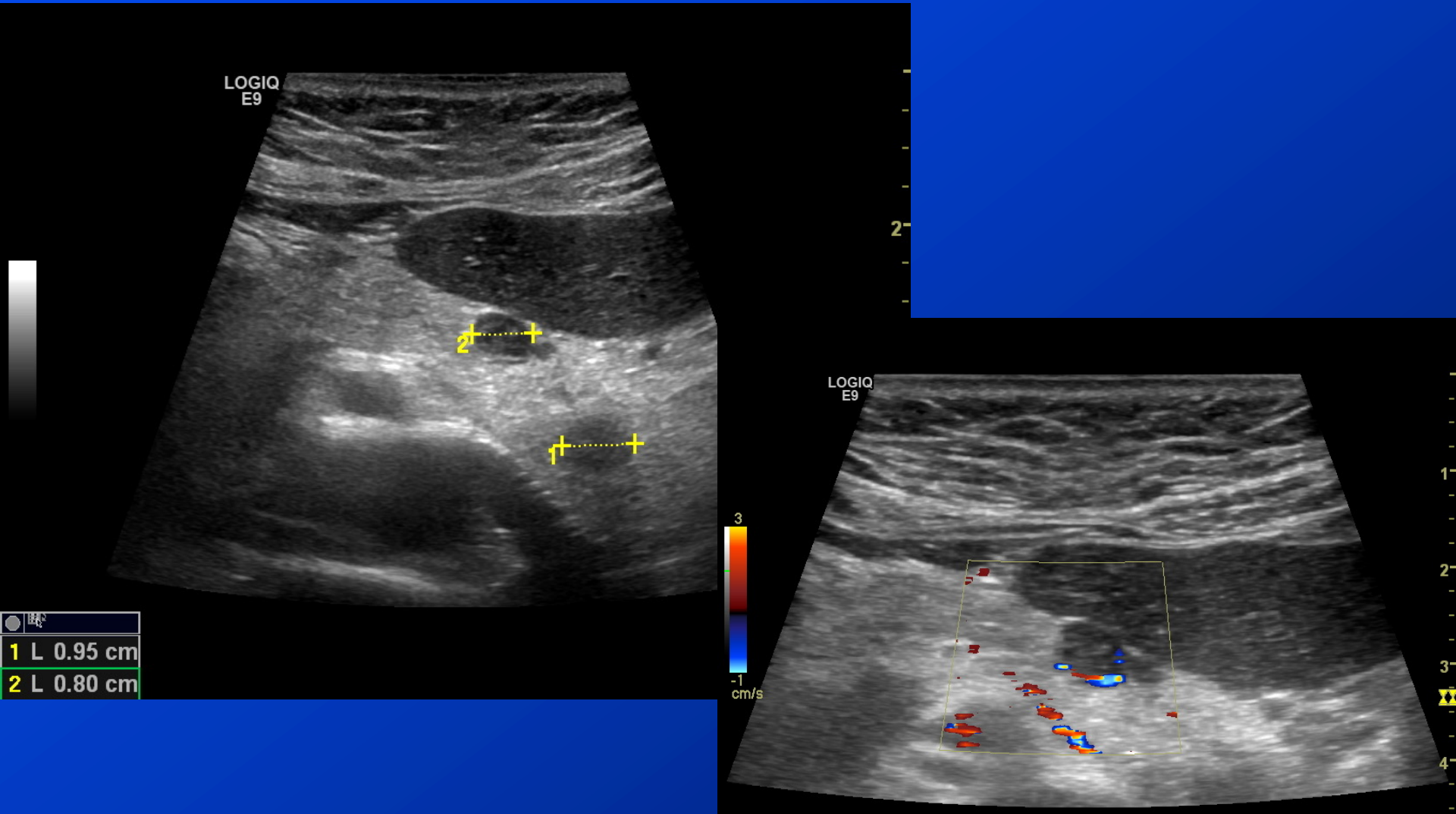
# Patient History

- Female, born 1961
- Watery diarrhoea since spring 2009
- Weightloss 10 kg
- CT: One lesion in the tail of the pancreas
- EUS: Showed 2 lesions in the pancreas
- External ultrasound...



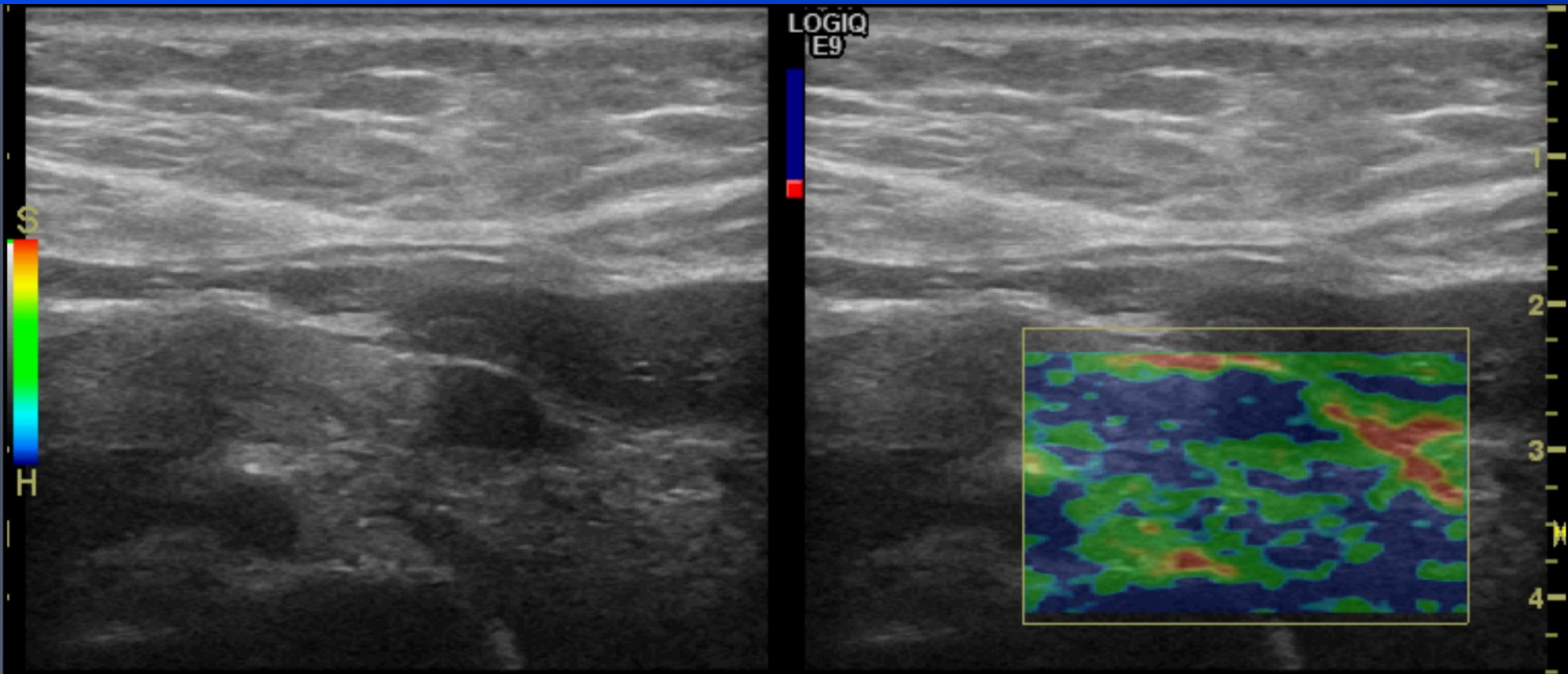


# B-mode Pancreatic Lesions



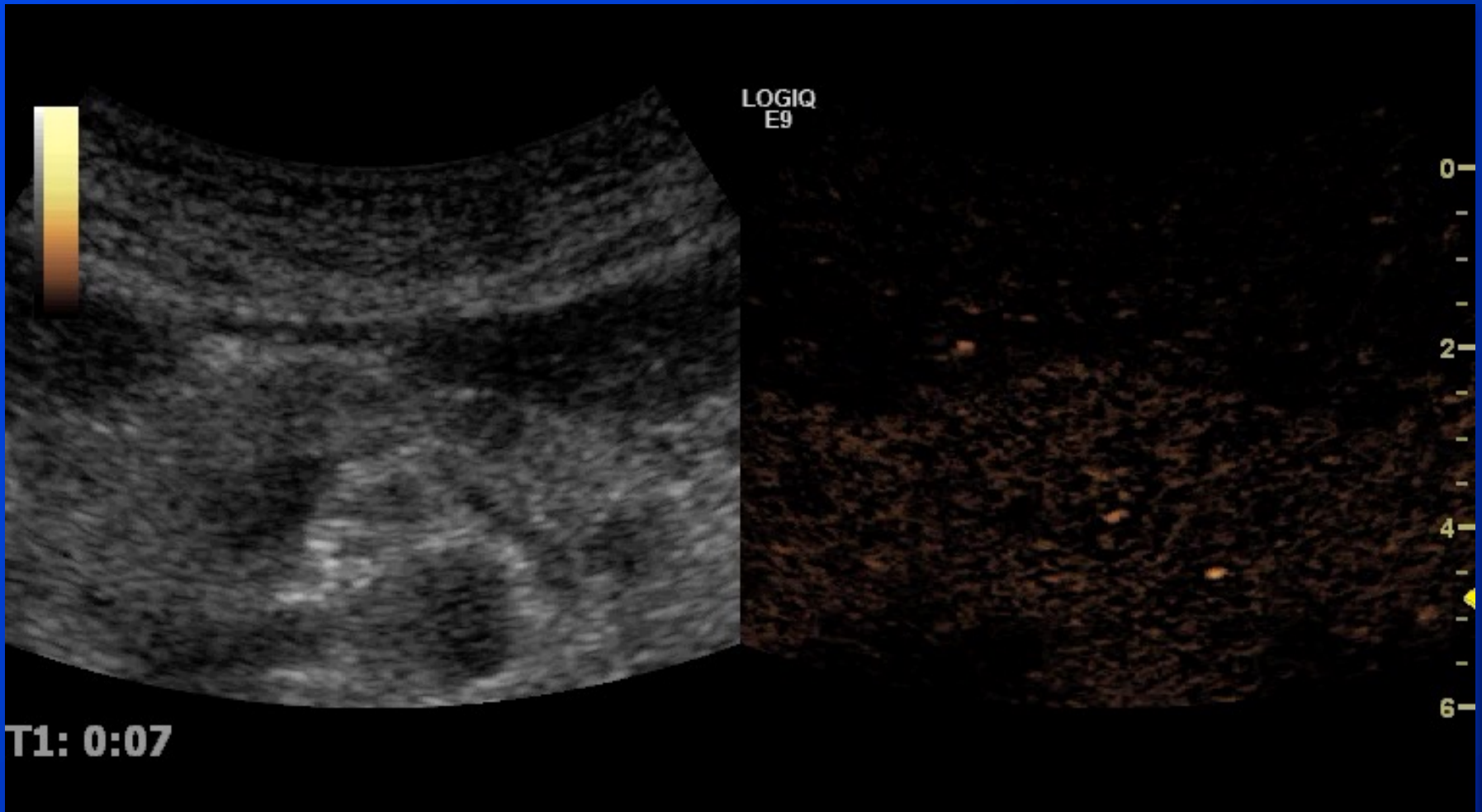


# Elastography



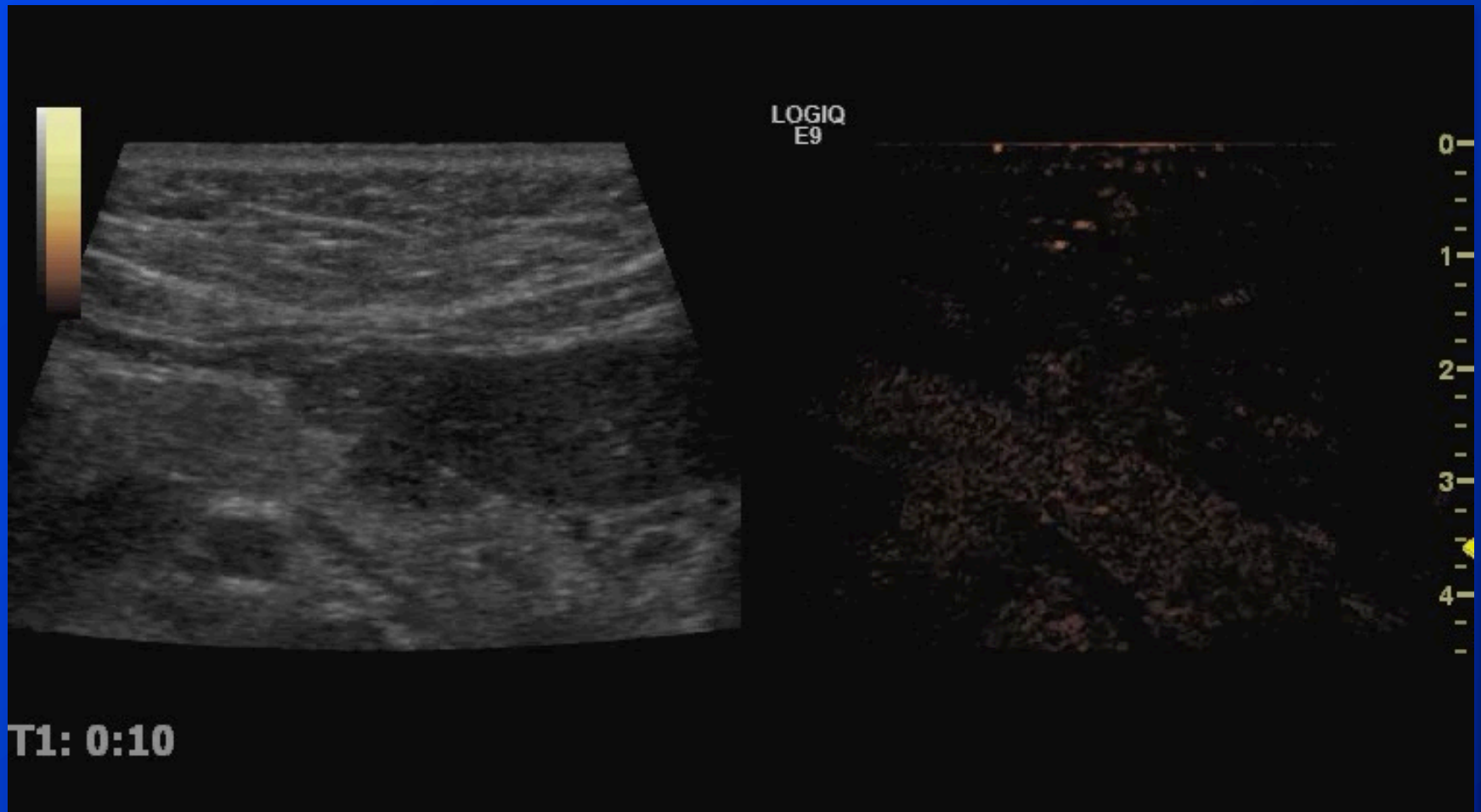


# CEUS with 3,5 MHz CLA probe





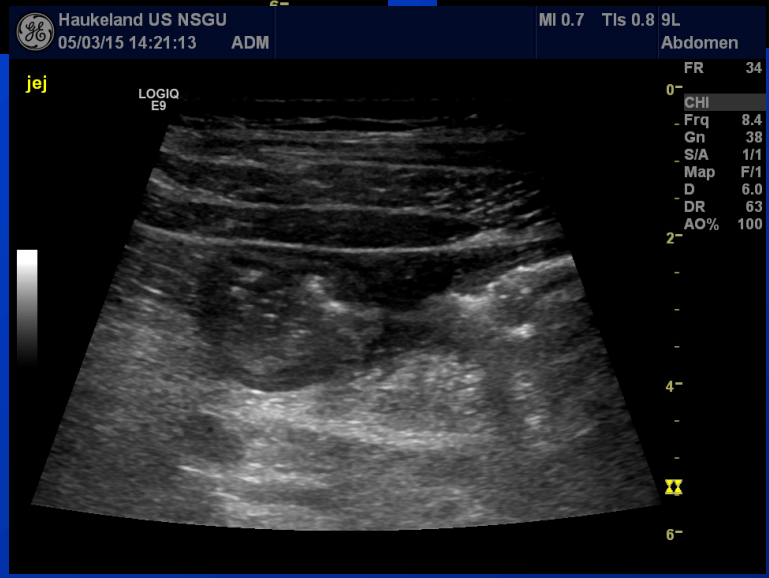
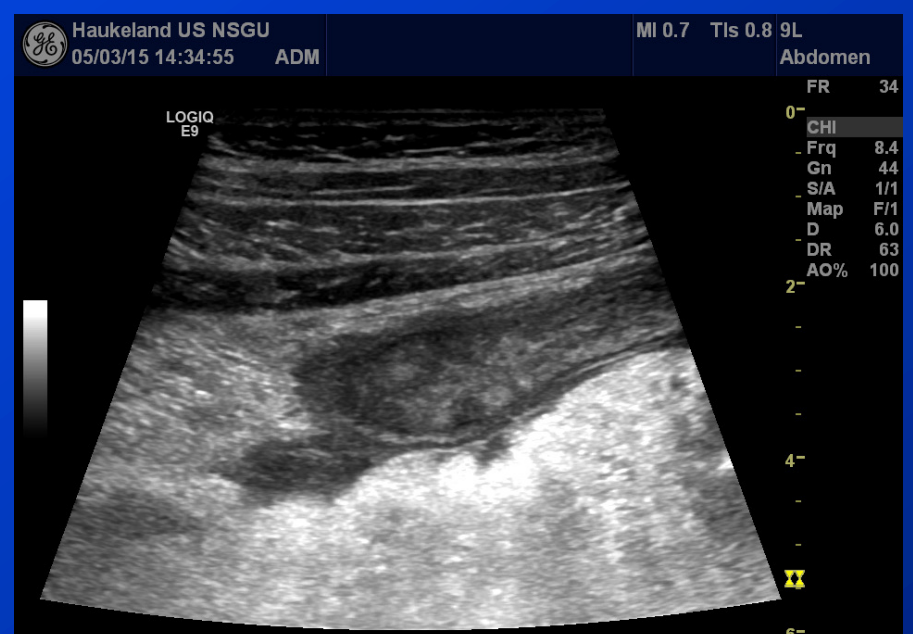
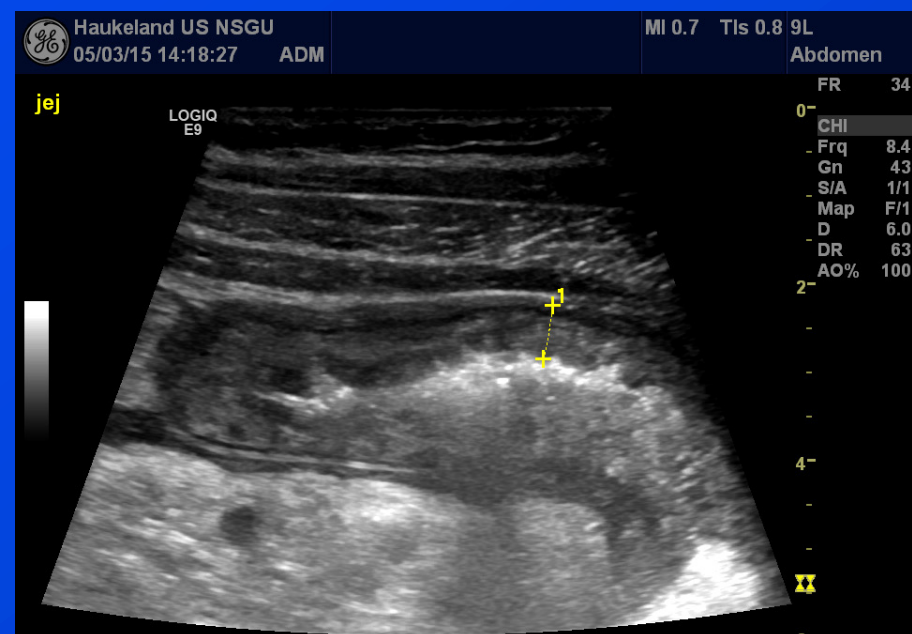
# Pancreatic Tumor – High-f CEUS



9 MHz linear probe

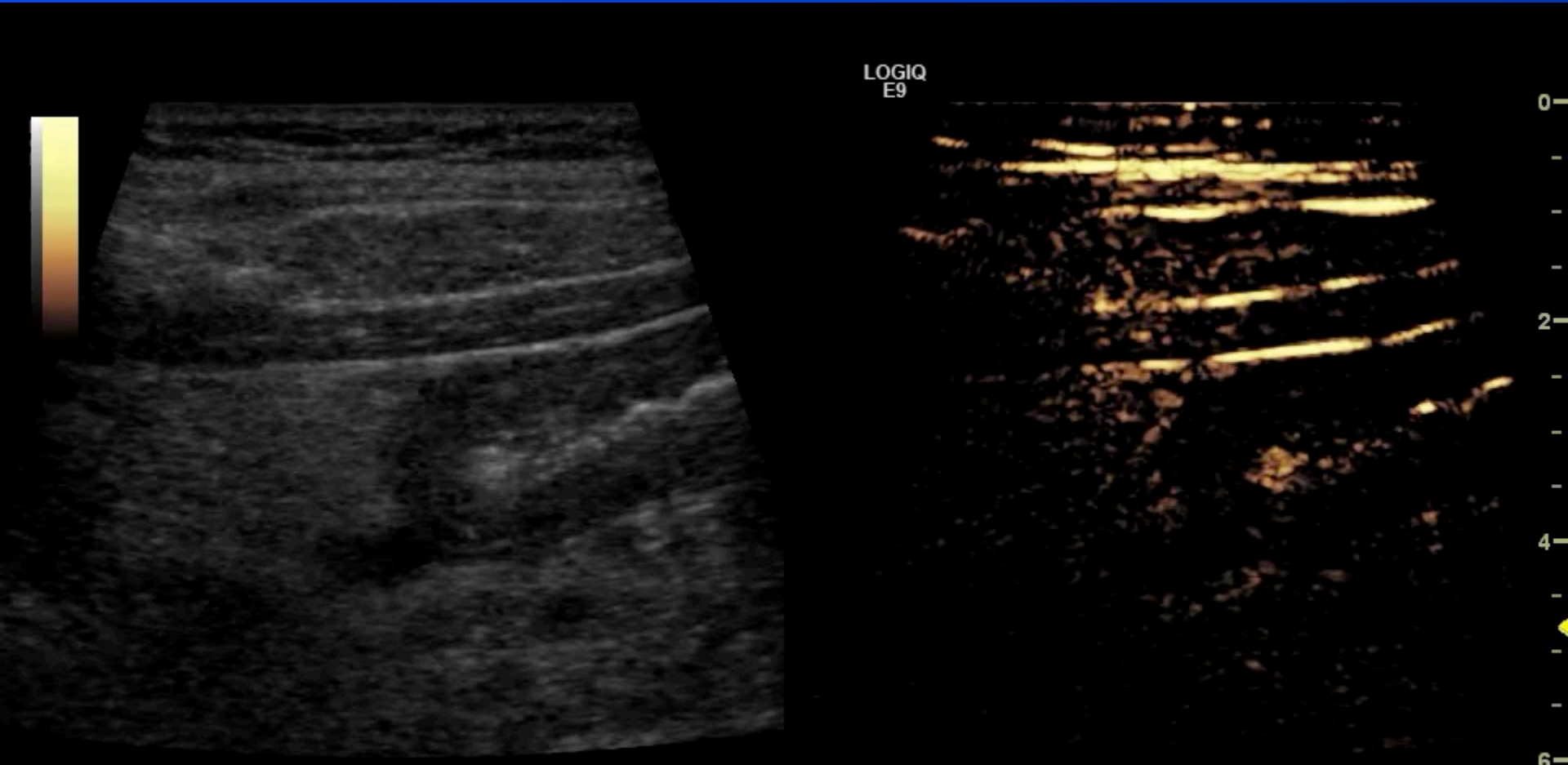


# Crohn Patient





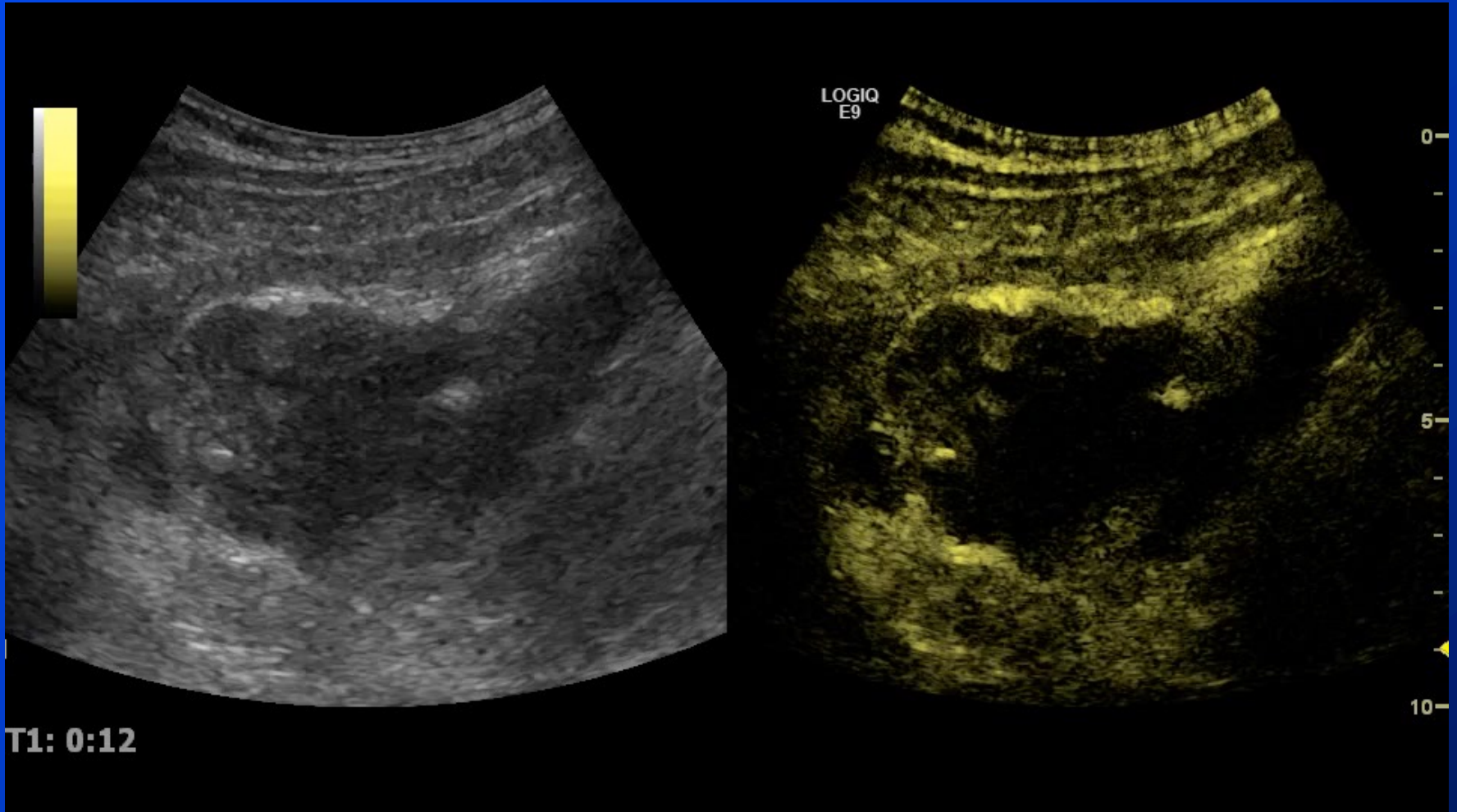
# CEUS of Jejunal loop and surrounding tissue



T1: 0:01



# Abscess detection in IBD



In right iliac fossa; note peritumoral hyperenhancement



# CEUS showing detailed intestinal perfusion in Crohn's disease







# Konklusjon

- Kontrast-undersøkelser har etablert seg i klinikken med over 30 indikasjoner
- SonoVue og Sonazoid er lett å anvende i klinisk praksis og forlenger ikke undersøkelsestiden mer enn 5-10 minutter
- Uklare CT-funn blir nå henvist til UL med kontrast
- Kontrastundersøkelser av fokale lever lesjoner diskriminerer mellom benigne og maligne lesjoner og bedrer karakteriseringen av benigne lesjoner
- CEUS er trygt å bruke bl.a. ved alvorlig nyresvikt

# Ultrasound

*Waves and bubbles that make a difference*