Contrast-enhanced EUS
Why? When? How?

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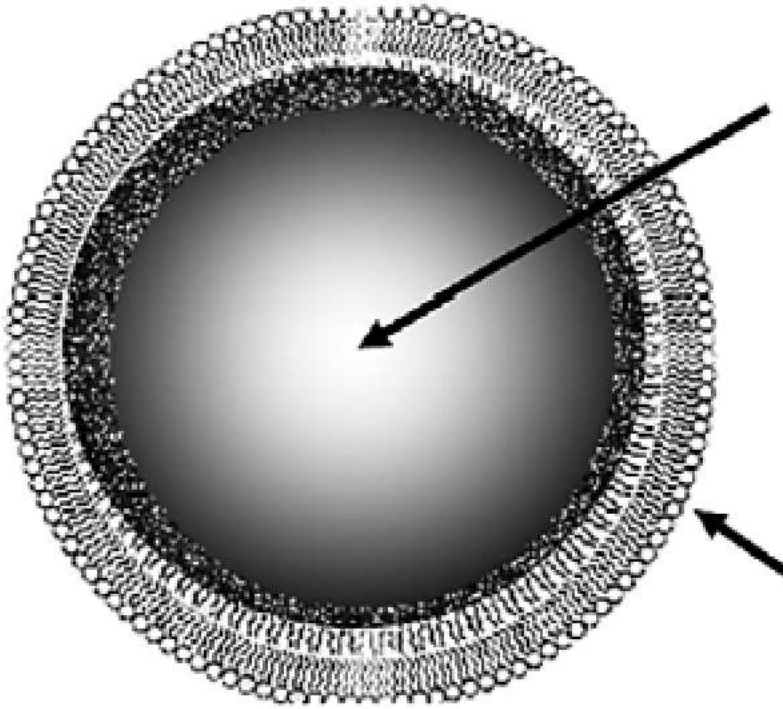
Content - Overview

Introduction – Basics in Contrast / agents – method

Sonovue – Preparation – Handling

Contrast-enhanced endoscopic ultrasound Cases

Ultrasound contrast agents (USCA)



Gas:
Levovist (Air)
Perfluorocarbon (Sonazoid, Definity)
Sulfur hexafluoride (SonoVue)

3-10 μm: pass the pulmonary capillary

Shell:
Galactose, palmitic acid (Levovist)
Phospholipid (Definity, SonoVue)
Lipids (Sonazoid)

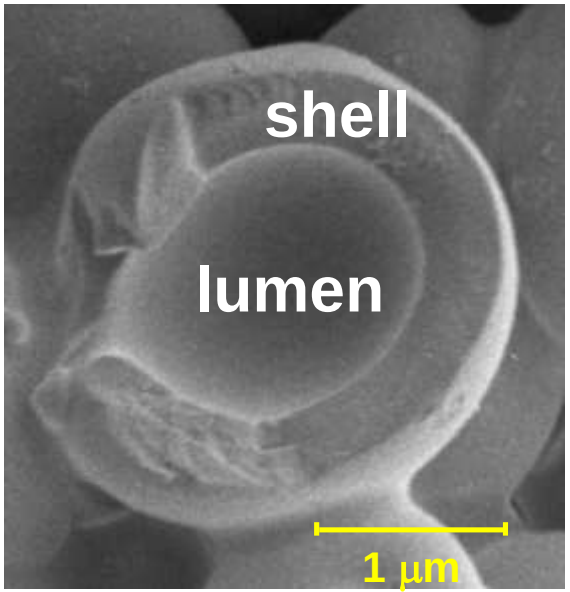
Microbubbles (MBs) of inert, stabilised gas

Ultrasound contrast agents (USCA)

Long persistence in the peripheral circulation

because:

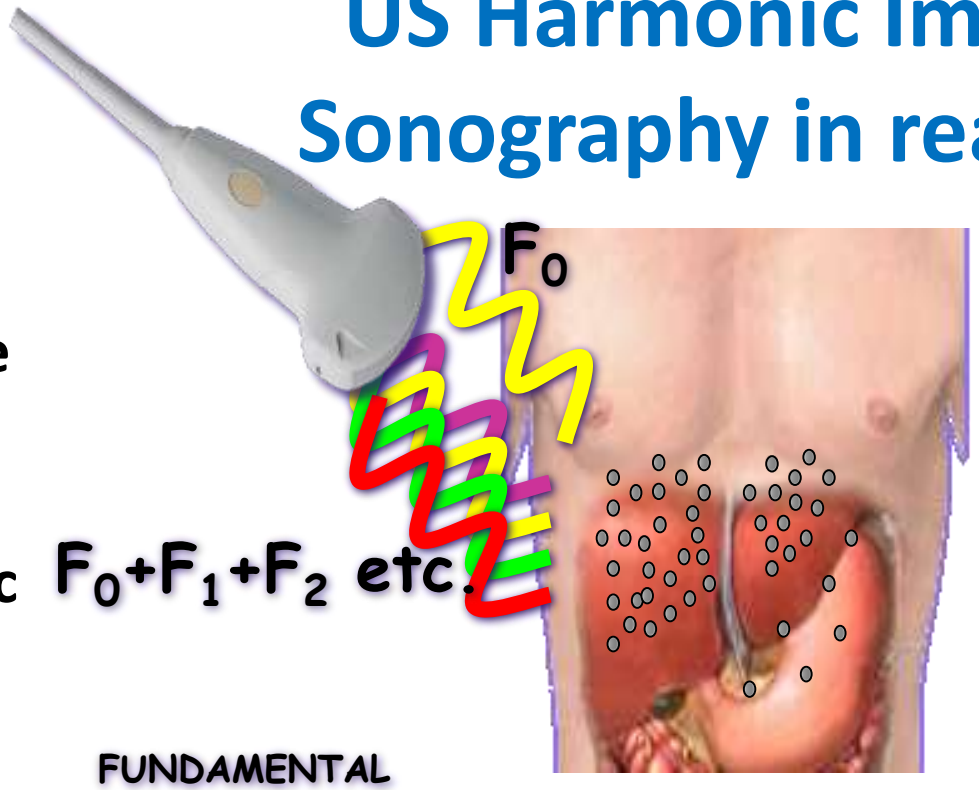
- **Shell of biocompatible material (lipids, albumin…)**
- **Low diffusion coefficient gas (sulphur hexafluoride or perfluorocarbon)**



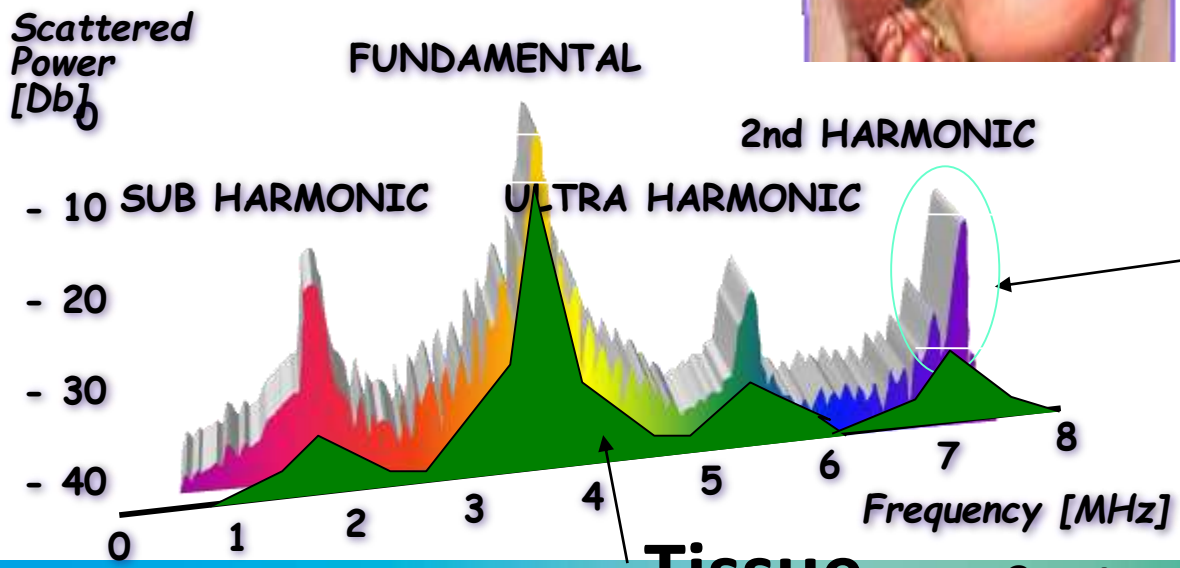
- **Specific acoustic proper**
  i.v. injected; they are limited to the intravascular space (blood pool agents)
- **enhance echoes from the entire blood pool until they are eliminated from the vascular space**

US Harmonic Imaging Sonography in real time

When the US beam hits a microbubble, it oscillates and sends back to the US machine both the fundamental and the harmonic frequencies.



By specific software, it is possible to exclude the fundamental frequency and keep only the harmonics



Courtesy of Prof. Fabio Piscaglia

Adverse reactions in CEUS CT and MRI

Contrast media	% of severe AR
SonoVue	0.009%
Ionics Iodate	0.1-0.25%
Not-ionics Iodate	0.01-0.1%
Gadolinium	0.005-0.2%

Piscaglia et al, Ultrasound Med Biol 2001

The EFSUMB Guidelines and Recommendations on the Clinical Practice of Contrast Enhanced Ultrasound (CEUS): Update 2011 on non-hepatic applications

ELSEVIER

Ultrasound in Med. & Biol., Vol. 39, No. 2, pp. 187–210, 2013

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2012.09.002

• *Guideline*

GUIDELINES AND GOOD CLINICAL PRACTICE RECOMMENDATIONS FOR CONTRAST ENHANCED ULTRASOUND (CEUS) IN THE LIVER – UPDATE 2012 A WFUMB-EFSUMB INITIATIVE IN COOPERATION WITH REPRESENTATIVES OF AFSUMB, AIUM, ASUM, FLAUS AND ICUS

Role of Contrast-Enhanced Ultrasound (CEUS) in Paediatric Practice: An EFSUMB Position Statement

In safety studies no organ-specific adverse effect

Blood tests are not required, no nephrotoxicity, no medical history data are required (except for previous allergic reaction to USCA)

SonoVue (Schwefelhexafluorid)

- 100-500 millions of MBs/mL
- Mean MB diameter = 2.5 μm
- Volume of gas within MB= 5μL/mL
- For a dose of 2.4 mL, total injected gas is 0.012 mL
- After reconstitution/reconstruction, remains stable for about 6 hours

Technical aspects of CEUS: preparation

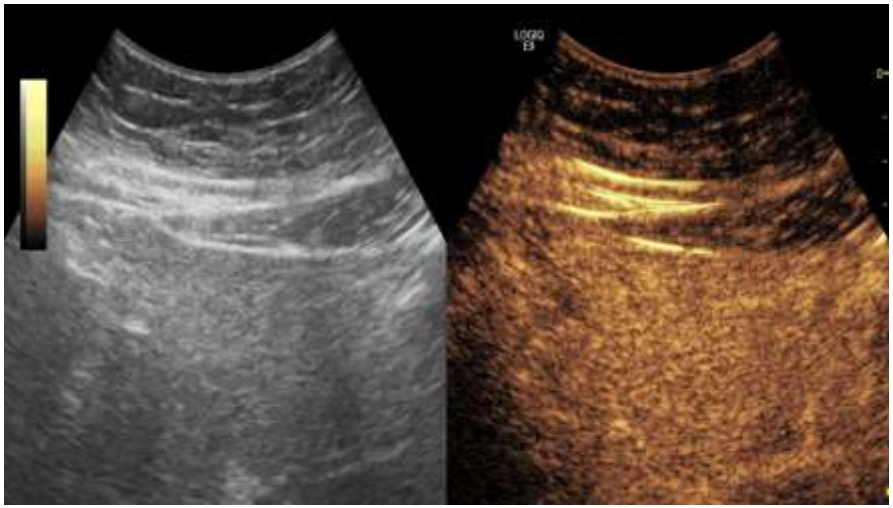
- Follow the manufacturer instructions
- Once reconstituted (after 30 seconds mixing), do not mix, violently shake or pass the liquid from and to the syringe (rupture of the microbubbles!)
- Eliminate any air contained in the syringe before the injection
- Prepare 5 ml saline solution in a separate syringe; this should be injected after the bolus of SonoVue
- Contrast media has to be prepared within 6 hours.
- Knowledge of the characteristics of each specific US machine is needed

Technical aspects of CEUS

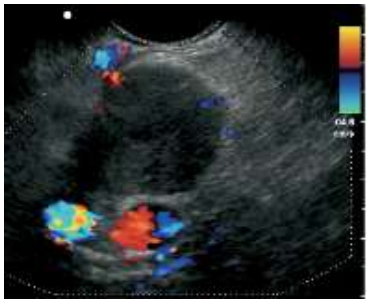
- Use a needle of at least 20 Gauge in a antecubital vein, keeping the access for at least 3 minutes before CEUS.
- Contrast injection: rapid bolus followed by a bolus saline solution (5 mL). Contrast media has to be prepared within 6 hours.
- Initial setting: in contrast images, only reference structures must remain visible (eg diaphragm, portal vein walls...) and the parenchyma must remain black (only slight noise).

CEUS for perfusion: turning the light on

- **Parenchyma: homogeneous uptake of contrast**



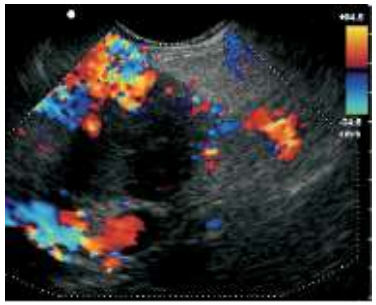
Contrast-enhanced (CE-) EUS



Conventional Doppler

✓ **Doppler/pw-Doppler mode**

= CE-EDUS

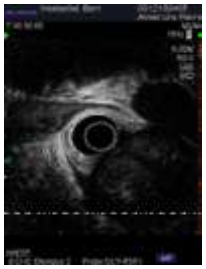


CE-pw-Doppler

influx + washout in target

can be observed in real time

microvasculature can be imaged in real time



✓ **Low mechanical index/Harmonic imaging**

= CE-LMI-EUS

European guidelines
Indications for Contrast-enhanced (CE)- EUS

Differential diagnosis*

*: Piscaglia et al. EFSUMB-guidelines: Ultraschall in Medizin 2012

- **solid** pancreatic tumor:
  - suspicion for NET
  - adeno-carcinom vs. chronic inflammation
  - improved tumor staging (venous invasion, N-status)[1]
  - help target FNA (particularly for small lesions) [2]

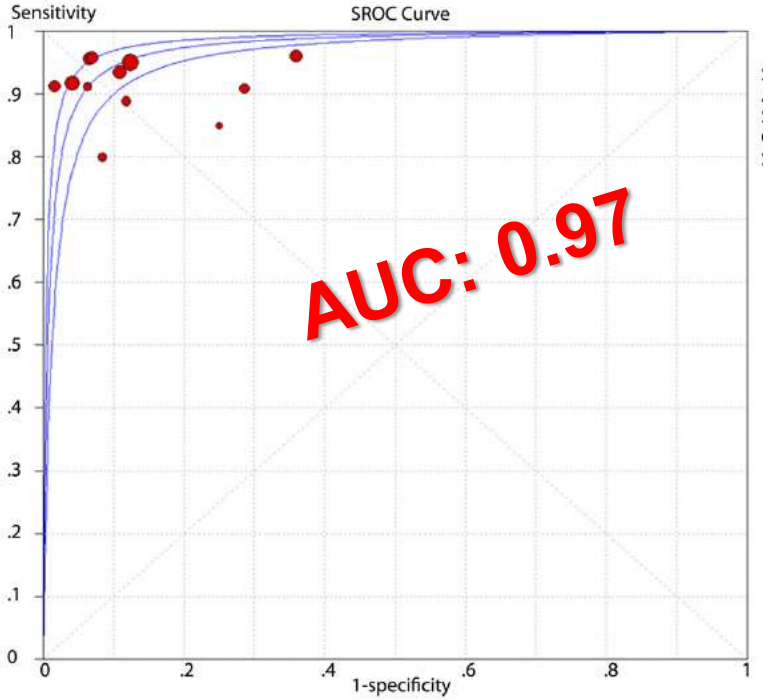
- **cystic** pancreatic tumor
  - discrimination from pseudocysts
  - help target FNA (e.g. Ohno-Classifiation) [3]

[1] Imazu ScandJGastro 2010; Kanamori A et al. AJG 2006; [2]: kitano m AJG.2012; 3: Ohno et al. Ann. Surg. 2009.

Solid pancreatic lesion: EUS-diagnostic performance

B-mode: diagnostic accuracy moderate (< 80%)

Contrast-enhanced: diagnostic accuracy excellent



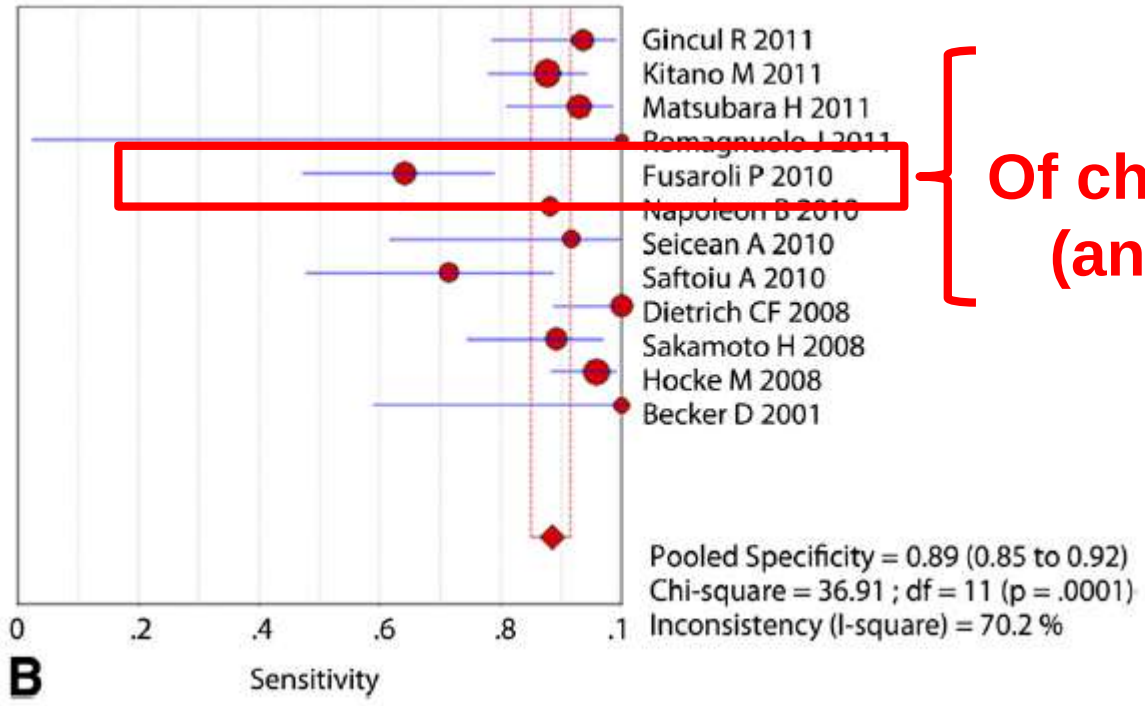
Meta-Analysis:

12 studies

1139 solid lesions

[1]Hocke et al. Z.Gastro 2012 2: Gong TT GIE 2012

CE-EUS: Meta-Analysis: Pancreatic solid lesion



Highest rate
Of chronic pancreatitis
(and severe forms)

Gong TT GIE 2012

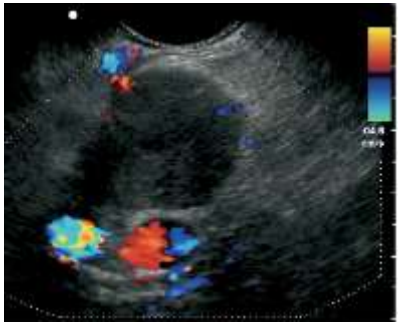
EUS-FNA: Problems in Differentiation chronic pancreatitis (CP)- Carcinoma

	No pts./ With CP	Sensitivity Without CP %	Sensitivity With CP %	P-Value
Fritscher-Ravens 2002	200/ 74	89.3%	**53.5%**	-
Varadarajulu 2005	300/75	91.3%	**73.9%**	0.02

Significantly lower sensitivity of EUS-FNA in CP due to:

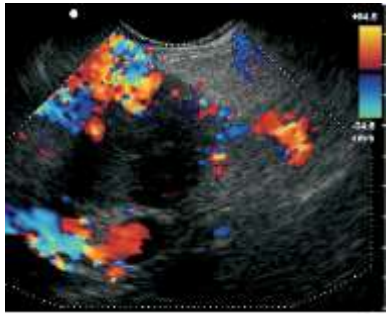
- ✓ Calcified stones can hamper vision
- ✓ desmoplastic stroma traps cancer cells, yielding only a scant aspirate.
- ✓ Collaterals make FNA challenging: considering expert-recommendation of «funnel-technique» and > 7 passes/per puncture
- ✓ Occasional atypical cells can mimic malignancy
- ✓ *Well-differentiated Ca* overlooked (lack hyperchromasia; modest increase N/C-ratio

Contrast Enhanced (CE) endoscop. Doppler US (EDUS) High-Mechanical Index (HMI)-EUS



Conventional Doppler

Adeno-Ca vs. inflammation



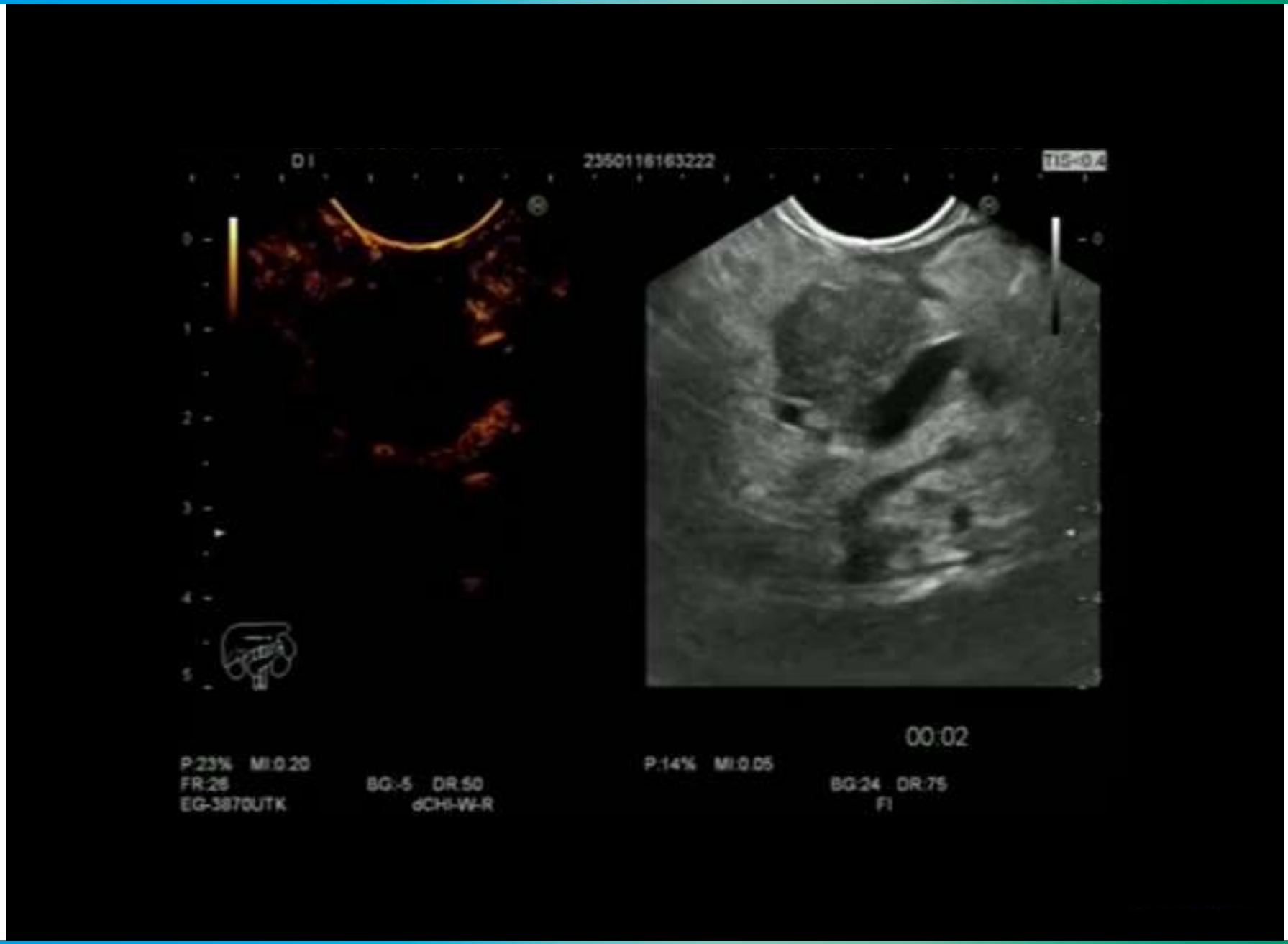
CE-pw-Doppler

- > 90% ductal adeno-carcinoma: hypoenhancing in all phases with irregular, rareficied vasculature + lack of venous vessels inflammation: homogenous network arterial + venous vessles

- Ca: due to desmoplastic reaction, low mean vascular density[1]
- Lesion size, margins and relationship with peripancreatic vessels better visualised with CE-EUS than conventional US[2]
- Positive vessel sign: associats with longer overall-survival[3]
- Differentiation diagnostic accuracy 90%

[1] Numata K et al. J Gastroenterol 2005; [2]Faccioli N et al. Pancreas 2008; 37: 265–268; 3: Yamashita et al. Pancreas 2013

Dietrich C ClinGastroHep.2008


D I
2360116163222
TIS<0.4
00:02
P:23% MI:0.20
FR:26
EG-3870UTK
BG:-5 DR:50
dCHI-W-R
P:14% MI:0.05
BG:24 DR:75
FI


R D
170709163211
41y
P:100%
MI 0.4
TIS 0.4
FR:26
EG-3870UTK
BG:14 DR:70
dTHI-W-R

Neuroendocrine Tumor: contrast-specific enhanced lesion

EUS after 2.5 ml SonoVue i.v:

Irregular Margins and/or Size>20mm are associated with malignancy In non-hypoenhancing Pancreatic lesions.

Crino et al EJOUS 2019

CE-EUS for NET:

CE-EUS hyperenhancement = NET with

AUC 0.92

even for small lesions (<15 mm)

Kitano et al. AJG 2012

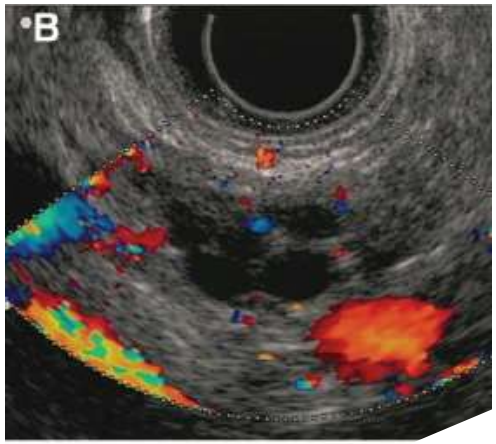
Pancreatic NET[2]

[1:] Piscaglia et al. Leitlinie;

. 2: Rosch T et al. N Engl J Med 1992


1641102163226
M
P:100%
FR:14
EG-3870UTK
BG:14 DR:70 CG:40 CF:M
dTHI-W-R 1kl5.0MHz

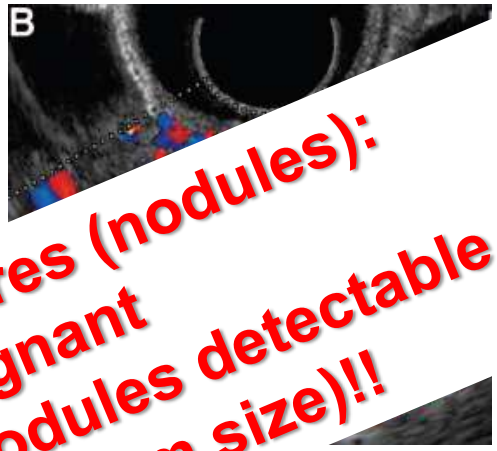
Contrast-Doppler-EUS and IPMN: risk stratification ?



Typ I:

low papillary
Nodule

Fine pro

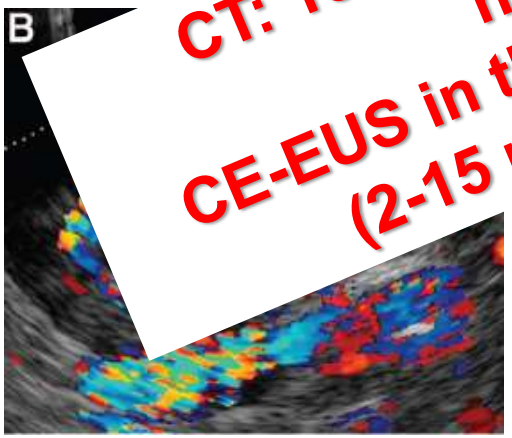


Typ II:

polypoid
Nodule

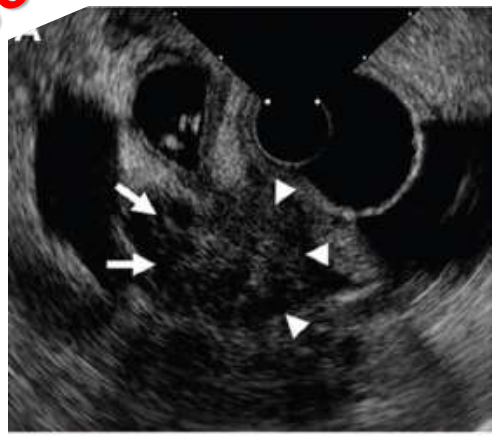
oth surfaced
Component protr.

CT: 15 no malignant features (nodules):
histology: malignant
CE-EUS in these cases: nodules detectable
(2-15 mm, in average 6 mm size)!!



papillary
Nodule

Protruding+
Thickend wall



Typ IV:

invasive
Nodule

Ill-defined
Hypoechoic area

Ohno et al. Ann Surgery 2009

CE/- EUS and Gallbladder (GB) diff[illegible]tial diagnosis

EUS supposed to be superi[illegible] US:

Proximity to duodenum + highe[illegible] vs. 5 MHz)*

Stevens P et al. In: Gress F. Endoscop[illegible]well; 2009:151–159.

- **GB-wall-thickening[illegible] chron. –itis, adenomatosis**

  MDCT (≥ 2 ph[illegible] histopatholog. correlation

  B-EUS vs[illegible] (98.5% vs. 95%) p=0.1 (n.s.)

  ->p[illegible]R 5), hypoechoic internal -enicity (OR 6.6)

  CE-[illegible]-EUS[2]: overall diagnostic accuracy ▲ (p<0.05)

  -> pred[illegible]ogenous CE-distribution (OR 72)

[illegible]Kim et al. DigDisSci 2012, [2]:Imazu et al. DIgDisSci 2014;

Talk to surgeon: if
B-mode: wall > 10 mm + disruption of 2 layers
(particularly if NO gallstones)
Urge your surgeon: if additionally
CE-EUS: + inhomogenous contrast

Thank you for your attention