**Contrast Enhanced Ultrasound**

Andrei Lyshchik, MD, PhD.
Department of Radiology
Thomas Jefferson University Hospital

**Microbubbles**

- Encapsulated heavy gas/air mixture (PFC, SF6)
- Lipid, albumin, or polymer shell
- Diameter 2-10 μm
- Administered by intravenous injection
- Dissolve in circulation (~15 min)
  - Shells metabolized by liver
  - Gas excreted by lungs

Kaufmann and Lindner, 2007

**Available contrast agents**

- Definity (Lantheus Medical Imaging)
- Optison (GE Healthcare)
- Lumason (Bracco Diagnostics)

**Definity preparation**

**Lumason preparation**

**Optison preparation**

http://www.escardio.org/
**Contrast dose**

Liver / Renal Imaging

- Definity: 0.2 – 0.3ml
- Lumason: 1.0 – 2.4ml
- Optison: 0.5 – 1.0ml

- The dose could be adjusted for individual patient and application.

**Contraindications**

- Right-to-left or bi-directional cardiac shunts
- Prior hypersensitivity reactions
- Intra-arterial injection

**Adverse effects**

- Usually very mild
  - Headache, dizziness
  - Flushing
  - Allergic reactions
  - Shortness of breath
  - Back, renal, or chest pain
  - Hyper- or hypotension

**Clinical applications**

- Liver tumors
- Renal masses
- Adnexal masses
- Interventional procedure guidance

**Focal Nodular Hyperplasia**

Baseline

Arterial Phase

Portal Phase

Late Phase
LI-RADS® v2017 CEUS Core

DIAGNOSTIC CATEGORIES

Definitely benign

Probable benign

Intermediate probability of malignancy

Probably HCC

Definitely HCC

Definitely HCC with tumor in vein

Not categorizable (due to image omission or degradation)

Step 1. Apply CEUS LI-RADS® Diagnostic Algorithm

1. ceus LI-RADS® Diagnostic Algorithm

2. CEUS LR-1

3. CEUS LR-2

4. CEUS LR-3

5. CEUS LR-4

6. CEUS LR-5

Step 2. Optional: Apply CEUS Ancillary Features (AF)

CEUS ancillary features may be used at interpreter's discretion for:

- Increased confidence or category adjustment

For category adjustment (upgrade or downgrade), apply CEUS AF as follows:

- ≥ 1 AF favoring malignancy: upgrade by 1 category up to LR-4
- 1 AF favoring malignancy: upgrade by 1 category up to LR-4
- 1 AF favoring malignancy: downgrade by 1 category

AFs cannot be used to upgrade to LR-5

CEUS Diagnostic Table

<table>
<thead>
<tr>
<th>Arterial phase hyperenhancement (APHE)</th>
<th>No APHE</th>
<th>APHE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation size (mm)</td>
<td>&lt; 20</td>
<td>≥ 20</td>
</tr>
<tr>
<td>Washout</td>
<td>No</td>
<td>CEUS LR-1</td>
</tr>
<tr>
<td>Late and mild washout</td>
<td>CEUS LR-2</td>
<td></td>
</tr>
<tr>
<td>Marked washout</td>
<td>CEUS LR-3</td>
<td></td>
</tr>
</tbody>
</table>

* No rim enhancement
* Not peripheral discontinuous globular (indicates hemangioma)

If unsure about APHE or any major feature, characterize that feature as absent.

Renal masses
$E_{\text{max}} = 0.41 \, \text{dB}$

$T_{1/2} = 7.5 \, \text{sec}$

$AUC = 15.3 \, \text{sec}$

$E_{\text{max}} = 17.6 \, \text{dB}$

$T_{1/2} = 15.5 \, \text{sec}$

$AUC = 424 \, \text{sec}$
E\text{\textsubscript{max}} = 27.9 \text{ dB}

T\text{\textsubscript{\textfrac{1}{2}}} = 128 \text{ sec}

AUC = 2693.7 \text{ sec}

Targeting of the needle in the vascular, viable areas of several tumors

Avoiding necrotic / avascular areas in larger tumors or in those with frequent necrosis;

Targeting of otherwise invisible lesions or those hardly visible (small nodules of HCC on cirrhosis, adenocarcinoma's areas in the prostate)
Investigational uses of US contrast include:

- Plaque characterization / assessment of cardiovascular risks
- Evaluation of trauma / detection of bleeding
- Detection and characterization of sentinel lymph nodes / staging of cancer
- Therapeutic procedures / treatment of thrombus and malignant tumors

Investigational uses of CEUS

- Evaluation of sentinel lymph nodes in patients with cancer is necessary to
  - stage disease
  - determine proper therapy
  - predict patient prognosis

Contrast-enhanced ultrasound detection of sentinel lymph nodes (SLNs)

- Evaluation of sentinel lymph nodes in patients with cancer is necessary to
  - stage disease
  - determine proper therapy
  - predict patient prognosis

Three-dimensional CEUS of multiple lymphatic channels (arrows) and SLNs (S) identified after injection of contrast at tumor site

CEUS assisted biopsy

CEUS assisted liver RFA

CEUS: Monitoring tumor therapy response

Two different patients with renal cell carcinoma metastasis treated with Sorafenib®

Patients were considered “good responders” or “bad responders” based on the results of CT done at 6 months

Courtesy Dr. Lassau, France
CEUS appearance of SLNs

- Normal SLNs demonstrate uniformly increased echogenicity (i.e., contrast enhancement)
- SLNs with metastases demonstrate filling defects (i.e., non-uniform enhancement)

SLNs as small as 4mm can be detected

SLN with metastatic tumor deposits (T)

Guidelines

GUIDELINES AND GOOD CLINICAL PRACTICE RECOMMENDATIONS FOR CONTRAST ENHANCED ULTRASOUND (CEUS) IN THE LIVER – UPDATE 2012
A VUMBIF-ESUMRI INITIATIVE IN COOPERATION WITH REPRESENTATIVES OF AFUMB, ASUM, FLAM, IACUS AND IUCS

Michel Claudon,1* Cristina F. M. Dias,1* Beting Hs Chao,2 Denis O. Caudron,3 Massimiliano Kolb,4 Christian F. Niggli,5 Fiona Pecckull,5 Sophie R. Wodicka,6 Richard G. Robb,7 Matteo C. Crisafulli,8 Nino G. Chinnock,9 Min-Huei Chen,10 Dina Andric-Cvetkovic11 jan Michel,12 Craig Dink,13 Fumio Fujisawa,14 J. Brian Fyfe,15 Robert N. Gobbin,16 Barry B. Goldberg,17 Saedal Rahi,10 Edward L. S. Lin,7 Robert F. Monk,17 Fumio Fujisawa,14 Louis Sorel,4 Ho-Ping Wannet12 and Ho-Sung Xu12

* Guideline

General overview, steering committee and contributions

<table>
<thead>
<tr>
<th>Section</th>
<th>Responsibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREAMBLE</td>
<td>Michel Claudon, Christian F. M. Dias, Beting Hs Chao, Denis O. Caudron, Massimiliano Kolb, Sophie R. Wodicka, Richard G. Robb, Matteo C. Crisafulli, Nino G. Chinnock, Min-Huei Chen, Dina Andric-Cvetkovic, jan Michel, Craig Dink, Fumio Fujisawa, J. Brian Fyfe, Robert N. Gobbin, Barry B. Goldberg, Saedal Rahi, Edward L. S. Lin, Robert F. Monk, Fumio Fujisawa, Louis Sorel, Ho-Ping Wannet, and Ho-Sung Xu</td>
</tr>
<tr>
<td>1. GENERAL CONSIDERATIONS (TECHNICAL ASPECTS)</td>
<td>Michel Claudon, Christian F. M. Dias, Beting Hs Chao, Denis O. Caudron</td>
</tr>
<tr>
<td>2. CEUS FOR CHARACTERIZATION OF LOCAL LIVER LESIONS</td>
<td>Cristina F. M. Dias, Beting Hs Chao, Denis O. Caudron, Massimiliano Kolb, Sophie R. Wodicka, Richard G. Robb, Matteo C. Crisafulli, Nino G. Chinnock, Min-Huei Chen, Dina Andric-Cvetkovic,</td>
</tr>
</tbody>
</table>