Where Contrast Administration Makes a Difference
Contrast 2017
State of the Art

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No disclosures
Contemporary Ultrasound Contrast Agents

Stabilized gas microspheres sized to pass through the smallest capillaries

Microsphere: 2-5 µm

RBC: 6-8 µm

Currently available agents

<table>
<thead>
<tr>
<th>Name</th>
<th>Shell</th>
<th>Gas</th>
<th>Size (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optison</td>
<td>Albumin</td>
<td>Octafluoropropane</td>
<td>2-4.5</td>
</tr>
<tr>
<td>Definity</td>
<td>Lipid/surfactant</td>
<td>Octafluoropropane</td>
<td>1.1-3.3</td>
</tr>
<tr>
<td>Imagent</td>
<td>Lipid/surfactant</td>
<td>Perfluorohexane</td>
<td>6.0</td>
</tr>
<tr>
<td>Sonovue/Lumason</td>
<td>Lipid</td>
<td>Sulfur hexafluoride</td>
<td>1.5-2.5</td>
</tr>
</tbody>
</table>
Interaction of Ultrasound and Microbubbles

- Linear resonance
- Nonlinear resonance
- Transient scattering

- Fundamental enhancement
- Harmonic enhancement
- Bubble disruption


Principles of Harmonic Imaging

- Tissue and blood reflect at the fundamental frequency
- Microbubbles reflect at both the fundamental and the harmonic frequencies

It’s all about signal to noise!
**Machine Settings**

- **For most applications**
  - Aim to maximize non-linear harmonic reflecting responses (MI 0.1-0.4)
    - Improves signal to noise vs tissue
- **Equipment**
  - Optimized settings (presets)
    - Contrast agent specific
    - Transducer specific
- **For perfusion applications**
  - Controlled bubble destruction
  - Works best with equipment specifically equipped to do perfusion imaging

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GUIDELINES AND STANDARDS

Guidelines for the Cardiac Sonographer in the Performance of Contrast Echocardiography: A Focused Update from the American Society of Echocardiography

Thomas R. Potter, MD, FASE (Chair); Sahar Abdelmoneim, MD; Todd Bevila, BS, RCS, RDMS, FASE; Mari L. McCollough, MBA, RDMS, FASE; Sharon L. Mulcahy, MD, FASE; Jason J. Olson, BS, RDMS, BVSI, FASE; Charlene Porcelli, BS, RDMS, RDCS, FASE; Jesse M. Punti, MD, and Kevin Wei, MD, FASE; Omaha, Nebraska; Minneapolis, Minnesota; Portland, Oregon; Houston, Texas; Chesapeake, South Carolina; Rio Ponsa, Brazil

(J Am Soc Echocardiogr 2014;27:797-810.)

Keywords: Echocardiography, Sonography, Contrast, Imaging

APPROPRIATE USE CRITERIA

ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 Appropriate Use Criteria for Echocardiography

A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Cardiology, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance

Endorsed by the American College of Chest Physicians

Table 1A. Contrast Use in TTE/TEE or Stress Echocardiography

<table>
<thead>
<tr>
<th>Indication</th>
<th>Appropriate Use Score (1-9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>201. A routine use of contrast. All LV segments visualized on noncontrast images</td>
<td>1 (L)</td>
</tr>
<tr>
<td>202. A selective use of contrast. &gt;2 contiguous LV segments are not seen on noncontrast images</td>
<td>A (B)</td>
</tr>
</tbody>
</table>
GUIDELINES AND STANDARDS

Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

Roberto M. Lang, MD, FASE, FESC, Luigi P. Badano, MD, PhD, FESC, Victor Mor-Avi, PhD, FASE, Jonathan Allen, MD, MSc, Anderson Armstrong, MD, MSc, Laura Ernande, MD, PhD, Frank A. Flachskampf, MD, FESC, Ellye Foster, MD, FASE, Steven A. Goldman, MD, Tatiana Kuznetsova, MD, PhD, Patrik Lanciloti, MD, PhD, FESC, Dennis Munzur, MD, PhD, Michael H. Picard, MD, FASE, Ernst R. Rietzschel, MD, PhD, Lawrence Rudski, MD, FASE, Kirk T. Spencer, MD, FASE, Wendy Tsang, MD, and Jens-Uwe Vogt, MD, PhD, FESC, Chicago, Illinois; Padua, Italy; Montreal, Quebec and Toronto, Ontario, Canada; Baltimore, Maryland; Civitavecchia; France; Uppsala, Sweden; San Francisco, California; Washington, District of Columbia; Leuven, Liege, and Ghent, Belgium; Boston, Massachusetts

Contrast agents should be used when needed to improve endocardial delineation when two or more contiguous LV endocardial segments are poorly visualized in apical views. As per published guidelines.1

IAC Standards and Guidelines for Adult Echocardiography Accreditation

Use of Contrast for Suboptimal Image Quality – Contrast is indicated for use when two contiguous segments are not visualized in any three of the apical views (poor endocardial border definition) as it provides greater accuracy as determining left ventricular function.7

1.6.3.1B If contrast is used, there must be a written policy for the use of contrast agents.

1.6.3.2B If contrast is not able to be used there must be a policy for alternative imaging

Comment: Poor endocardial border definition is defined as the inability to detect two or more contiguous segments in any three of the apical views.
Case Examples

Left Ventricular Opacification

62 yo female with aortic and mitral valve disease
Is the EF <60%
Accurate LVEF needed for clinical decision making
LVEF 64%  

Stress echo
With thanks to Sharon Mulvagh

62 yo female with atrial fibrillation (spontaneously converted) and dyspnea
Dx: Apical HCM
Not CAD

Another myopathy
52 yo male with NYHA Class III Heart Failure
76 yo female with syncope
32 yo male with atrial fibrillation and family history of SCD
Dx: ARVD
Myocardial Contrast Perfusion

Thanks to Tom Porter, MD

Post PCI

Thanks to Tom Porter
Safety Concerns
Class Box Warning

WARNING: Serious Cardiopulmonary Reactions

Serious cardiopulmonary reactions, including fatalities, have occurred uncommonly during or following microsphere administration (see Warnings and Precautions (5.1)). Most serious reactions occur within 30 minutes of administration.

- Assess all patients for the presence of any condition that precludes administration (see Contraindications (4)).
- Always have resuscitation equipment and trained personnel readily available.

Old contraindications

CONTRAINDICATIONS

Do not administer to patients with known or suspected right-to-left, bidirectional or transient right-to-left cardiac shunts, by intra-arterial injection, or to patients with known hypersensitivity to
Current for all agents

CONTRAINDICATIONS:
Do not administer to patients with known or suspected hypersensitivity to

INDICATIONS AND USAGE:
LUMASON is an ultrasound contrast agent indicated for use:

- in echocardiography to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border in adult patients with suboptimal echocardiograms
- in ultrasonography of the liver for characterization of focal liver lesions in adult and pediatric
CARPA

Complement Activation Related Pseudo-Allergy

CARPA Signs and Symptoms

- Angioedema
- Bronchospasm
- Cyanosis
- Hypotension
- Low back pain
- Pruritis
- Urticaria
- Tingling sensation
- Hypoxemia
- Sneezing
Acute Hypersensitivity Reactions

IgE mediated type I
- Reaction after repeated exposure
- Reaction is stronger upon repeated exposure
- Reaction does not cease without treatment

CARPA
- No prior exposure necessary
- Reaction is milder or absent upon repeated exposures
- Spontaneous resolution

Szebeni J. Toxicology 2005:216:106-121

Note that prior “allergic” reaction is contra-indication to use of same/similar agent
## Event Rates for Commonly Performed Cardiovascular Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Event Rate</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary Angiography</td>
<td>1:1000</td>
<td>Death</td>
</tr>
<tr>
<td>Exercise Treadmill Testing</td>
<td>1:2500</td>
<td>MI or Death</td>
</tr>
<tr>
<td>SPECT Exam or Radionuclide Ventriculography</td>
<td>1:1000 to 1:10,000</td>
<td>Fatal Malignancy</td>
</tr>
<tr>
<td>Contrast Echocardiography</td>
<td>1:500,000</td>
<td>Death</td>
</tr>
</tbody>
</table>

### Pulmonary Hypertension
Using propensity matching, CE associated with a 28% lower mortality at 48 h in comparison with patients undergoing nTTE.
Interatrial Shunt

Safety of Ultrasound Contrast Agents in Patients With Known or Suspected Cardiac Shunts

Jeremy M. Parker, MD\textsuperscript{a}, Mark W. Weller, JD\textsuperscript{b}, Linda Maiman Feinstein, JD\textsuperscript{b}, Robin J. Adams, BS\textsuperscript{b}, Michael L. Main, MD\textsuperscript{b}, Paul A. Grayburn, MD\textsuperscript{d}, David O. Cosgrove, MD\textsuperscript{d}, Barry A. Goldberg, MD\textsuperscript{d}, Kassa Darge, MD, PhD\textsuperscript{e}, Petros Nihoyannopoulos, MD\textsuperscript{f}, Stephanie Wilson, MD\textsuperscript{f}, Mark Monaghan, PhD\textsuperscript{f}, Fabio Piscaglia, MD\textsuperscript{f}, Brian Fowlkes, PhD\textsuperscript{f}, Wilson Mathias, MD\textsuperscript{f}, Fuminari Moriyasu, MD, PhD\textsuperscript{f}, Maria Christina Chammas, MD, PhD\textsuperscript{d}, Lennard Greenbaum, MD\textsuperscript{f}, and Steven B. Feinstein, MD\textsuperscript{f, g}

Parker JM et al. \textit{Am J Cardiol} 2013;112:1039-1045
Cost-effectiveness
Thx to Michael Main


And yet contrast is underutilized

Contrast Echocardiography as a Percentage of Total Echocardiography

Thx to Michael Main
Obstacles

• “Internal” (Lab operations)
  • Time
  • Orders
  • Consent
  • Personnel with IV skills / Scope of practice
  • Access to agent

• “External”
  • Cost considerations
  • Black box warning

STREAMLINE

- Decision
- Order/Consent
- Personnel
- Agent
- Machine Optimization / Protocols
- Reduce/eliminate time to obtain order
  - Incorporate order for contrast into order for echocardiogram
  - Standing orders
    - a written document containing rules, policies, procedures, regulations, and orders for the conduct of patient care in various stipulated clinical situations
  - Develop policy for consent
- Have ready access to personnel trained to insert IV and administer agent
  - Create staffing model that ensures that echo labs have qualified non-sonographer personnel available
    » RN
    » Cardiology fellow
  - Cross-train sonographers (scope of practice/personal preference)
- In hospital on floors
  - In-service for nursing staff
– Have ready access to agent/equipment
  • Consider storing in high use sites (ICU's)
• Optimize machine settings
  – Presets
    • Agent specific
    • Transducer specific
    • Frequency specific
  – Focal zone

• Protocols
  – Infusion rate
  – Look at more than the LV blood pool
    • RV
    • Great vessels
    • Doppler

• Resource person
Cost Considerations

“There is inadequate reimbursement to cover the cost of contrast “

Solutions:
For outpatient studies, there is reimbursement
  Document guideline driven indication
For inpatient studies, cost of agent can be recaptured by reduction in other costs
  Create/defend contrast budget

<table>
<thead>
<tr>
<th>Indication for Study</th>
<th>Quality of Images</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>poor</td>
</tr>
<tr>
<td>Chest pain - angina?</td>
<td></td>
</tr>
<tr>
<td>LV Thrombus</td>
<td></td>
</tr>
<tr>
<td>Stress echo</td>
<td></td>
</tr>
<tr>
<td>ΔLVEF (chemo)</td>
<td></td>
</tr>
<tr>
<td>LVEF for ICD or BiV</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td></td>
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<tr>
<td>Aortic dissection</td>
<td></td>
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<tr>
<td>Atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td>Valve disease</td>
<td></td>
</tr>
<tr>
<td>Pericardial disease</td>
<td></td>
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</table>

With thanks to Jonathan Lindner
Summary

• Contrast has been repeatedly shown to improve the accuracy and reproducibility of LV volume /EF assessment
  – Multiple off label uses
• Safety profile is excellent
• After “hit” triggered by black box warning utilization is increasing

Summary

• Thoughtful approach to streamlining all steps in utilization chain is essential to optimal utilization and appropriate use of health care resources