## When Do We Need Contrast? How Can ItBe Implemented?

Anthony DeMaria

Judy and Jack White Chair in Cardiology

University of California, San Diego

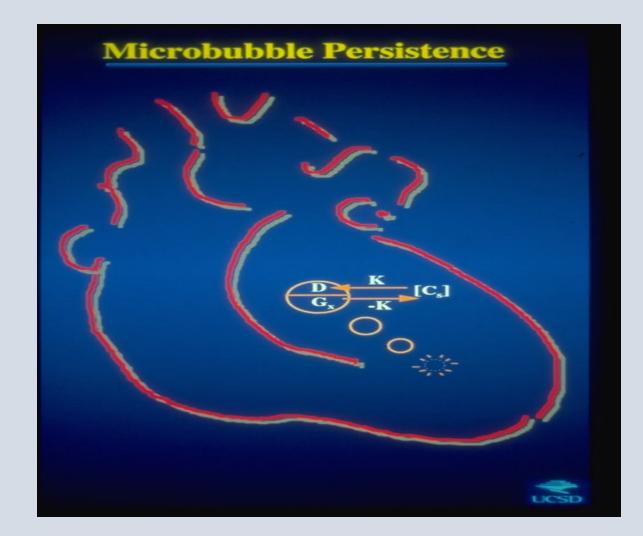
#### **Contrast Echo: General Concepts**

- Terminology: Contrast Agents vs Enhanced Ultrasound Agents
- Contrast Agents are Microbubbles and are Safe
- The Intersocietal Accreditation Commission has required that policies be in place for UEA use
- Reimbursement is established for LV Opacification
  - Hospital (DRG), Hospital Lab (folded into CPT), Office or IDTF add on
- The American Medical Association CPT Panel approved a category III ("emerging technology") CPT code (+0439T) for "myocardial contrast perfusion echocardiography" as an add-on for ischemia/viability

#### Microbubbles Make Contrast

- Large acoustic impedance difference
  - Low density and high compressibility
- Oscillate at frequency of ultrasound
  - Linear signals (low energy)
  - Harmonics or non-linear signals (high energy)
- Thus, both reflect and generate signals
- Optimal size 4-6 micron
  - Too small to embolize; big enough to reflect

#### Microbubble Properties: Shell and Gas



#### Contrast Agent Properties

Agent	Mean Size (u)	<u>Gas</u>	<u>Shell</u>	
Levovist	2-3	Air	(Galactose)	
Optison	4.7	Perflouropropane	albumin	
Definity	1.5	Perflouropropane	phospholipid	
Imagent	5.0	Perflourohexane-N	Surfactant	
Lumason (Sonovue)	2.5	Sulfur hexaflouride	Phospholipid	
Cardiosphere	4.0	Nitrogen	Polymer	
Acusphere	2.0	Perflourocarbon	Polymer	

#### Hypersensitivity Reactions to Contrast

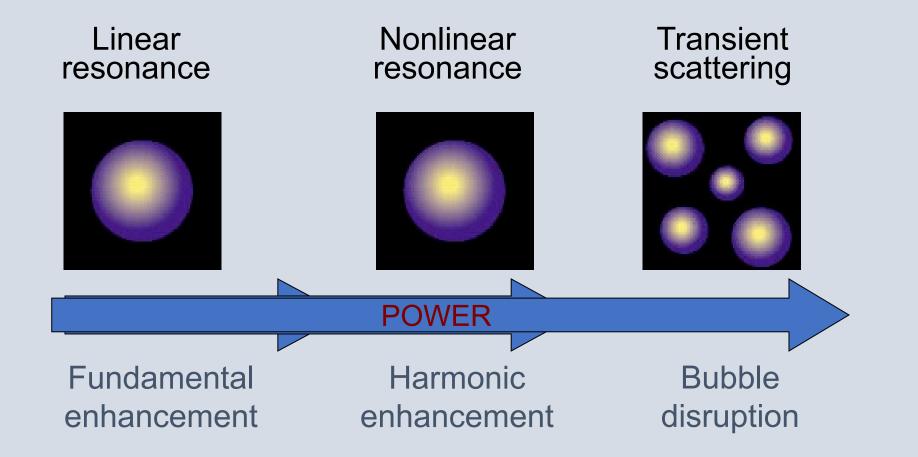
- Complement activation-related pseudoallergy (CARPA)
  - Most common form of immune related events
- e IgE-mediated Type I hypersensitivity reactions to PEG components
  - Polyethylene glycol contained in vehicle or shell

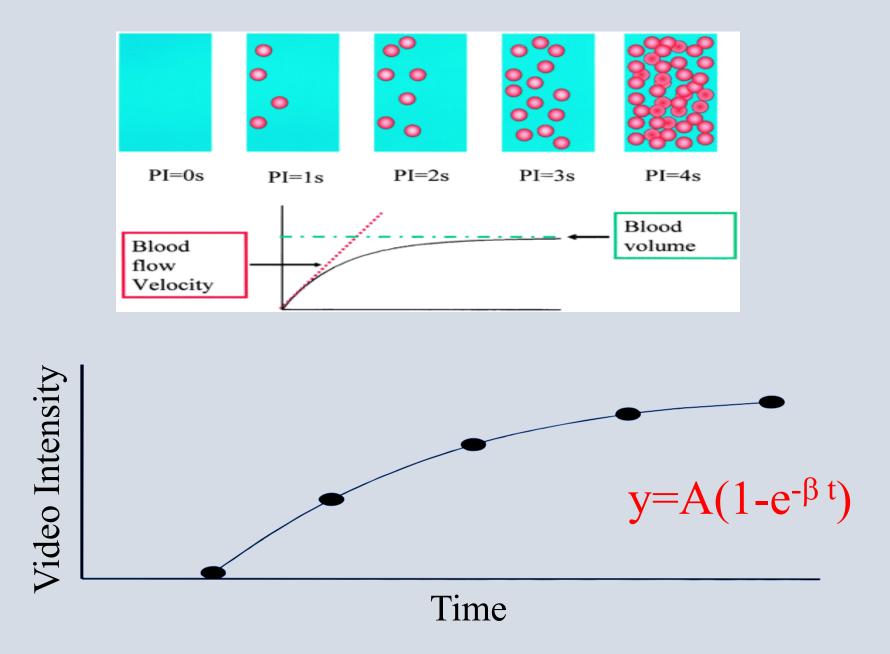
Both are treated similarly: epinephrine, steroids, antihistamines, support

#### Studies on the Safety of Contrast Agents

Study	Design	UEA	Total patients	UEA patients	Control patients	Inpatient/outpatient	Rest/stress	Outcomes
Aggeli <i>et al.</i> (2008) <sup>7</sup>	Prospective	Sonovue	5,250	5,250	NA	NR	Stress	No deaths or myocardial infarctions
Gabriel <i>et al.</i> (2008) <sup>8</sup>	Retrospective	Definity or Optison*	9,798	4,786	5,012	95% Outpatients	Stress	No increased rate of SAEs or mortality at 24 h in UEA patients
Herzog <i>et al.</i> (2008) <sup>9</sup>	Retrospective	Definity or Optison	16,025	16,025	NA	Both	Both	No short-term mortality; SAEs in 0.031%
Kusnetzky <i>et al.</i> (2008) <sup>10</sup>	Retrospective	Definity	18,671	6,196	12,475	Inpatients	Rest	No increased mortality in UEA patients
Main <i>et al.</i> (2008) <sup>11</sup>	Retrospective	Definity	4,300,966	58,254	4,242,712	Inpatients	Rest	No increased mortality in UEA patients
Shaikh <i>et al.</i> (2008) <sup>12</sup>	Retrospective	Definity or Optison	5,069	2,914	2,155	Both	Stress	No increased risk for SAEs in UE patients
Wei <i>et al.</i> (2008) <sup>13</sup>	Retrospective	Definity or Optison	78,383	78,383	NA	Both	Both	Severe allergic reactions in 0.019 and anaphylactoid reactions ir 0.006%
Abdelmoneim <i>et al.</i> (2009) <sup>14</sup>	Retrospective	Definity or Optison	26,774	10,792	15,982	Both	Stress	No increased short- or long-term mortality in UEA patients
Anantharam <i>et al.</i> (2009) <sup>15</sup>	Retrospective	Definity or Lumason <sup>†</sup>	3,704	1,150	2,554	Both	Stress	No increased SAEs in UEA patients
Dolan <i>et al.</i> (2009) <sup>16</sup>	Retrospective	Definity or Optison	66,220	42,408	23,812	NR	Both	No increased mortality in UEA patients
Abdelmoneim <i>et al.</i> (2010) <sup>17</sup>	Retrospective	Definity or Optison	16,434	6,164	10,270	Both	Stress	No increased risk for myocardia infarction or mortality in UEA patients with pulmonary hypertension
Exuzides <i>et al.</i> (2010) <sup>18</sup>	Retrospective	Optison	14,500	2,900	11,600	Inpatients	Rest	No increased mortality in UEA patients
Goldberg <i>et al.</i> (2012) <sup>19</sup>	Retrospective	Definity	96,705	2,518	94,187	Both	Both	No increased mortality in UEA patients
Weiss <i>et al.</i> (2012) <sup>20</sup>	Prospective	Definity	1,053	1,053	NA	NR	Both	No deaths or SAEs
Wever-Pinzon <i>et al.</i> (2012) <sup>21</sup>	Retrospective	Definity	1,513	1,513	NA	Inpatients	Both	No deaths or SAE attributed to UEA in pulmonary hypertension patients
Platts <i>et al.</i> (2013) <sup>22</sup>	Retrospective	Definity	5,956	5,956	NA	Both	Both	No increased mortality in UEA patients
Main <i>et al.</i> (2014) <sup>23</sup>	Retrospective	Definity	32,434	16,217	16,217	Inpatients	Rest	Lower mortality in UEA patients
Wei <i>et al.</i> (2014) <sup>24</sup>	Prospective	Optison	1,039	1,039	NA	Outpatients	Both	No deaths or SAEs

# Interaction of Ultrasound and Microbubbles





Wei et al; Circ. 97:1998

#### Technical Concepts for Contrast Echo

- Second harmonic imaging
- Low mechanical index imaging
- Flash (high energy) capability to destroy microbubbles
- Pharmaceutical grade microbubble agents with high persistence
  - High molecular weight gas with low diffusivity and solubility
  - Shell encasing the bubbles
- Contraindications
  - Optison: allergy to perflutren, albumin, blood
  - Definity: allergy to perflutren or lipid components
  - Lumason: allergy to sulfur hexafluoride, lipids or other components

#### **Contrast Recording Techniques**

#### Destructive

- high energy, unipulse
- Most sensitive
- Triggered, no motion
- Can get tissue signals
- Power Doppler
- Ultraharmonics

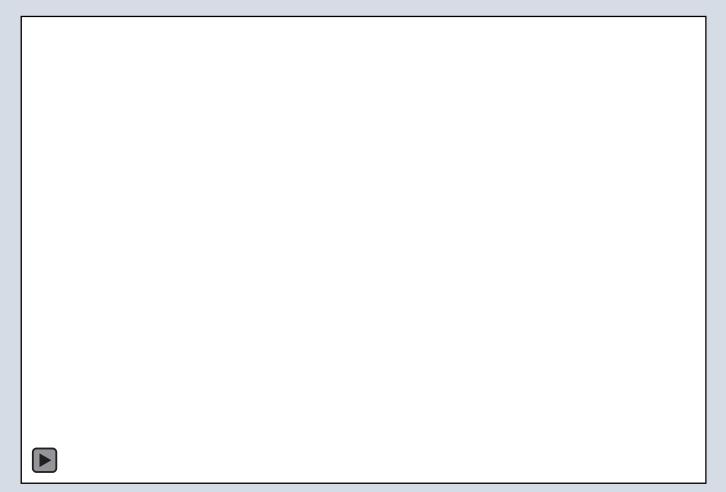
#### Non-destructive

- *low energy*,multipulse
- Real-time, motion
- Ease of use
- Less sensitivity
- Non-linearity methods
  - Pulse inversion
  - Power modulation
  - Coherent imaging

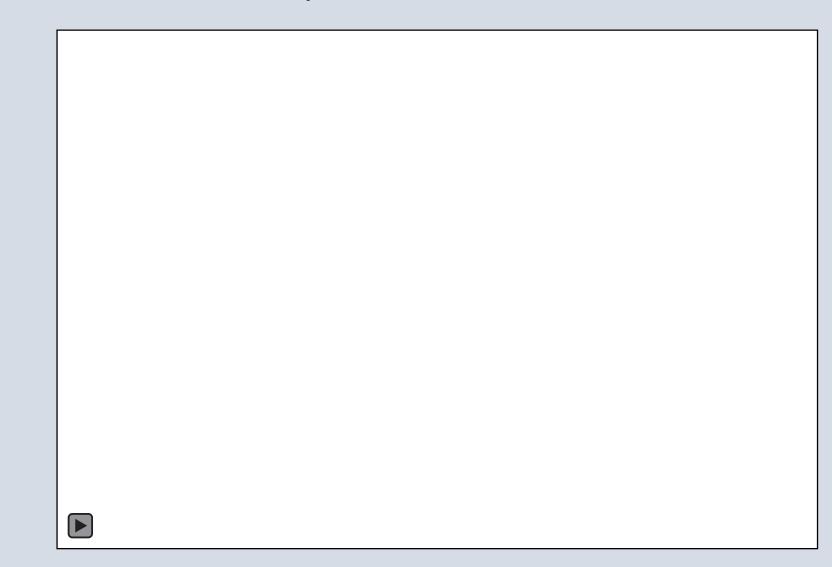
#### Contrast for LV Opacification



#### Baseline 65 yo male with COPD



#### Baseline 65 yo male with COPD



#### Indications for Contrast from Guidelines

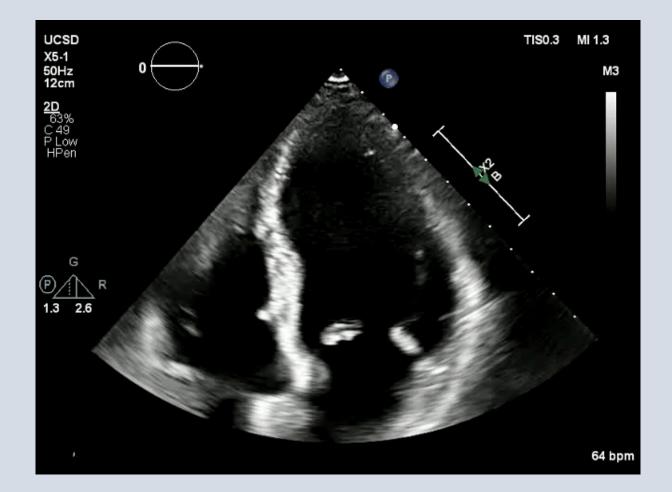
Current ASE guidelines for cardiac chamber quantification provide recommended standards for reporting LV internal diameters derived from the parasternal long-axis view, LV volumes by a biplane method, and normalization to body surface area; *use of UEAs is advised if this information cannot be readily obtained because of the poor quality of endocardial visualization.* 

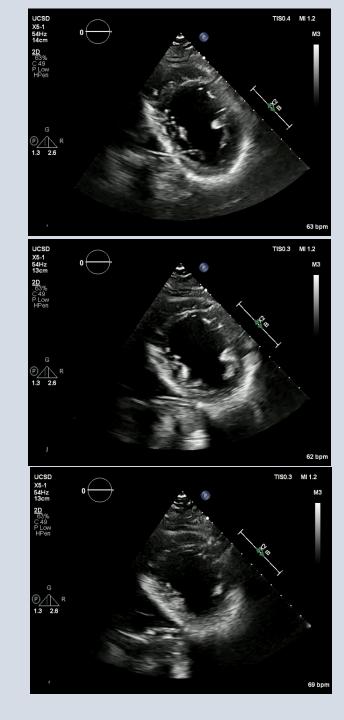
#### Patients Most Likely to Benefit from Contrast

- Obesity
- Congestive heart failure
- Chronic obstructive pulmonary disease
- Mechanical ventilation, circulatory support (ICU)
- Chest deformity (barrel chest)
- Patients with limited acoustic windows
  - Inadequate imaging of 2/6 segments in any single view
  - Incomplete Doppler velocity profiles

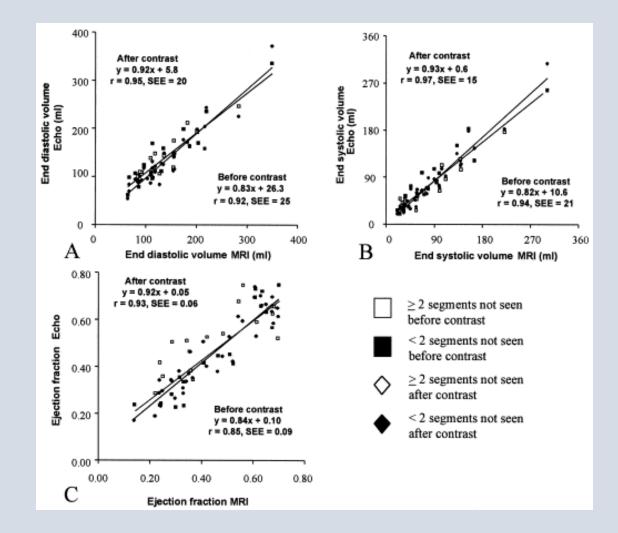
#### Who Must Have Contrast LVO?

- Indication for echo is evaluate LV function (EF)
- Endocardial border not visualized in either apical or *non-apical views*
- LV shape difficult to determine
- Epicardial motion not or poorly visualized





#### Contrast LVO for LV Volumes/EF vs MRI



Hundley et al; JACC, 1998

## Published Trials in Which EF was Part of the Entry Criteria (Partial List)

- SOLVD Treatment Trial
- SOLVD Prevention Trial
- SAVE
- US Cravedilol Trials
- MERIT-HF
- CIBIS 1 & 2
- COPERNICUS

- CAPRICORN
- RALES
- ELITE 1 & 2
- Val-HEFT
- PRAISE 1 & 2
- OVERTURE
- CHARM
- PARADIGM

#### 2012 ACCF/AHA/HRS Focused Update Incorporated Into the ACCF/AHA/HRS 2008 Guidelines for

**Device-Based Therapy of Cardiac Rhythm Abnormalities** 

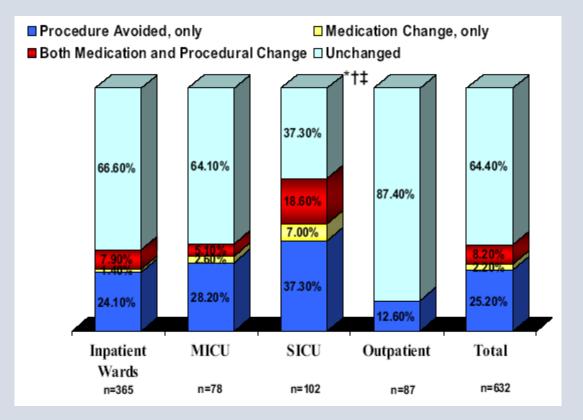
A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

#### RECOMMENDATIONS FOR CARDIAC RESYNCHRONIZATION THERAPY IN PATIENTS WITH SYSTOLIC HEART FAILURE

2. AVR is recommended for asymptomatic patients with severe AS (stage C2) and an LVEF less than 50% with decreased systolic opening of a calcified aortic valve with an aortic velocity 4.0 m per second or greater or mean pressure gradient 40 mm Hg or higher (61, 62). (Level of Evidence: B)

#### Monitor Cancer Chemotherapy

## Impact of LVO on Management



Kurt et al: JACC, 2009

#### LV Opacification Echo Other Than Border Definition

- Cardiac Shunts
- Doppler enhancement
- Cardiac Masses
  - Tumor vs Clot
- 3D enhancement
- Noncompaction
- Vascular enhancement

### A Practical Approach to Echo Contrast

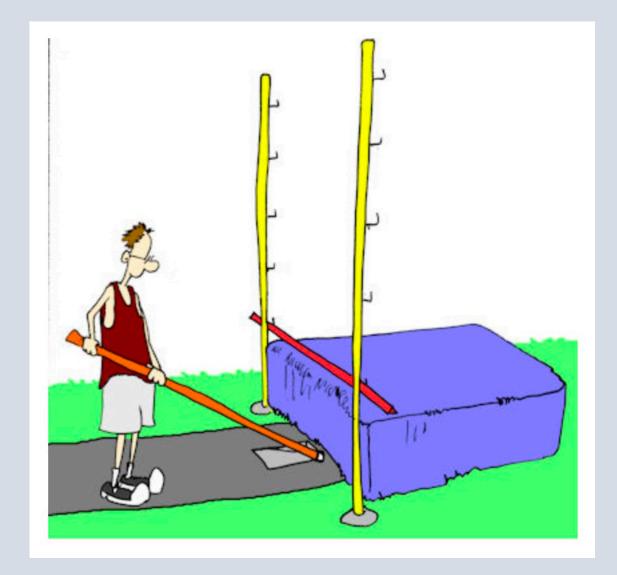
- Studies indicate about 15 to 30% of echo studies are inadequate (1)
  - The definition of inadequate is subjective
  - Stress echoes and those in ICU are more often inadequate
- Data suggests that less than 5% of echo studies receive contrast (2)
- Clearly, contrast echo is majorly underutilized
- Technical and procedural factors contribute greatly to underutilization
- Philosophical outlook on the role of contrast is critical
  - 1. Kurt M et al; JACC: 2009; Waggoner AD et al; JASE:2001; Platts D et al; Crit Care Resuscitation: 2011)
  - 2. 2. Decision Resources LLC, Toronto, Canada

## A Practical Approach to Echo Contrast

#### • It all begins at the top

- Physicians differ widely on *what constitutes a suboptimal study*
- Contrast can take too much time and personnel
- The definition of "noninvasive" varies
  - The tradition of "totally noninvasive" ultrasound is entrenched
- Considerable inertia exists to expanding the examination
- Interpretation of the studies may be more complex
- A contrast friendly philosophy must be fostered

#### How High is the Quality Bar Set?



#### **Establish Protocols for Studies**

- Team roles
  - Physician, Sonographer, Nurse
- Patient selection protocol
- Imaging protocols
- Administration protocols

## **Selecting Patients For Efficiency**

- Identify patients likely to benefit from contrast quickly; eliminate struggle time
- Incorporate contrast early in imaging protocols
- If parasternal views are poor, advance quickly to apical views

Or

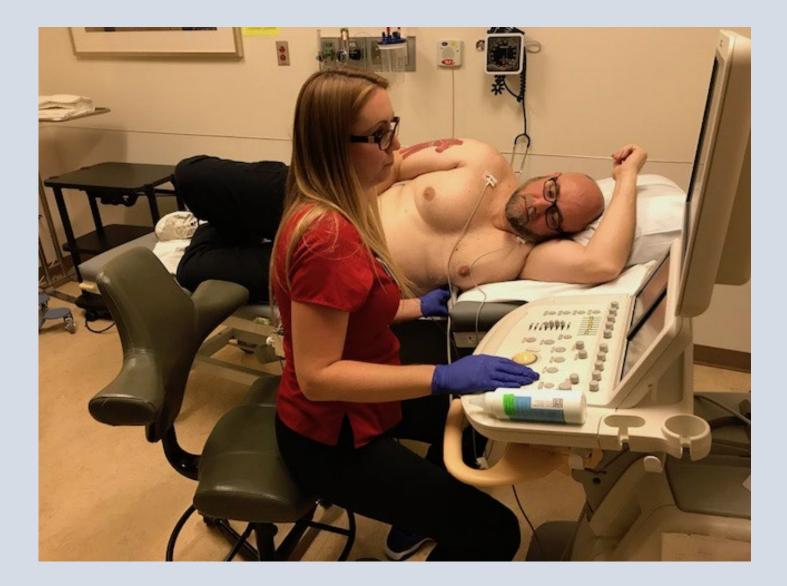
Begin with apical views

• Procedures should often be sonographer-driven















#### Efficacy and time-efficiency of a "sonographerdriven" contrast echocardiography protocol in a high-volume echocardiography laboratory

Ramon Castello, MD,<sup>a</sup> Jonathan N. Bella, MD,<sup>a</sup> Aleksandr Rovner, MD,<sup>a</sup> Jimmy Swan, MD,<sup>a</sup> John Smith, RN,<sup>a</sup> and Leslie Shaw, PhD<sup>b</sup> *Cleveland, Obio, and Atlanta, Ga* 

"After very extensive examinations in those technically difficult cases, adequate information may not be obtained in 25% to 50% of them.11,13 By eliminating **"Struggle time"** and reducing the decision and administration times, the total time used in performing a contrast study may be less than that used with conventional imaging,"

A majority of suboptimal studies can be identified within 10 minutes The time required for contrast can be offset by reduced struggle time

### **Overcoming the IV Insertion Issue**

- Finding a good vein may be an epic task
- A system must exist for an experienced individual to be readily available to start the IV and inject contrast
- Traditionally this has been a nurse or fellow
- Sonographers can insert IVs



Scope of Practice and Clinical Standards for the Diagnostic Medical Sonographer

April 13, 2015



#### PARTICIPATING ORGANIZATIONS

The following organizations participated in the development of this document. Those organizations that have formally endorsed the document are identified with the "†" symbol. Supporting organizations are identified with the "\*" symbol.

- American College of Radiology (ACR) \*
- American Congress of Obstetricians and Gynecologists (ACOG) \*
- American Institute of Ultrasound in Medicine (AIUM) \*
- American Registry for Diagnostic Medical Sonography (ARDMS) \*
- American Registry of Radiologic Technologists (ARRT) \*
- American Society of Echocardiography (ASE) +
- American Society of Radiologic Technologists (ASRT) \*
- Cardiovascular Credentialing International (CCI) +
- Joint Review Committee on Education in Diagnostic Medical Sonography (JRC-DMS) †
- Joint Review Committee on Education in Cardiovascular Technology (JRC-CVT) \*
- Society of Diagnostic Medical Sonography (SDMS) †
- Society of Radiologists in Ultrasound (SRU) \*
- Society for Maternal-Fetal Medicine (SMFM) †
- Society for Vascular Surgery (SVS) †
- Society for Vascular Ultrasound (SVU) +
- Sonography Canada (formerly the Canadian Society of Diagnostic Medical Sonography) \*
- IV access and injection of ultrasound agents is included in the scope of practice by the Society of Diagnostic Medical Sonography

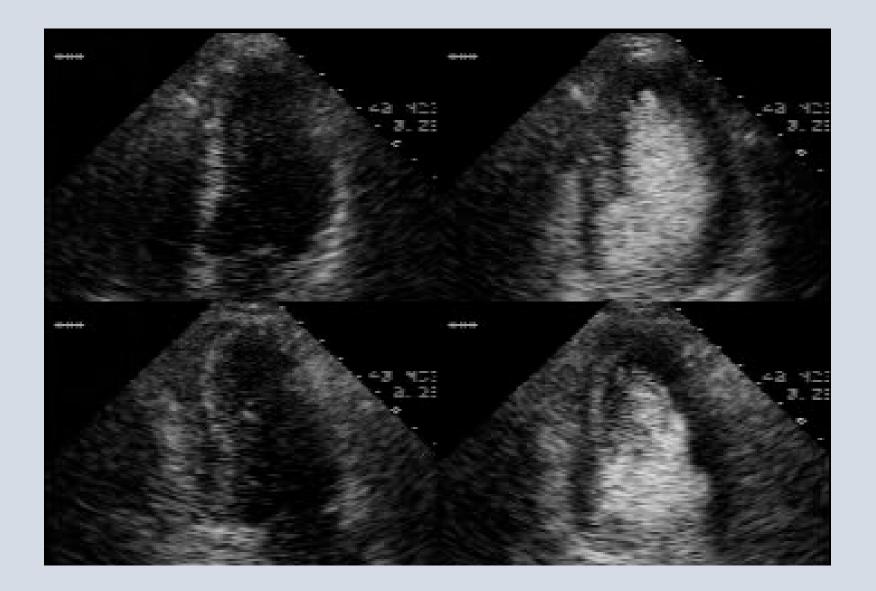
#### From ASE;

"in the interest of providing a timely patient diagnosis... a qualified cardiac sonographer can determine the need for a contrast agent and, if necessary, establish IV access and even potentially administer a contrast agent"

J AM Soc Echocardiogr 2001, 14:417-420

#### Contrast and Stress Echo

- Contrast has unique role in stress echo
- A stress echo is positive if there is abnormal contraction of any single myocardial segment
  - Therefore, to be negative, all myocardial segments must be visualized
- Contrast enhances endocardial definition
- Contrast improves image quality and confidence
- Contrast improves diagnostic accuracy
- Contrast enables prognostication
- Contrast provides myocardial perfusion



## How to Streamline Contrast-Enhanced Echo Studies

- Establish policy and procedures
  - Standing orders
  - Departmental guidelines
  - Reimbursement (coding, coverage, carrier)
- Determine staff roles and responsibilities
  - IV training
  - Combine with stress/cath RNs
  - Involve personnel outside echo lab
- Ensure availability of supplies
- Plan ahead when performing portable studies