Contrast Echo: Basic Principles

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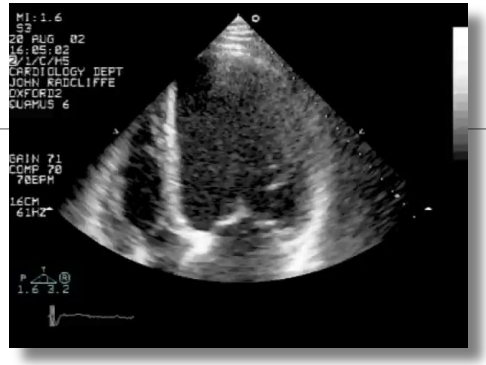
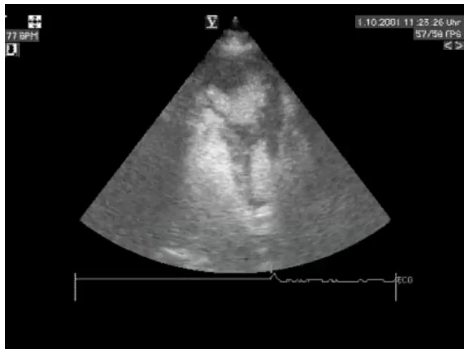
Layout

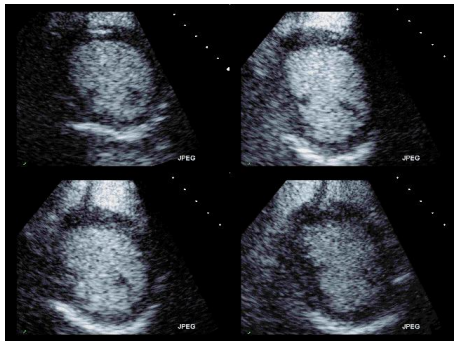
- Basic Science behind Contrast
- The Physics of Myocardial Contrast Perfusion Echocardiography
- Technique
  - Contrast preparation and contraindications
  - Equipment
  - Contrast delivery
  - Optimisation
  - Troubleshooting
  - Safety and Hurdles

An Introduction to Ultrasonic Contrast in Echocardiography

- Enhances endocardial definition
  - Estimate LV volumes, global and regional function in presence of suboptimal echo images
  - Increase feasibility, diagnostic confidence and accuracy during stress echocardiography
  - Opacification of apex for detection of thrombus, non-compaction, and hypertrophy
- Opacifies myocardial capillary bed and can be used to estimate myocardial blood volume
  - Detection of ischaemia
  - Detection of hibernating myocardium
  - Prognostication in patients with CAD



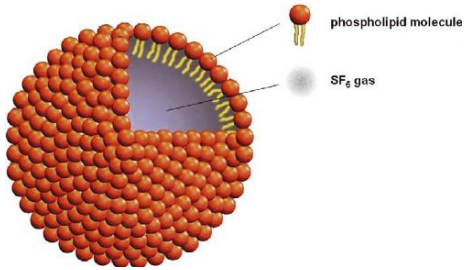


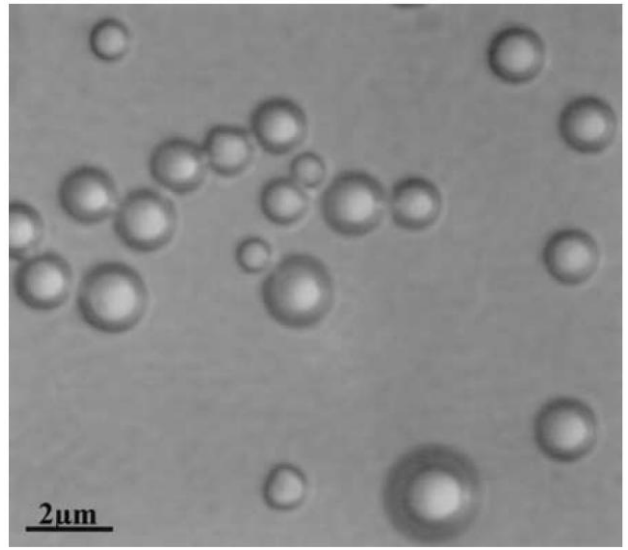



How Contrast Works

What is ultrasonic contrast?

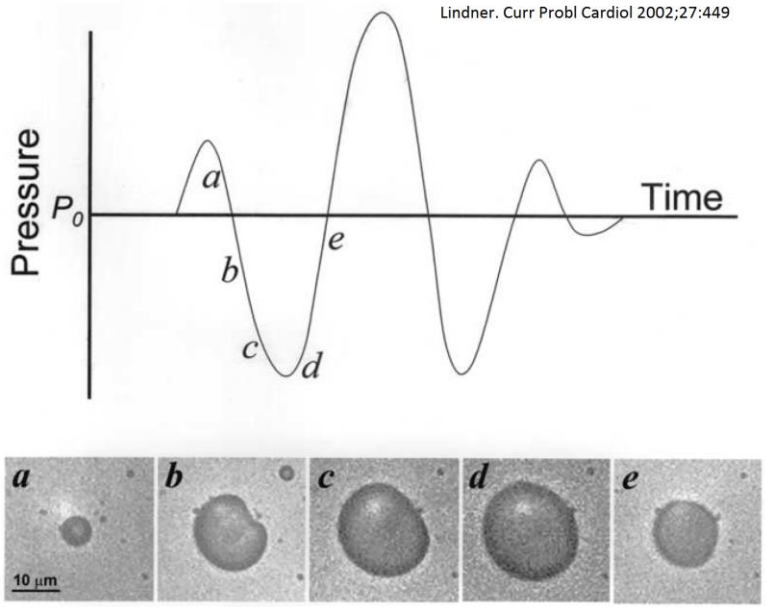
- Contrast bubbles desired properties
  - Non-toxic
  - Haemodynamically inert
  - Must interact with U/S to produce strong signal
  - Must be small enough to cross the pulmonary microcirculation
  - Must persist long enough to generate useful images
- Microbubbles consist of an outer shell (eg. albumin, galactose, lipid) and gas core containing a high molecular weight gas (eg. octafluoropropane, sulphur hexafluoride)
- Smaller than RBC's (1-4 micrometres), and easily pass through pulmonary circulation…in fact they behave exactly like RBC's





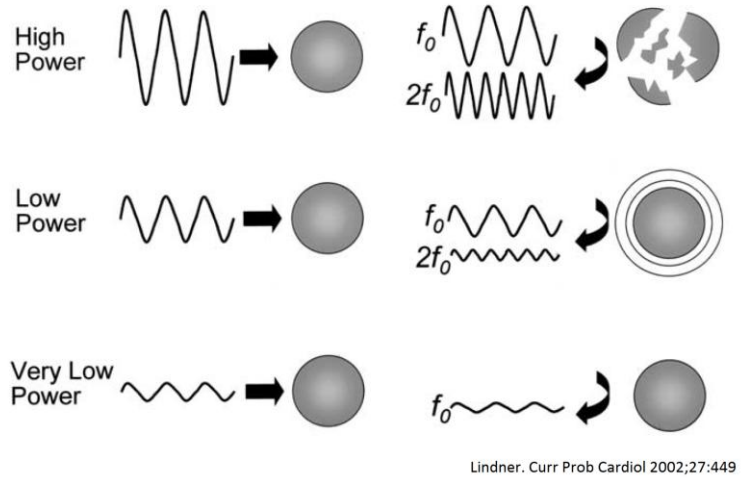
How *does contrast work?*

- When exposed to ultrasound the gas oscillates (compression and rarefaction) and reflect strong ultrasound waves
- Microbubbles in clinical use happen to have a resonant frequency in the range used for echocardiographic imaging (25 MHz)
- At this frequency the alternate compression and expansion are asymmetric and bubbles generate a non-linear response
- This non-linear behaviour generates harmonics, while tissue generates less signal at the harmonic frequency. Therefore, reception at twice the fundamental frequency increases contrast between blood and tissue
- Don't last long because they are destroyed by ultrasound and taken up by the immune system



Know the Physics – *acoustic response*

The response of bubbles exposed to U/S depends on the transmit power



Lindner. Curr Prob Cardiol 2002;27:449

The harmonic behaviour of bubbles

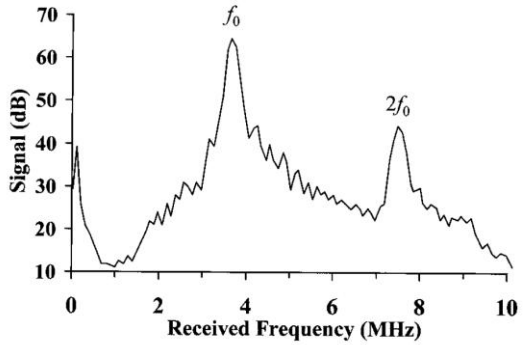
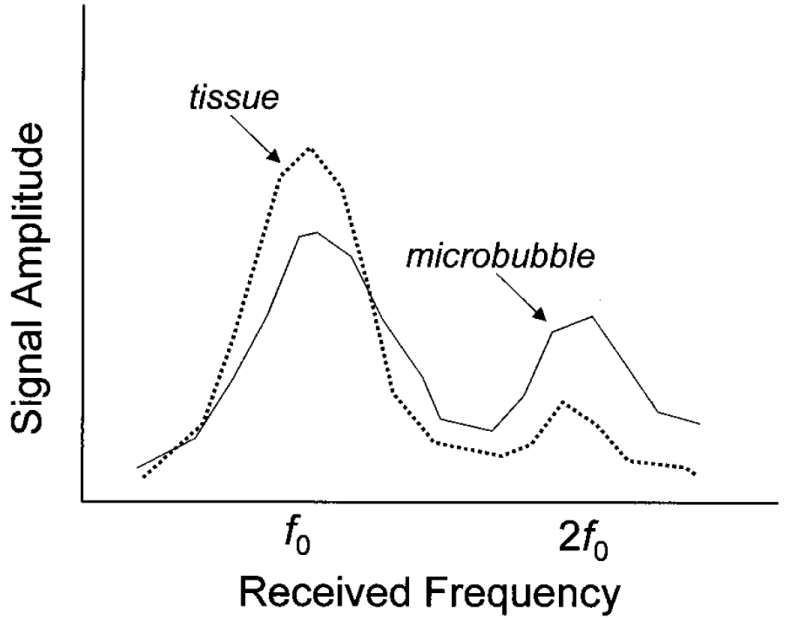


Fig 5. Acoustic signals returning from Levovist microbubbles during imaging at centerline frequency of 3.75 MHz. Returning signals contain both fundamental (f_0) and second harmonic ($2f_0$) signals. Reproduced with permission.[47]

The different response of tissue at harmonic frequencies



- U/S POWER = Mechanical Index: a measure of the ultrasound beam's non-thermal bioeffects:
  = Peak negative pressure/SQRT (centre frequency of beam)

Know the Physics – *Basic Scanner Settings*

- Manual: reduce MI and switch to harmonic imaging
- Automated: Needs low MI (< 0.3) (Left Ventricular Opacification Mode) or very low MI (<0.2) setting
- Vendors have different very low MI imaging modes, designed to increase non-linear response from bubbles and suppress linear responses from tissue
  - Pulse-inversion Doppler (GE)
  - Power modulation (Philips)
  - Contrast pulse sequencing (Siemens)
- High MI flash mode is optional

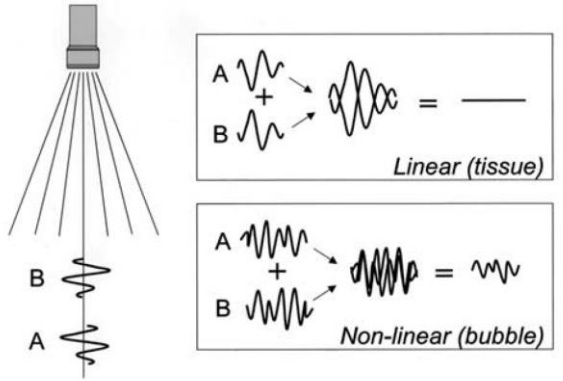
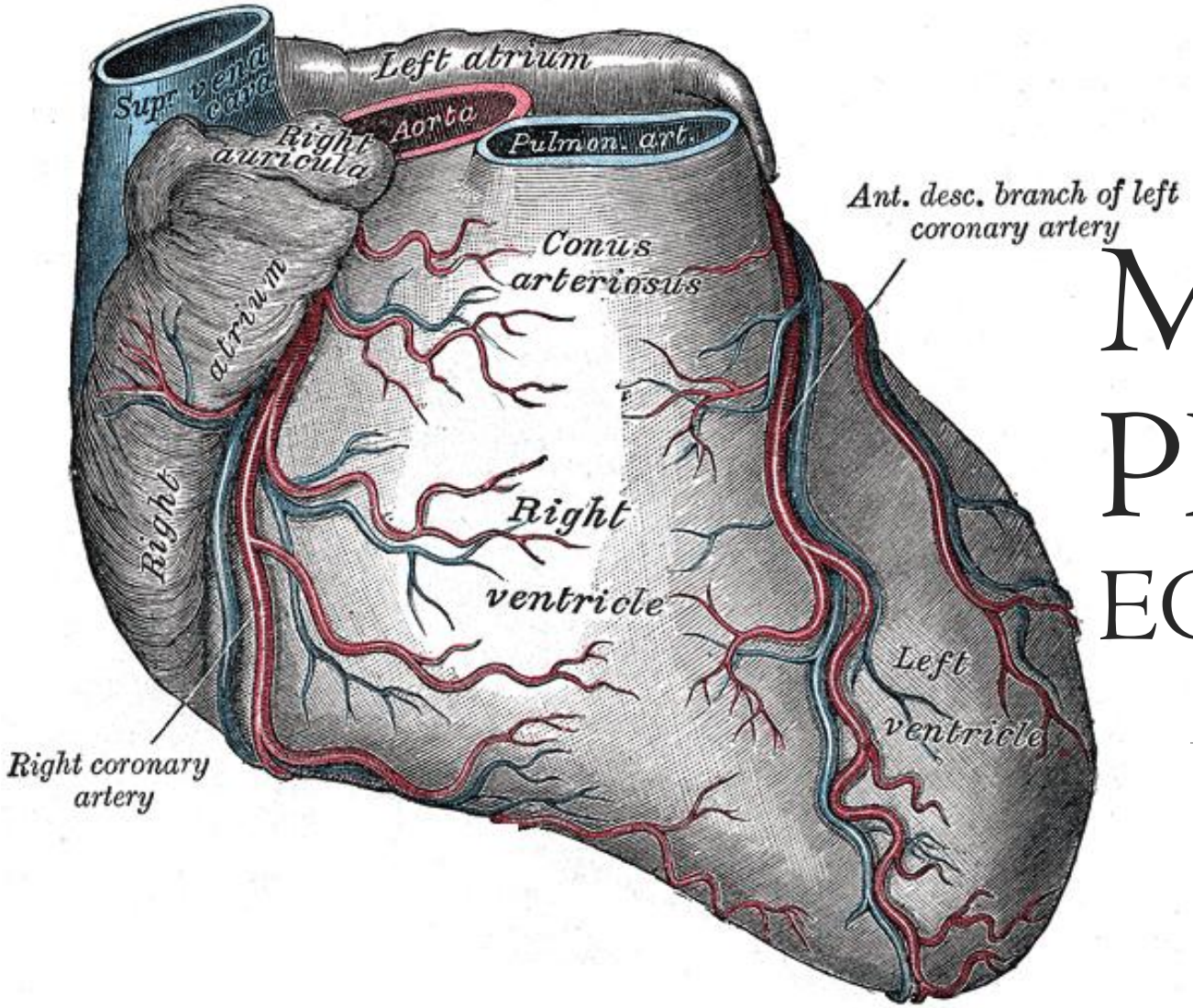


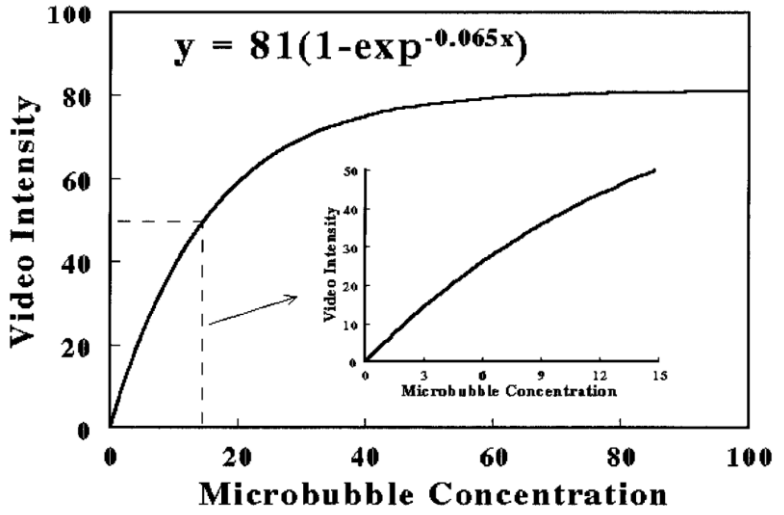
Fig 11. Schematic depicting methods used to improve microbubble signal relative to tissue with pulse-inversion imaging. Two or more sequential pulses are transmitted for each line, which are phase-inverted. By summing returning signals, tissue signal (linear scatterer at low-power) is eliminated whereas nonlinear microbubble signal is not.

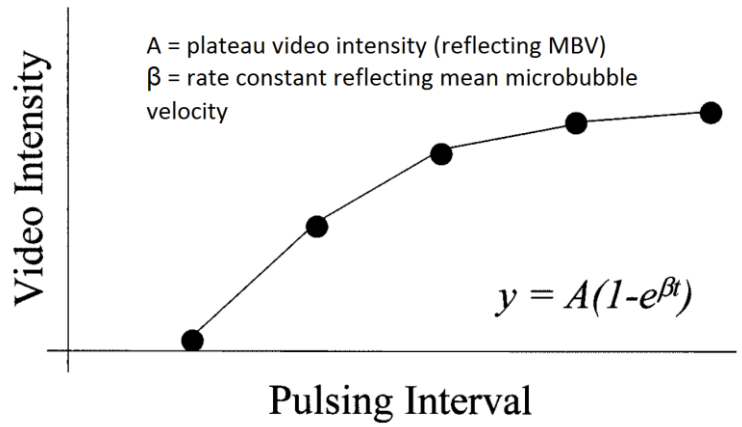


MYOCARDIAL PERFUSION ECHOCARDIOGRAPHY

The Physics of Myocardial Perfusion Echocardiography

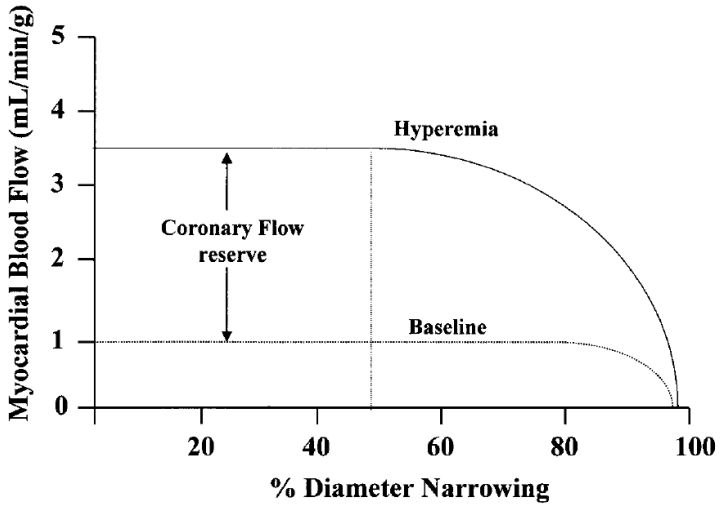
- Most of myocardial blood is within microcirculation – since contrast is completely intravascular, it reflects the myocardial capillary blood volume
- At low concentration of microbubbles, there is a linear relation between amplitude of returned signal and microbubble concentration
- Destruction of bubbles with a high MI pulse will be followed by replenishment of contrast, the rate of which reflects myocardial blood flow velocity
- The change of signal intensity over time is fitted into an equation to estimate MBV and MBF velocity





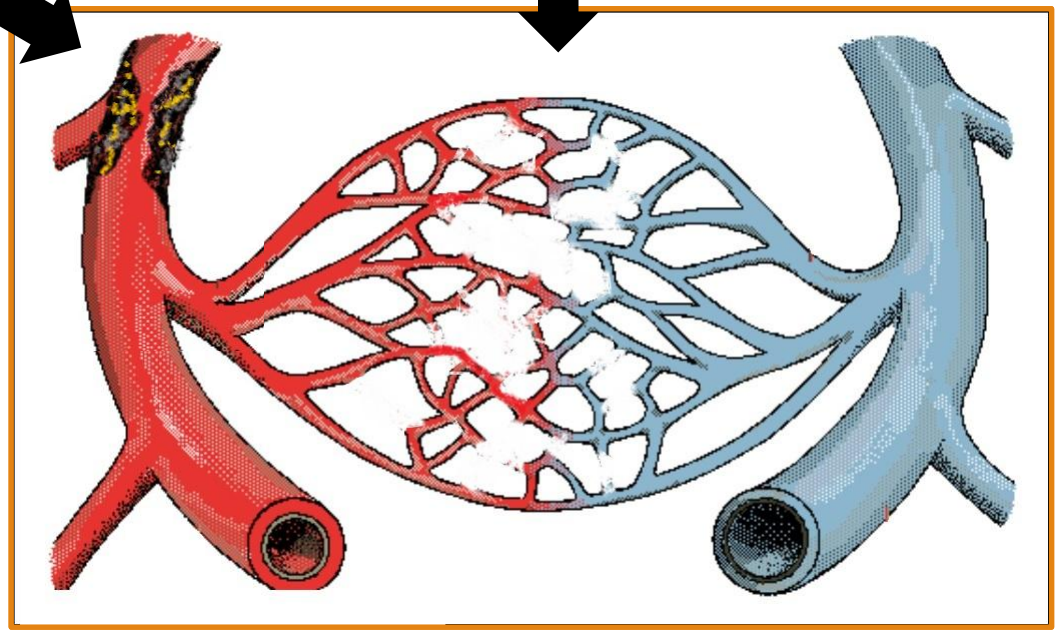
The effect of coronary stenosis on MBF

The use of hyperaemia for more sensitive detection of stenosis



Flow-limiting Stenosis

Capillary Decruitment = Increased MVR = reduced MBF

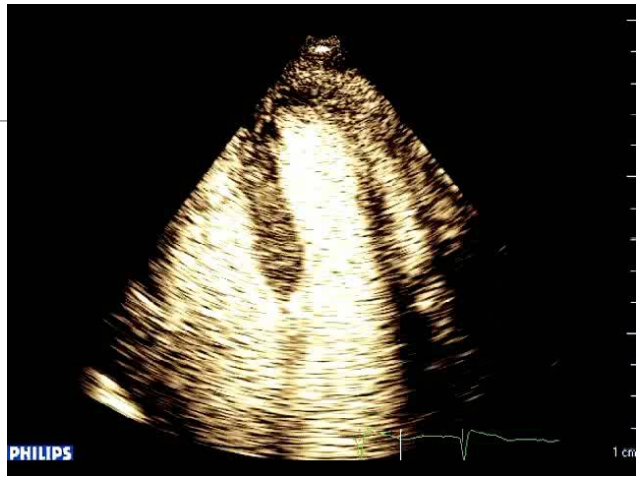


During maximal hyperaemia

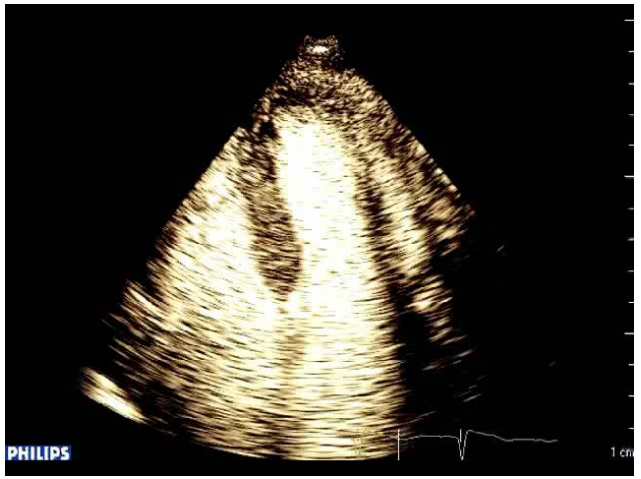
Performing Myocardial Contrast Perfusion

- Vasodilator (dipyridamole/adenosine) hyperaemia is used for early detection of the drop in filling pressure across significant stenosis
- Can also be performed with dobutamine or exercise
  - Benefit of assessing RWM
  - Tachycardia/respiratory motion may be a problem
- High MI flash (0.9) for 7 frames, and image acquisition for replenishment
  - Real-time
  - Triggered (end-systole)
- Normally microbubble replenishment takes 5 s at rest and 1-2 s at peak hyperaemia; takes longer if flow-limiting stenosis

Triggered Imaging

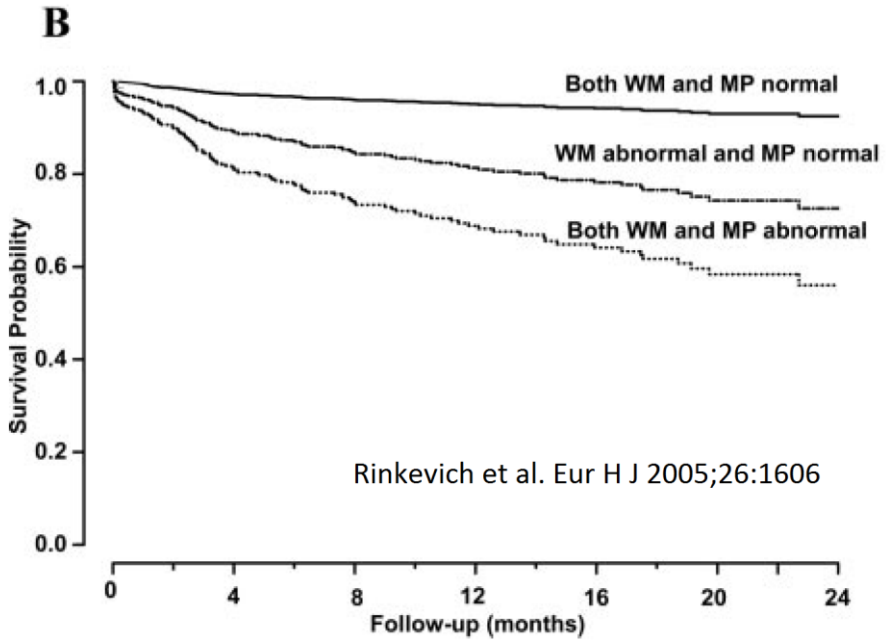


Continuous Capture



The clinical uses of Perfusion MCE

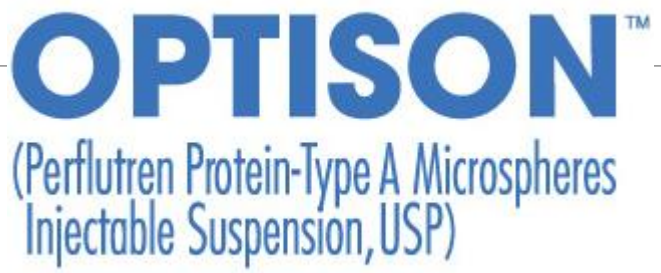
- **Detection of ischaemia - increased sensitivity compared to wall motion assessment alone (validated +++)[1*]**
- **Detection of viable/hibernating myocardium[2]**
- Assessment of area at risk after MI[3]
- Distinguishing ischaemic from non-ischaemic causes of cardiomyopathy[4]
- Prognosis in ischaemic heart disease[5]
- Identifying the myocardium supplied by first septal perforator in HCM septal ablation[6]



[1]Senior et al. JACC 2013;62:1353; [2]Shimoni et al. Circulation 2002;106;950; [3]Hayat S et al. Am J Cardiol 2006;97:1718; [4]Senior et al. Circulation 2005;112:1587; [5]Wejner-Mik et al. Eur J Echo 2011;12:762; [6]Nagueh et al. JACC 1998;32:225

The Technique

Know the Contrast Agent (2nd generation)



Commercially available contrast agents for echo	Shell	Gas	Size (µm)
Optison	Albumin	Octafluoropropane	2-4.5
Definity	Lipid/surfactant	Octafluoropropane	1.1-3.3
Sonovue	Lipid	Sulphur hexafluoride	2-3
Imagent	Lipid/surfactant	Perfluorohexane	6.0

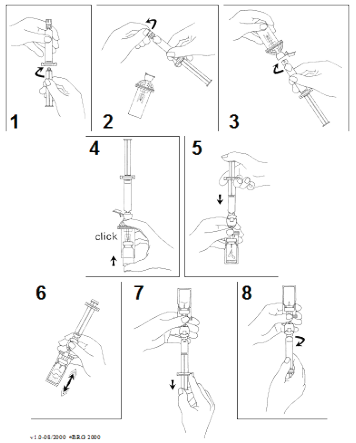
Safety of contrast

- 1:16,541 risk of anaphylactoid reaction[1]
- Minor adverse effects such as back pain, headache, nausea and rash in 0.27-0.35% of cases[2]
- The 2007 FDA black box warning against use of contrast in potentially unstable cardiovascular conditions has been reversed after large studies reported safety in all-comers,[2] critically ill patients,[3] post-MI[4] and patients with pulmonary hypertension[5]
- Only contraindications are now:
  - Known or suspected R-to-L shunts, bidirectional or transient R-to-L shunts
  - Intra-arterial injection
  - Known hypersensitivity to constituents

[1]Wei et al. JASE 2008; 21:1202; [2]Platts et al. Heart Lung Circ 2003;22:996; Weiss et al. JASE 2012;25:790; [3]Main et al. JACC Cardiovasc Imag 2014;7;40; [4]Nucifora et al. Eur J echo 2008;9:816; [5]Wever-Pinzon et al. EHJ Cardiovasc Imag 2012;13:857

Specific Features - SONOVUE

- Package containing
  - Powder
  - Solvent (0.9% NaCl)
  - Mini-Spike transfer system



- Shake vigorously to suspend bubbles after injecting solvent
- Flush with 5 mls of saline after injection
- Contraindications:
  - Hypersensitivity to the active substance(s) or to any of the excipients
  - right-to-left shunts, severe pulmonary hypertension (pulmonary artery pressure >90 mmHg), uncontrolled systemic hypertension, and in patients with adult respiratory distress syndrome.
  - Sonovue should not be used in combination with dobutamine in patients with conditions suggesting cardiovascular instability where dobutamine is contraindicated.
- Not to be used < 18 years of age; avoid in pregnancy
- Shelf life of 2 years
- No specific storage instructions
- Stable for 6 hours after reconstitution

Technique - Equipment

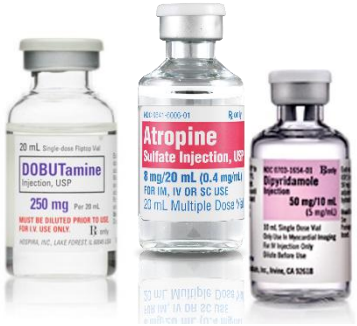
20G Venous cannula

Saline or Dextrose flush

Syringes

3-way connector/multilumen connector

Venting needle/ Optispike



Stressor Drugs

Resuscitation/anaphylaxis Equipment

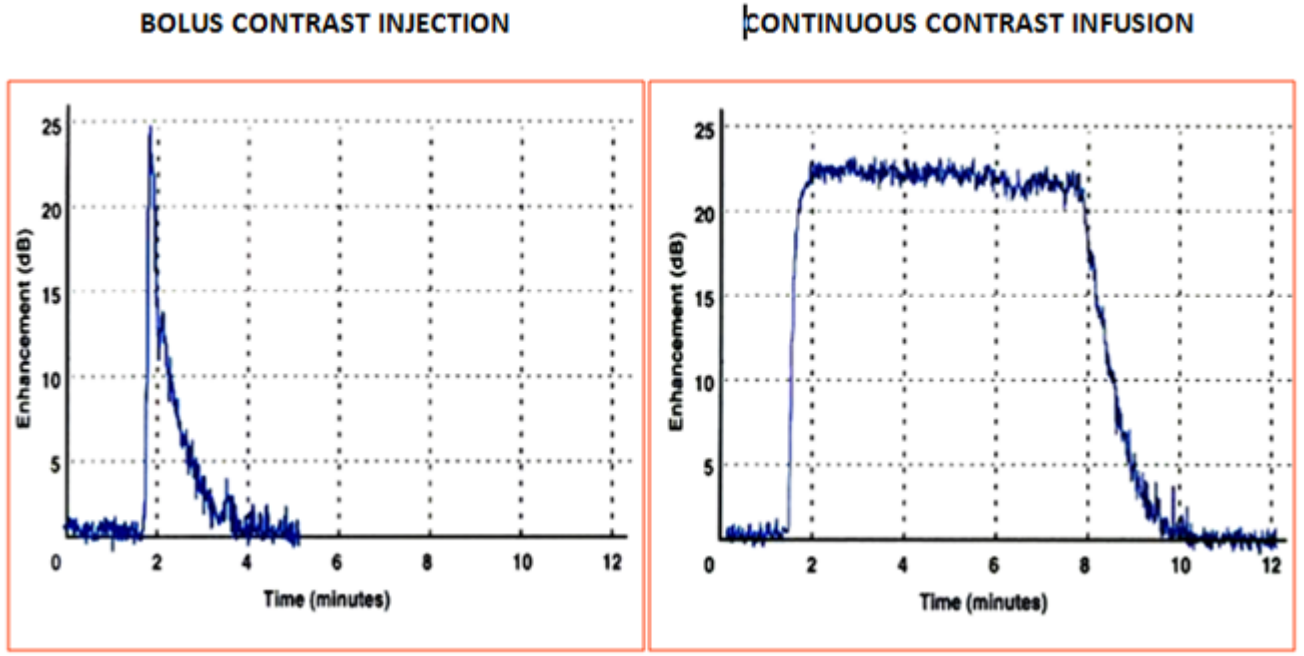
Contrast infusion pump/activating device

Technique – General Advice

- Ensure complete suspension (inspect for unsuspended powder)
- Learn how to use brand-specific equipment eg. MiniSpike transfer system for Sonovue, VIALMIX for Definity
- Do not insert a needle into phial more than once
- Vent phial before aspirating contrast to avoid destruction of bubbles
- Aseptic technique
- Need help from qualified nurse or doctor

Administration – bolus or infusion

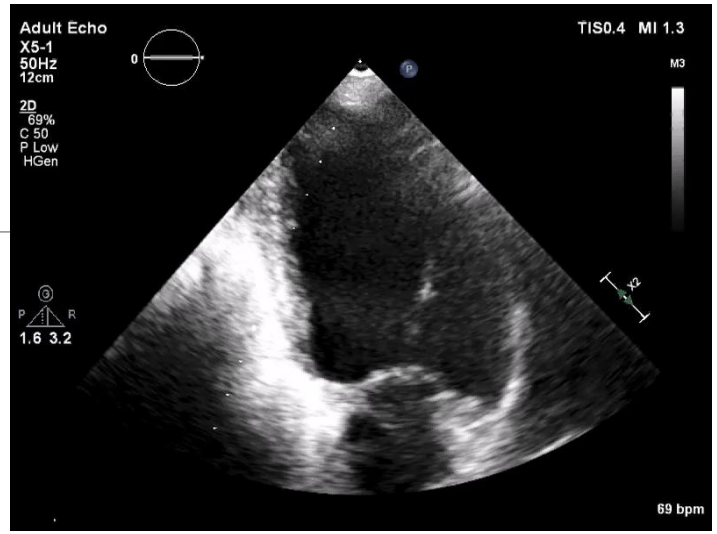
- SONOVUE:
  - BOLUSES:
    - 0.3 mls boluses, followed by 1-2 ml flush
    - Repeat as needed
  - INFUSION:
    - undiluted, at 0.8-0.9 mls/min
- Advantages of infusion:
  - More uniform contrast
  - Less artefacts
  - Easy to tailor to patient's needs
- Disadvantages:
  - Needs infusion pump and additional skills



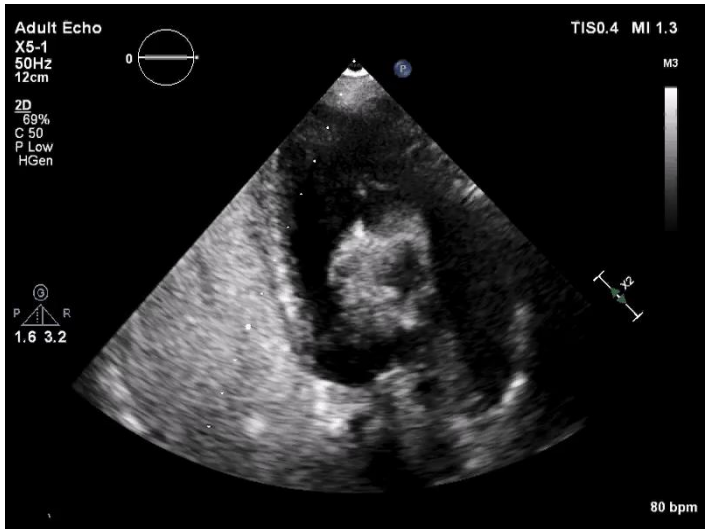
Technique – Optimisation and scanner settings

- Don’t forget to switch to LVO mode when you see contrast in RV!
- The initial inflow of contrast will cause a signal drop in the basal segments from the apical views - wait until uniform opacification (may take up to 90s)
- Adjust LGC for even myocardial and cavity brightness from apex to base
- Place focus at level of MV
- If apex is not filling, reduce MI or inject faster
- If base is attenuated, inject slower
- If contrast is dim, increase overall gain

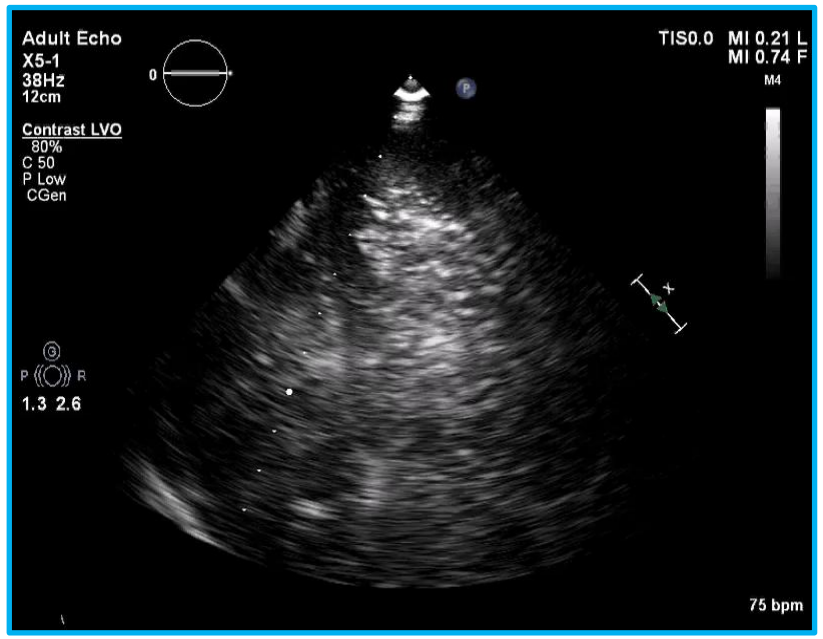
Contrast in RV – time to switch on LVO



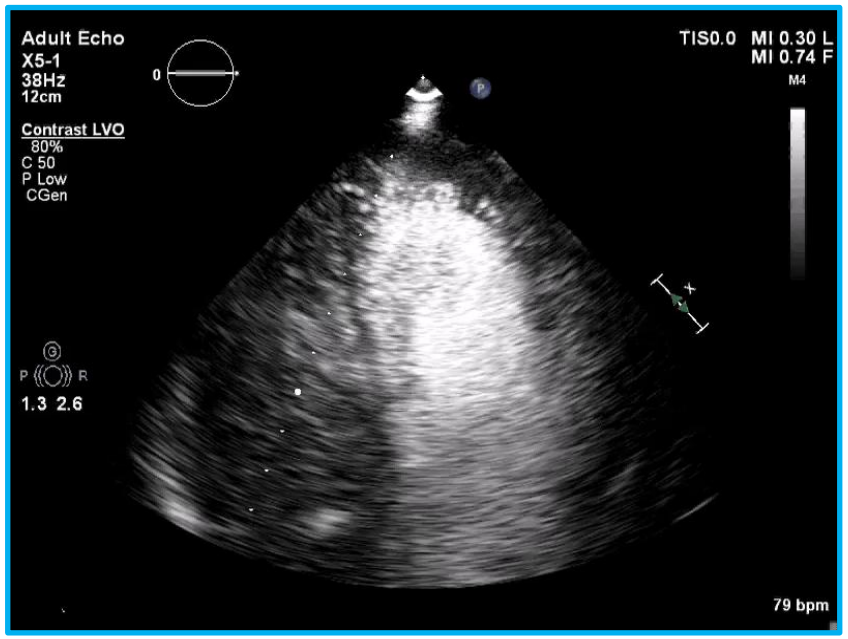
LVO not switched on!



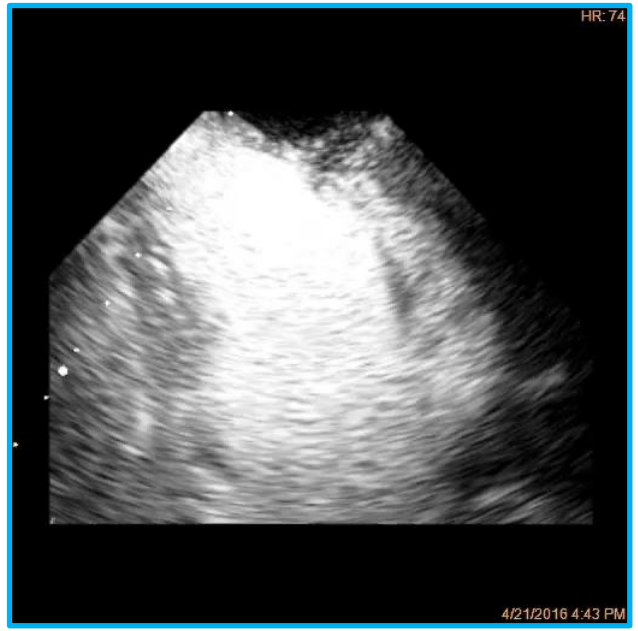
Technique – Optimisation



Too little contrast



Apical swirling



Optimal

Troubleshooting

Problem	Solution	Comments
Rib artefact	Spend time finding right echo window; ask patient to hold breath in expiration on inspiration or mid-inspiration	Need to remember the phase of respiration for subsequent imaging of same plane; may have to focus on, and acquire, a single wall
Overall or regional Low signal	Increase overall **gain** or **LGC**; may need to increase **MI** when penetration is reduced (eg. obese)	Gain will not affect microbubble persistence
Microbubble destruction + swirling in near field	Reduce **MI**, move **focus** into apex, increase contrast delivery rate	
Blooming (too much signal, giving false appearance of perfused myocardium)	Reduce **gain**	
Attenuation at base of heart	Wait, or decrease **rate of microbubble infusion**	May have to acquire a single wall rather than whole plane
Signal drop-out in far field	Move segment into middle of scan sector	

Final points

- SAFETY
  - Have a pathway for anaphylactic reactions
  - Lab Protocol and Designated personnel (pre-procedure checklist and consent, sonographer, venous cannulation, injecting contrast, post-procedure care)
  - Resusc trolley and trained personnel
  - ECG monitoring during contrast administration in unstable patients
  - PFO's are safe
- HURDLES
  - Time
  - Cost
  - Extra staff
  - Extra training
  - Need for cannulation
  - Train sonographers to cannulate and administer contrast

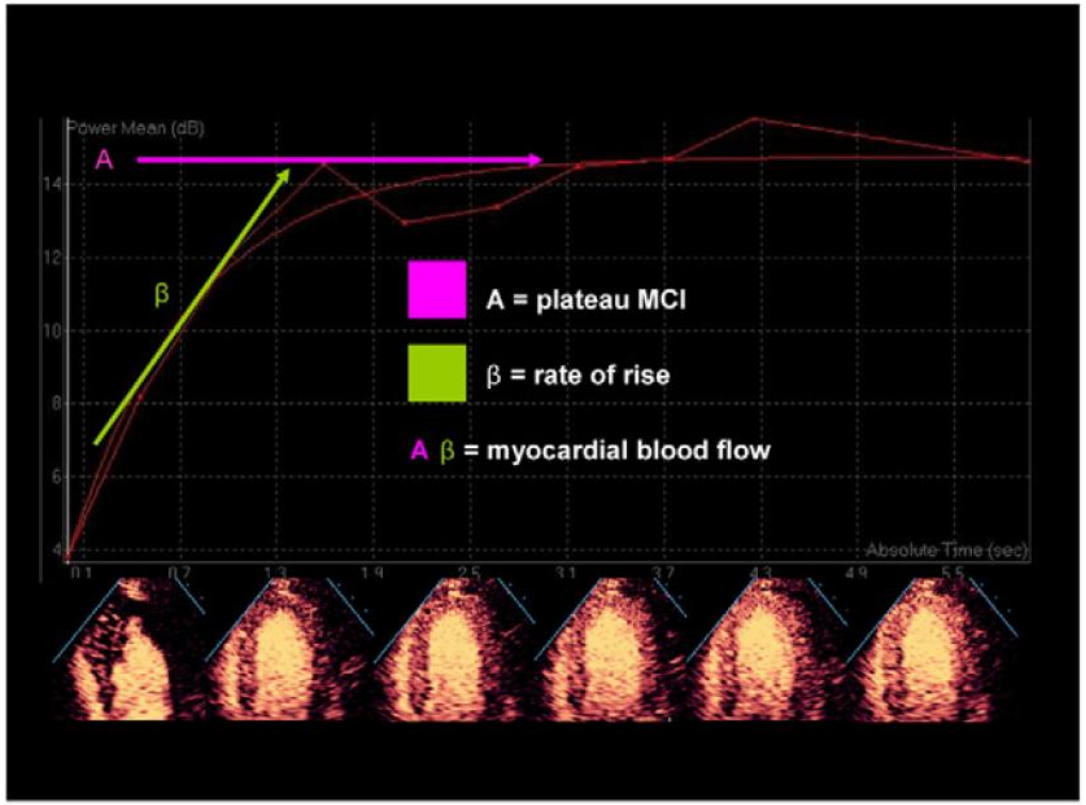
Conclusion

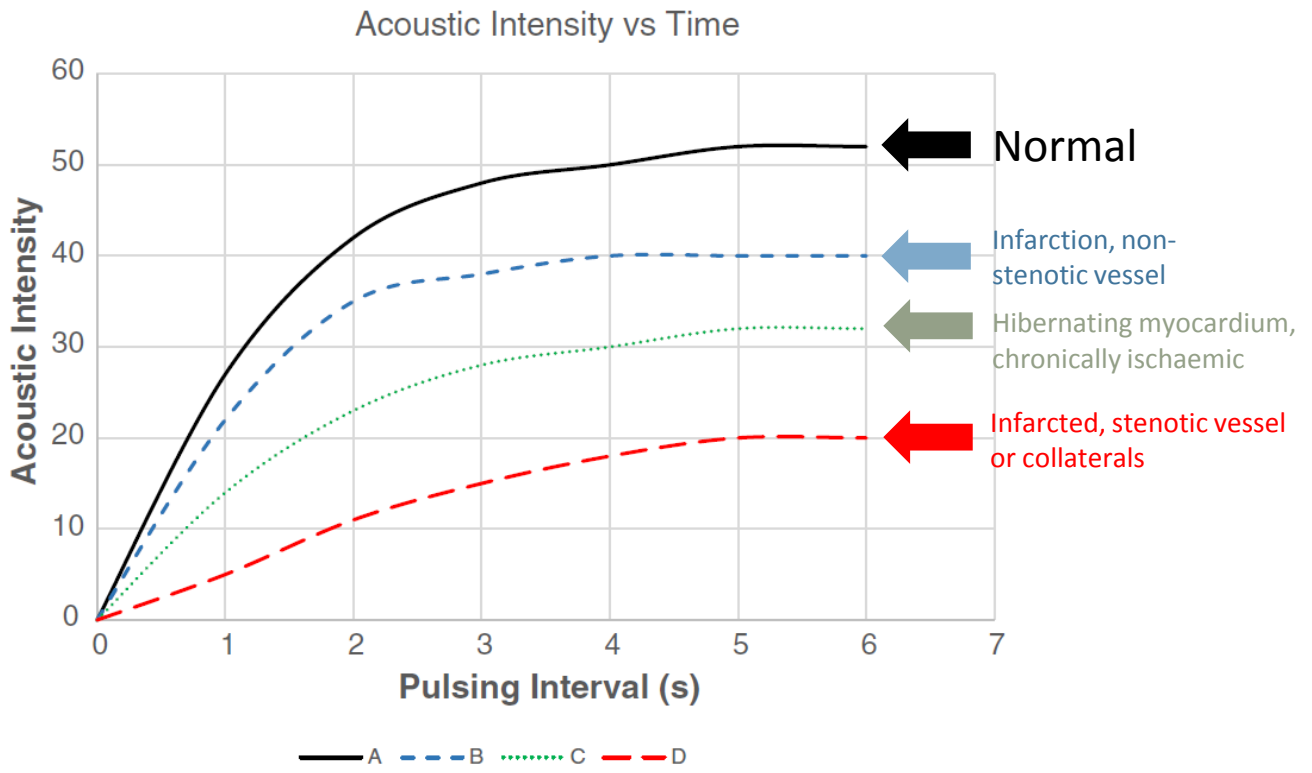
- Contrast Echocardiography
  - Increases diagnostic confidence
  - Increases accuracy
  - Provides economic benefits
  - Essential for a stress echo service
  - Perfusion
- Basic physics and machine settings must be appreciated
  - How contrast works
  - Preparation and storage
  - Low and very-low MI imaging modes
  - How scanner optimises signal from contrast
  - Machine settings and dealing with problems
- Develop Departmental protocol and safety policy

The End

THANK YOU

The Physics of Myocardial Perfusion Echocardiography 2





Specific features - OPTISON

- Box containing 5 x 3ml-phials
- Invert or gently rock-and-roll phial
- Check for an opaque solution, vent with 18G needle or spike, and withdraw solution
- Contraindications
  - Known or suspected R-to-L shunts, bidirectional or transient R-to-L shunts
  - Intra-arterial injection
  - Known hypersensitivity to perflutren, blood, blood products or albumen
- Storage
  - Upright
  - At 3-8^{o}C
  - Stable at room temp up to 24 hrs
- Use
  - Do not use if upper white layer is absent
  - Do not use if re-suspended solution is clear rather than opaque
  - Caution in pregnancy and lactating mothers
- The most frequently reported adverse reactions following clinical trial use of Optison were headache, nausea and/or vomiting, warm sensation or flushing, and dizziness

Contrast makes a difference when you need it most: stress echo

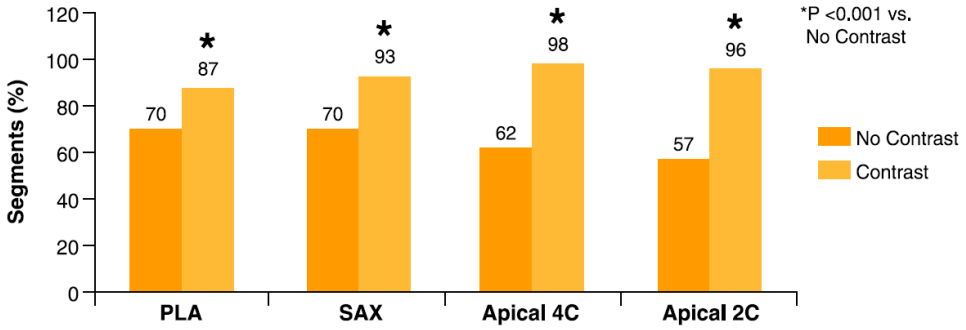


Figure 2. Visualization of Segments by View at Peak Stress: Contrast Agent Versus Noncontrast Enhancement

An improvement in image quality…

JACC: CARDIOVASCULAR IMAGING
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A Randomized Cross-Over Study for Evaluation of the Effect of Image Optimization With Contrast on the Diagnostic Accuracy of Dobutamine Echocardiography in Coronary Artery Disease

The OPTIMIZE Trial

Juan Carlos Plana, MD, FACC, Issam A. Mikati, MD, FACC, Hisham Dokainish, MD, FACC, Nasser Lakkis, MD, FACC, John Abukhalil, RT(R), Robert Davis, RDCS, Brian C. Hetzell, MS, William A. Zoghbi, MD, FACC
Houston, Texas

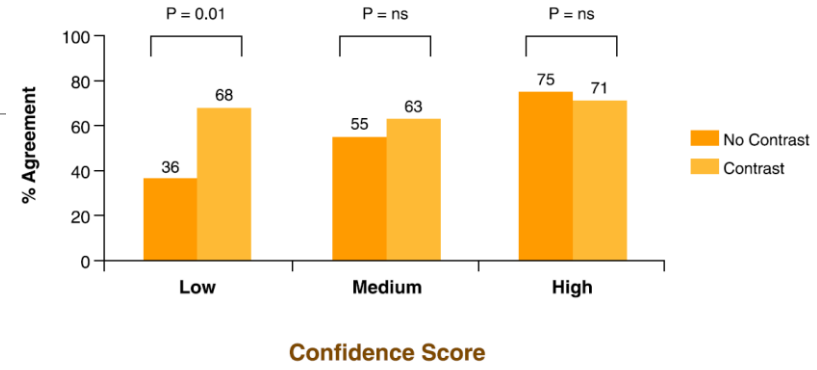

Figure 5. Impact of Contrast Agent Use on Accuracy of DSE in Relation to Confidence of Interpretation in Unenhanced DSE Studies

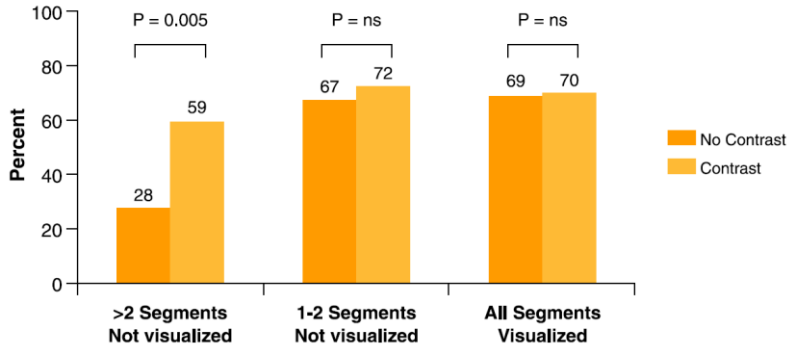

Figure 7. Effect of Contrast Agent Use on Accuracy of DSE in Relation to the Number of Segments Visualized

…which translates into better accuracy

Rationale behind perfusion