

# Ultrasound Contrast Agents

# Microbubbles

- Gas core
- Shell
- Diameters 1-10  $\mu\text{m}$
- Administration: Intravenous Injection

# Microbubbles differences

- There are a variety of microbubbles contrast agents.
- Microbubbles differ in their:
- Gas core
- Shell
- Whether or not they are targeted

# Effects of microbubble shell

1) Selection of shell material determines .....

- how easily the microbubble is taken up by the immune system.
- A more hydrophylic material →
- Taken up more easily →
- Reduces the microbubble residence time in the blood circulation →
- Reduction of the available time for imaging

# Effects of microbubble shell

2) The shell material also affects mechanical elasticity of microbubble.

- The more elastic the material →
- The more acoustic energy

# Microbubble shell materials

- Microbubble shells are composed of the material such as:
- Albumin
- Lipid
- Galactose
- Polymers

# Microbubble gas core

- The gas core is the most important part of the ultrasound contrast microbubble.
- ?
- It determines the echogenicity

# Microbubble gas core

- Gas cores can be composed of:
  - Air
  - Heavy gases like perfluorocarbon
  - Heavy gas/air mixture
  - Nitrogen
- 
- Heavy gases:
  - Less water soluble →
  - Less leak out from the microbubble



# Microbubble size

- Smaller than red blood cells →
- Allows them to flow easily through the blood circulation as well as the microcirculation

# Natural frequency

- The frequency at which microbubbles resonate most strongly
- Frequency of microbubbles is determined by:
  - Composition of the gas and the shell
  - Size
- Smaller bubbles resonate at high frequencies

# Range of resonance frequencies

- Microbubbles in the 1-10 $\mu$  range have their resonance at the frequencies used in diagnostic ultrasound (1-20MHz).

# Blood pool marker

- Microbubbles (at 1-7 $\mu$  diameter) do not diffuse across the endothelium, so that there is no interstitial phase of enhancement. →
- They are essentially markers for the blood pool.
- Vascular enhancement: During a few minutes

# Microbubbles uptake

- Some microbubbles are taken up by the phagocytic cell systems →
- They have liver/spleen specific effects

# Safety

- While it may seem unwise to inject gas bubbles intravenously, the total amount used is low and their small size makes embolisation most unlikely

# Clinical applications

- LVO – Left Ventricular Opacification
- Liver tumor detection and characterization
- Myocardial perfusion
- Kidney (transplants), breast, prostate
- Stroke
- Research for targeted/molecular imaging
  - Combined with drug delivery
- The most important example is in echocardiography.

# Ultrasound contrast agents

- Currently there are two ultrasound agents approved for worldwide clinical use:
  - SonoVue
  - Optison
- They are packaged as freeze-dried powders which can be rehydrated in physiological saline solution just before they are to be injected into the patient's bloodstream.



# SonoVue

- SonoVue is an example of an important family of microbubbles.
- Gas: Sulphur hexafluoride (SF<sub>6</sub>) which diffuses slowly
- Shell: Phospholipid

# Optison

- Optison consists of microbubbles which contain **perfluoropropane gas** within a **serum albumen microsphere**.

# Microbubbles removal

- Filtered by liver
- Cleared ~ 15 minutes