

Ultrasound Contrast Agents



Ultrasound contrast agents rely on the different ways in which sound waves are **reflected** from interfaces **between** substances.

This may be the surface of a small air bubble or a more complex structure.

Commercially available contrast media are **gas-filled** microbubbles that are administered intravenously to the systemic circulation



Microbubbles have a high degree of **echogenicity** (the ability of an object to reflect ultrasound waves). There is a great difference in echogenicity between the gas in the microbubbles and the **soft tissue** surroundings of the body.

Contrast-enhanced ultrasound can be used to image

blood perfusion in organs,

measure **blood flow rate** in the heart and other organs, and for other applications



These micron-sized particles consist of a gas core **surrounded by a lipid shell**, and are injected intravenously into the circulatory system.

Understanding the **patterns of blood flow** is a powerful tool for evaluating the differences **between normal and pathological tissues**.

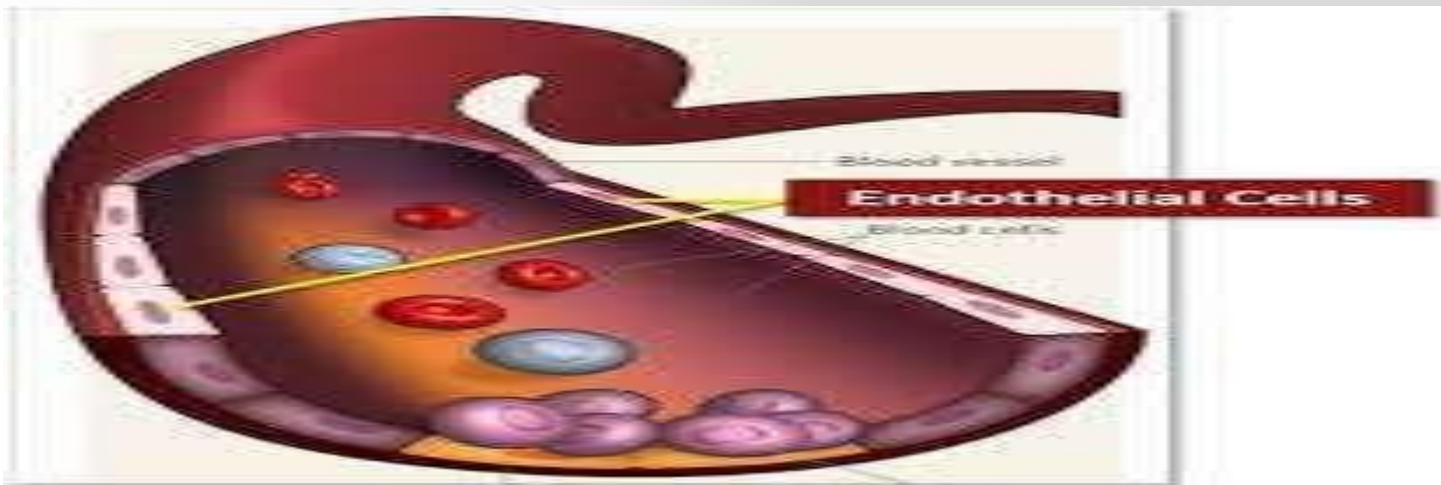
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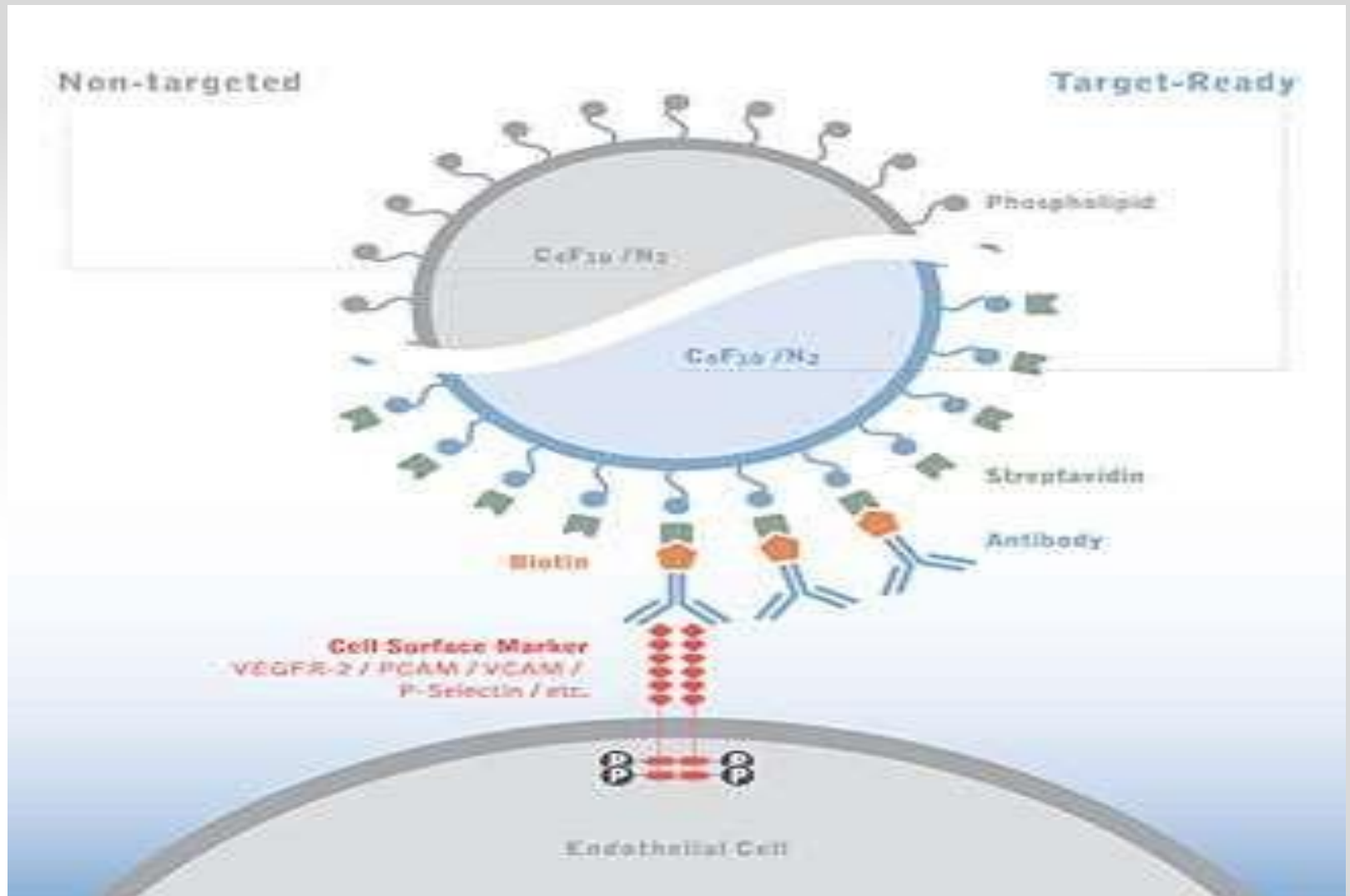
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Size of Microbubble is around 1 - 4 μm •

The Microbubble is nearly around the size of RBCs as it should not cross the vascular endothelium. •



types



Types

1. Non-targeted contrast-enhanced ultrasound

2. Targeted contrast-enhanced ultrasound

1. Non-targeted contrast-enhanced ultrasound

More common method

In this the microbubbles will remain in the systemic circulation for a certain period of time. During that time, ultrasound waves are directed on the area of interest. When microbubbles in the blood flow past the imaging window, the microbubbles' compressible reflect a unique echo.



Uses of Non-targeted contrast-enhanced ultrasound

To enhance the contrast at the interface between the tissue and blood.

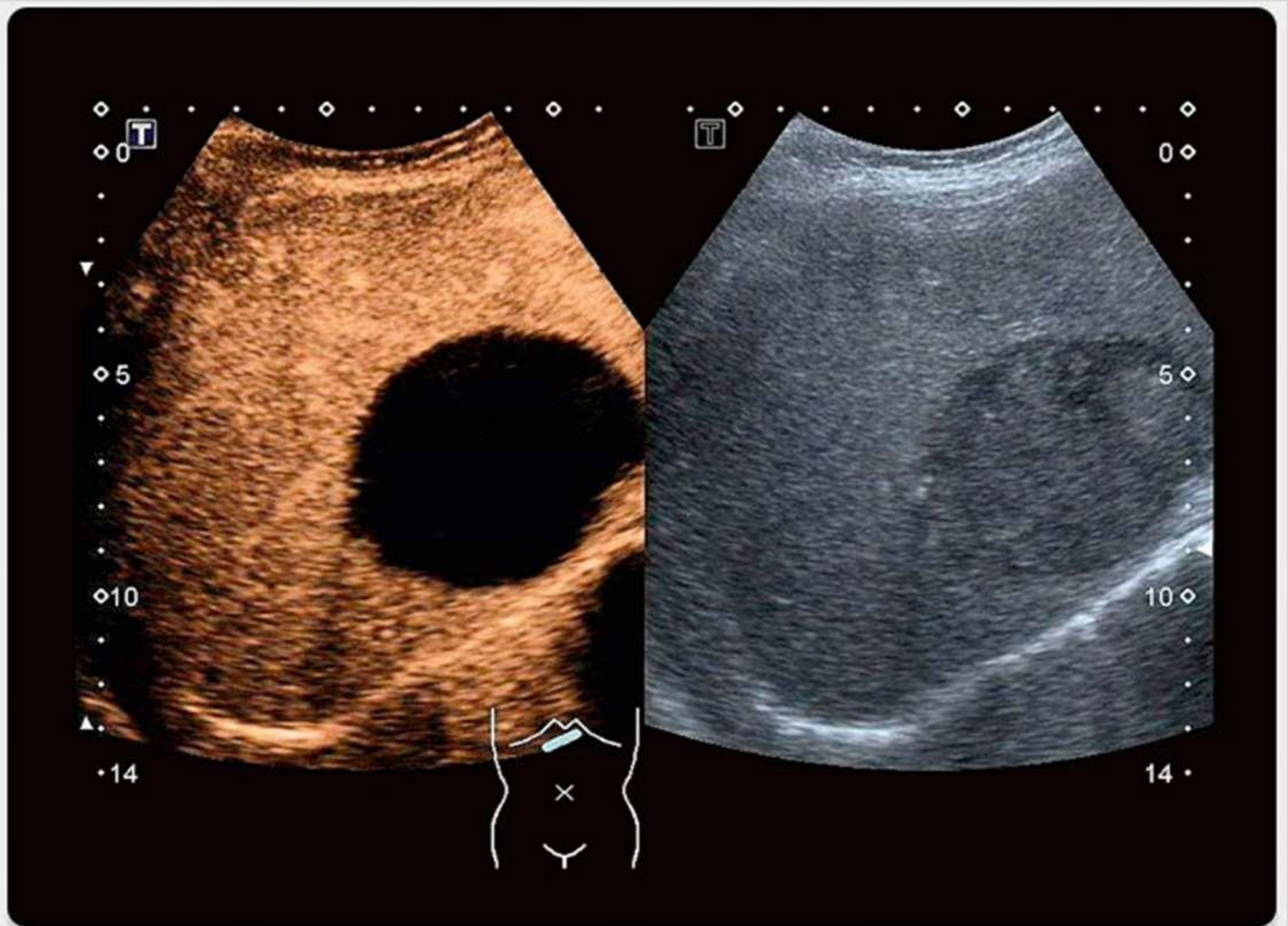
A clearer picture of the structure of an organ

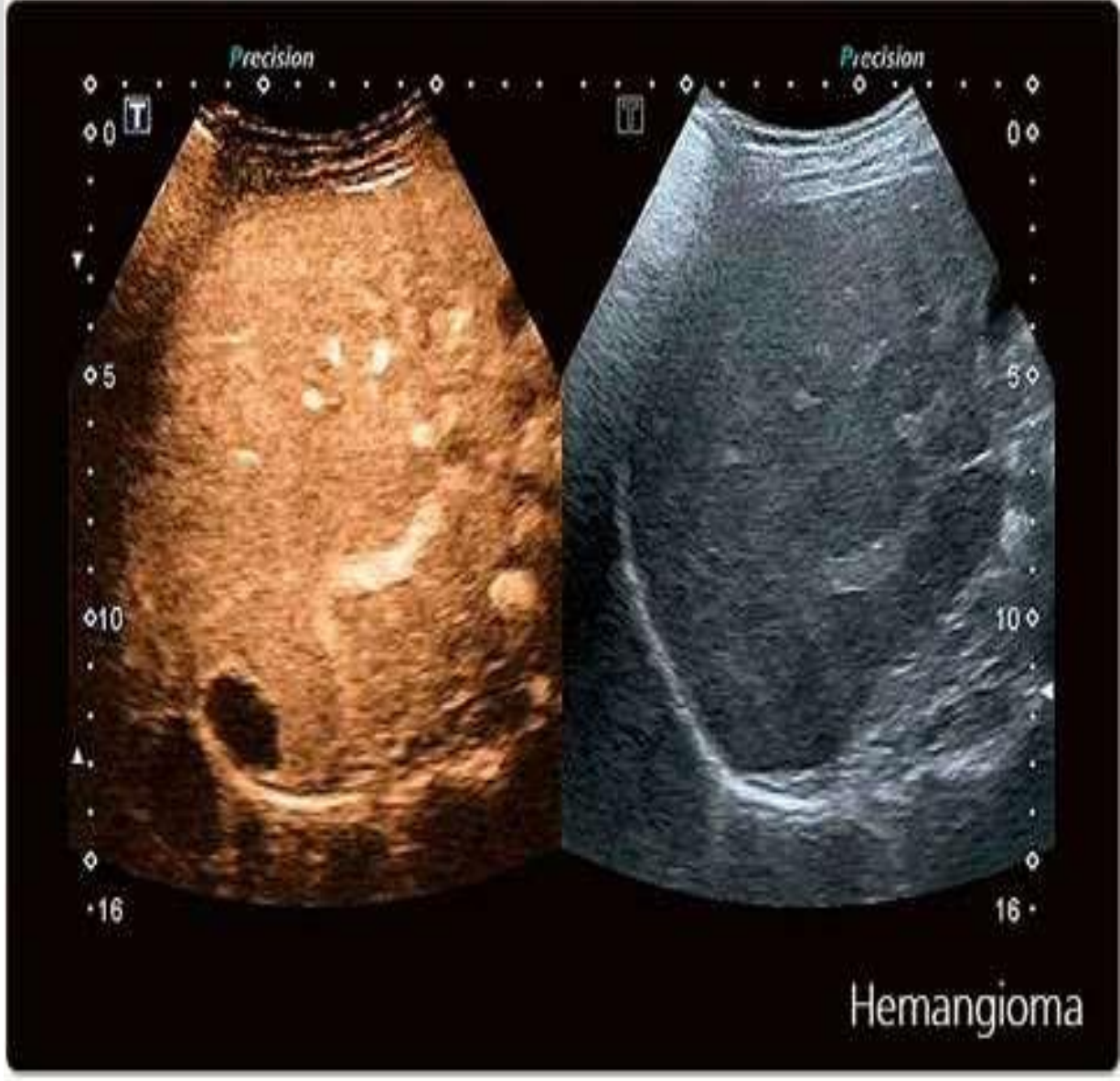
Evaluating the degree of blood perfusion and evaluating the blood volume in an organ or area of interest.

Differentiation between benign and malignant focal liver lesions



Liver abscess





Targeted contrast-enhanced ultrasound

Contrast agents designed to bind to specific molecules, which are then targeted at tissues expressing that substance.

Microbubbles targeted with ligands that bind certain molecular markers that are expressed by the area of imaging.

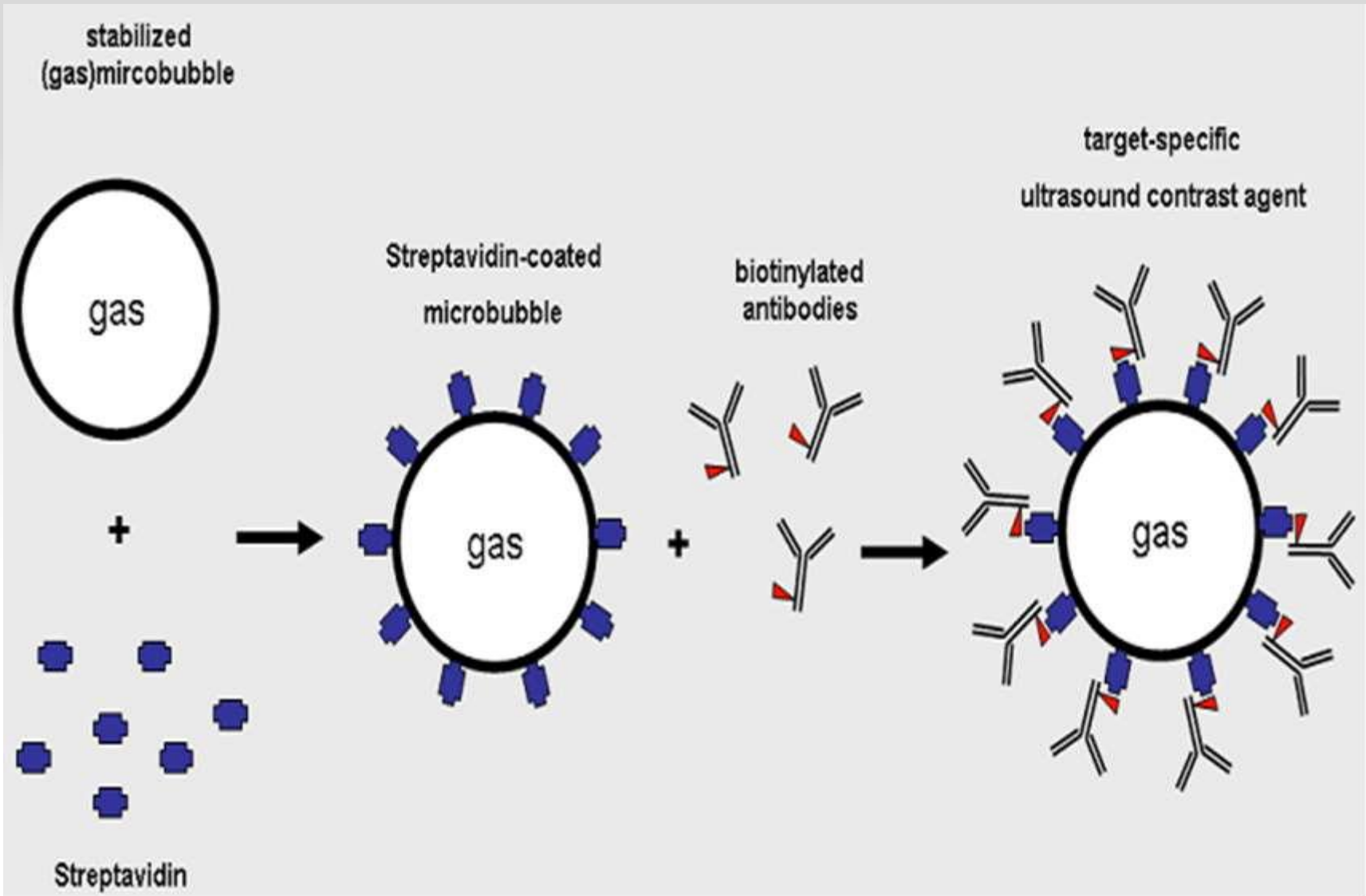
Microbubbles theoretically travel through the circulatory system, eventually finding their respective targets and binding specifically.

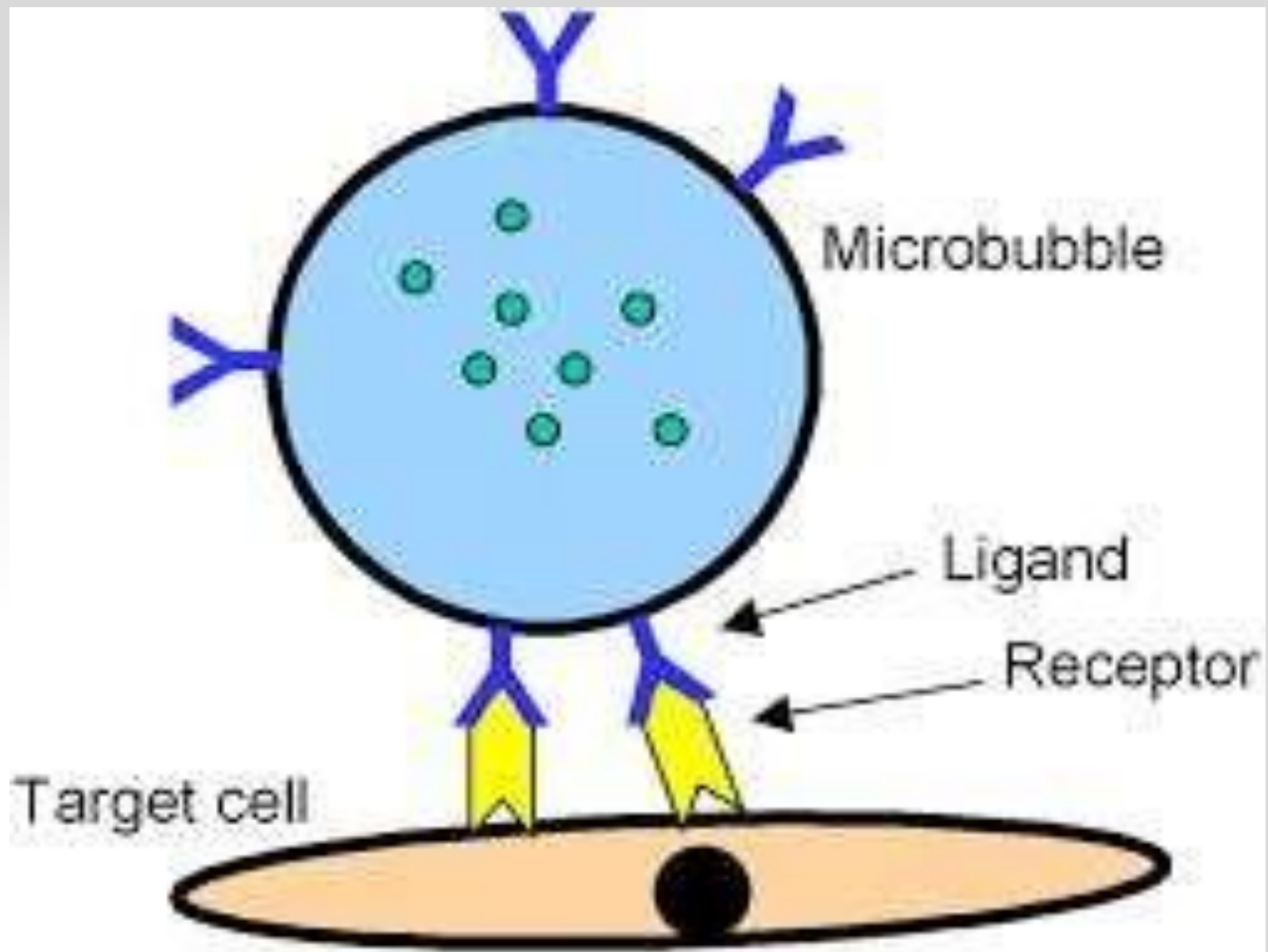
Targeting ligands that bind to receptors characteristic of intravascular diseases can be conjugated to microbubbles, enabling the microbubble complex to accumulate selectively in areas of interest, such as diseased or abnormal tissues.

This form of molecular imaging, known as targeted contrast-enhanced ultrasound, will only generate a strong ultrasound signal if targeted microbubbles bind in the area of interest.

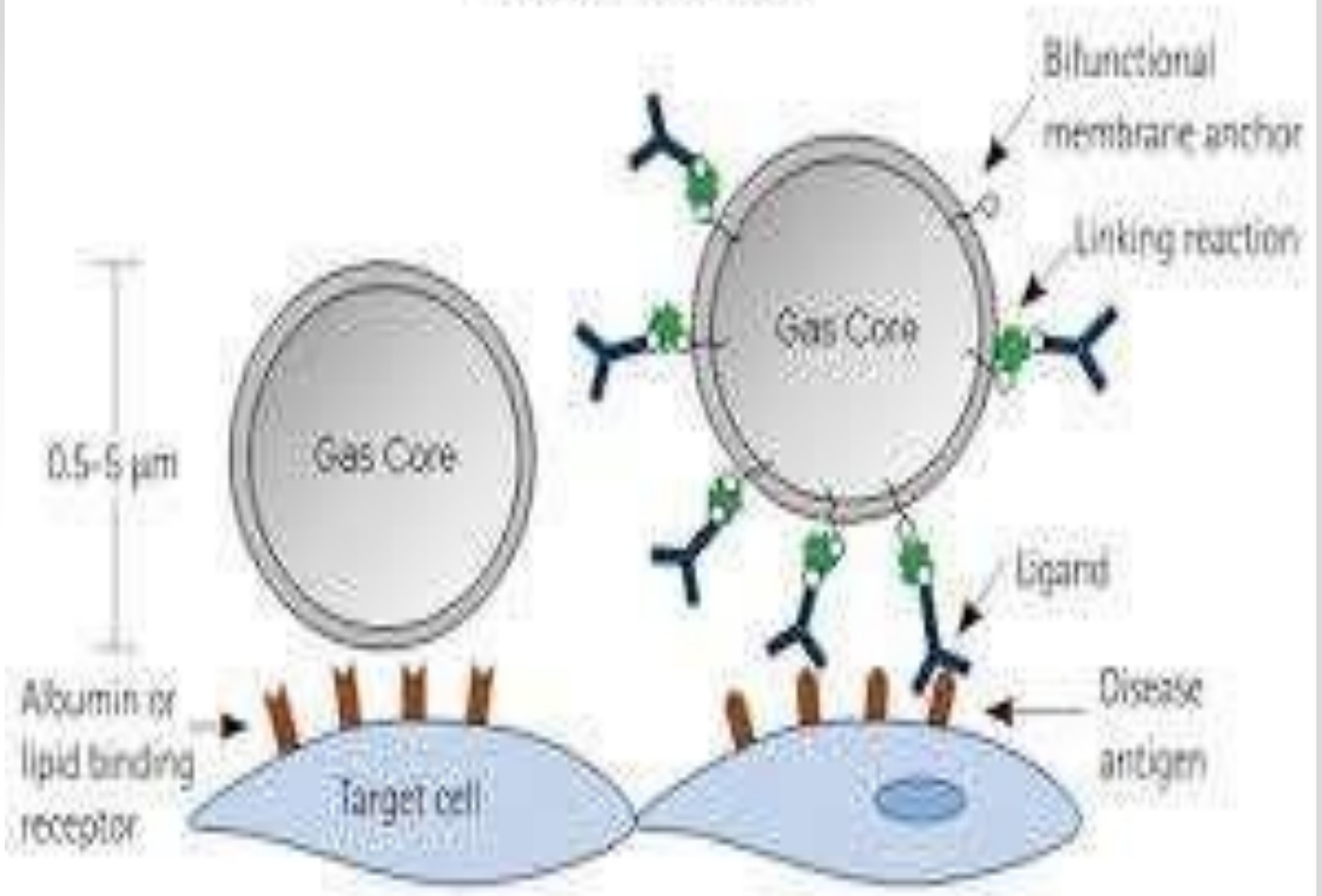
Targeted contrast-enhanced ultrasound may have many applications in both medical diagnostics and medical therapeutics.







Targeted microbubbles



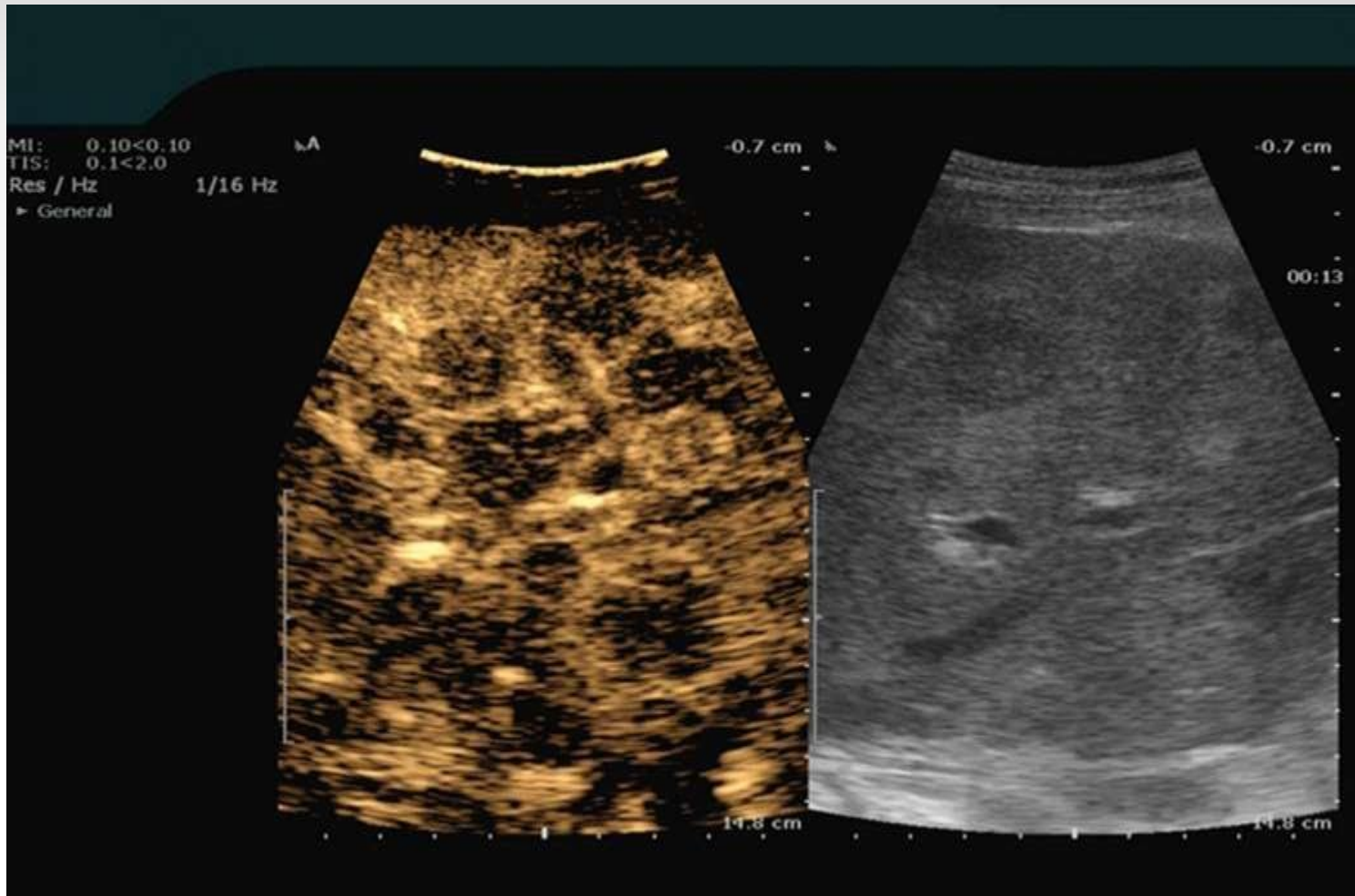
uses

Inflammation: Contrast agents may be designed to bind to certain proteins that become expressed in inflammatory diseases such as Crohn's disease, atherosclerosis, and even heart attacks

Thrombosis (is the formation of a blood clot inside a blood vessel) and thrombolysis: Contrast Agents specifically bind to activated platelets and allow real-time molecular imaging of thrombosis, such as in myocardial infarction, as well as monitoring success or failure of pharmacological thrombolysis.



Focal liver lesion



Prostate cancer

Medscape



contrast imaging techniques

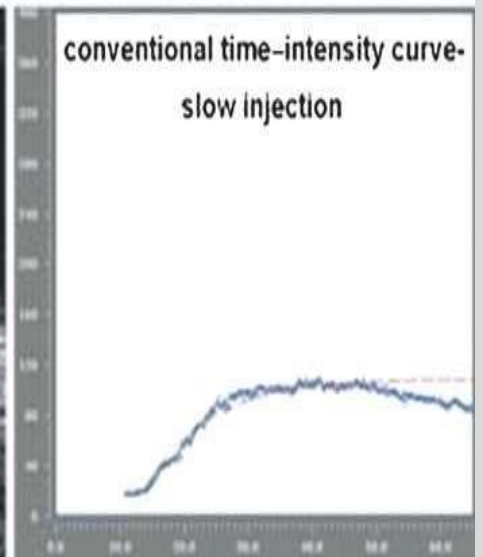
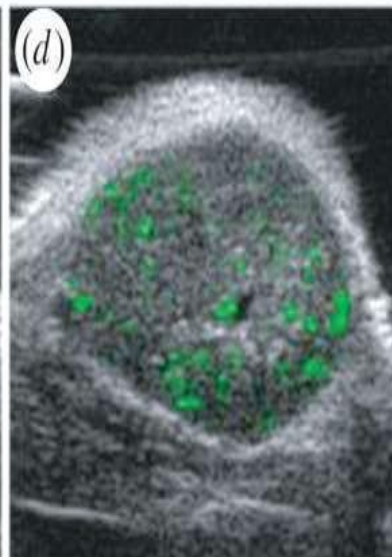
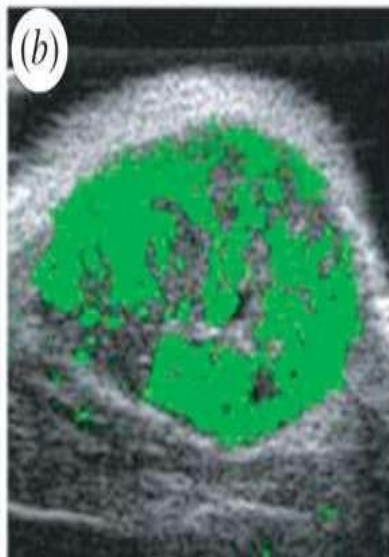
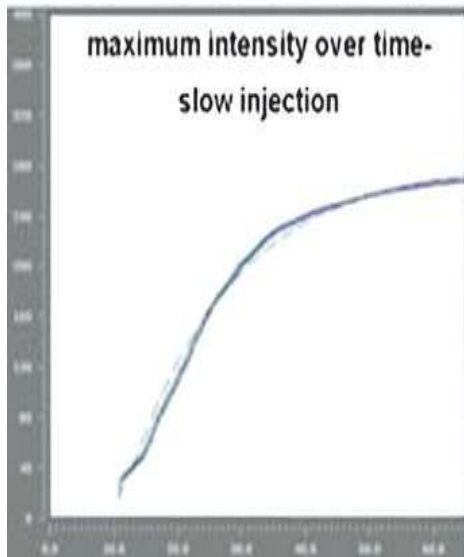
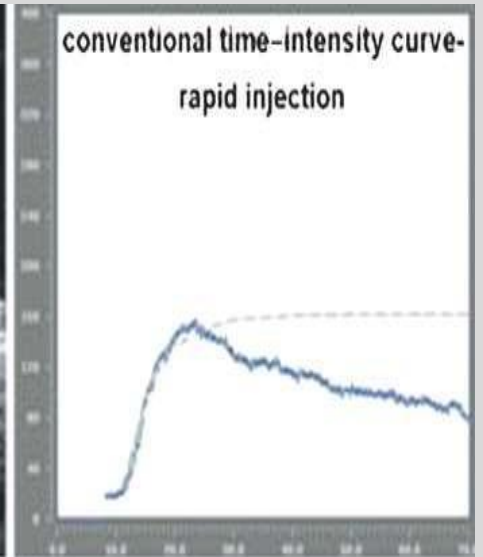
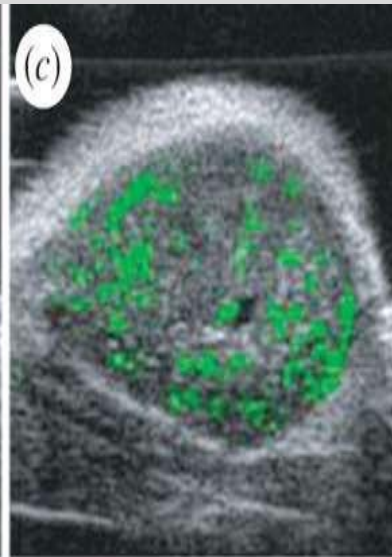
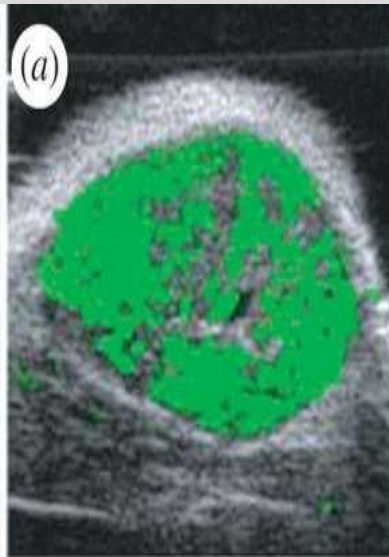
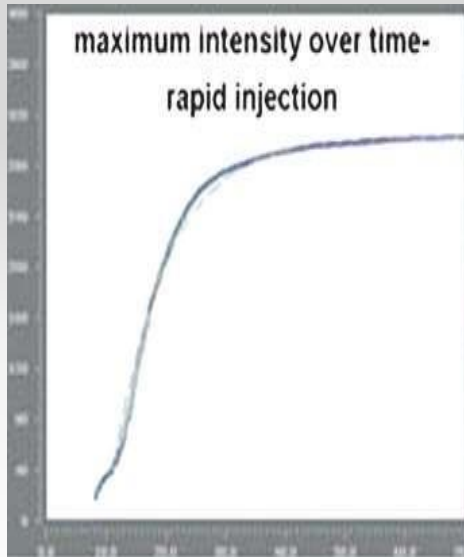
There are two contrast imaging techniques,
linear and
nonlinear.



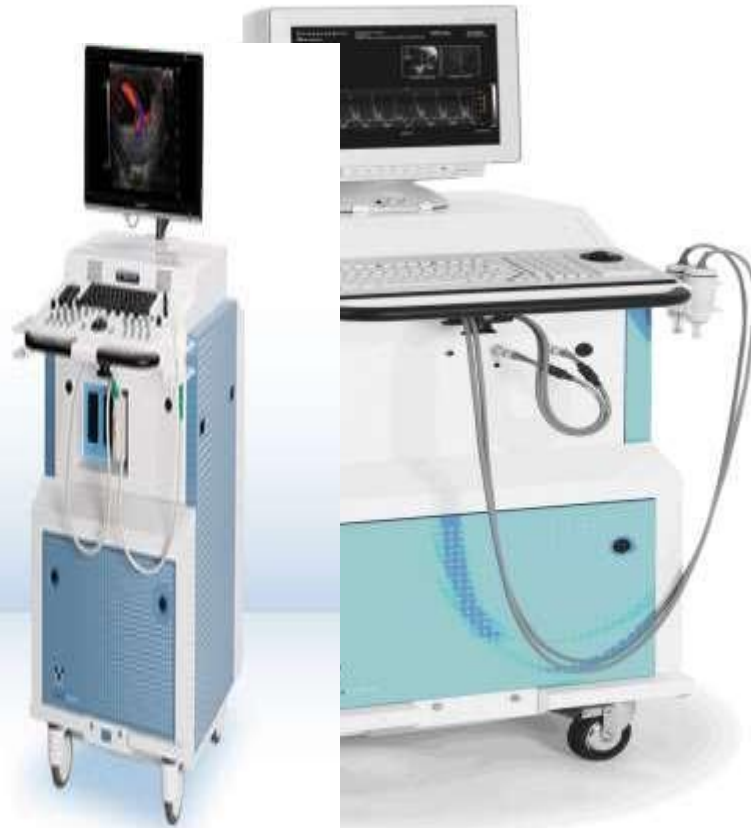
Linear contrast agent imaging refers to visualizing the microbubble contrast agents using **B-Mode** imaging and then applying a reference subtraction algorithm to apply a green contrast overlay on the image to aid in the visualization and quantification of the contrast specific signal.

This type of imaging is available both on the Vevo 770 as well as on the Vevo 2100 system.





 Vevo2100



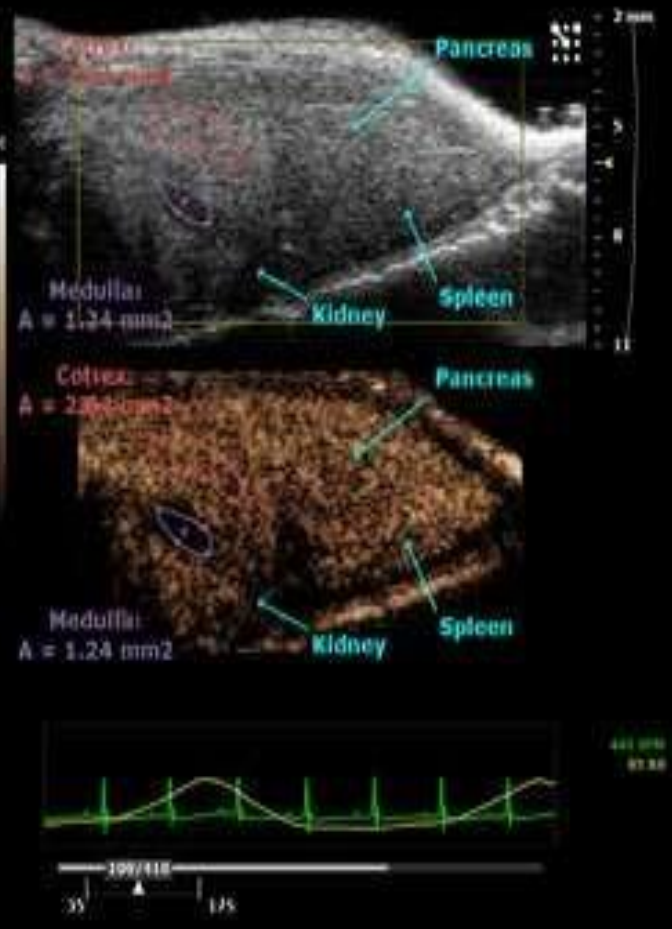
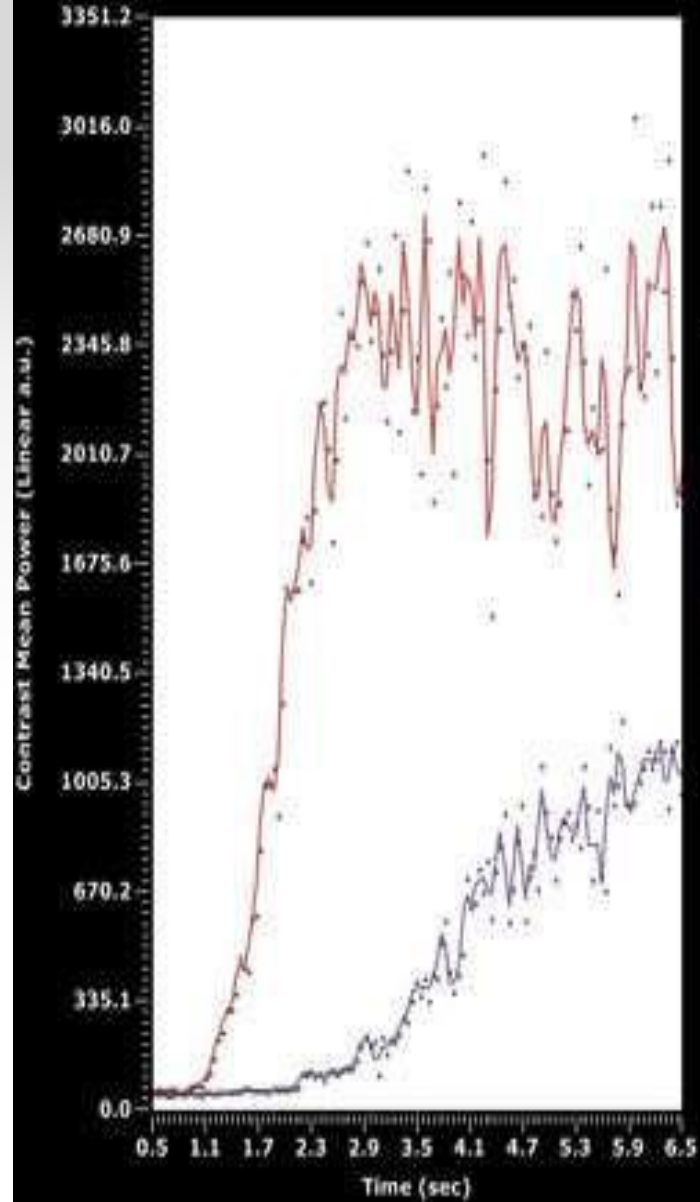
Nonlinear contrast agent imaging uses multiple ultrasound pulses in which the amplitude of the pulse is modulated, by performing this type of imaging the nonlinear response of the microbubbles to ultrasound pulses is utilized. The goal of this type of imaging is to suppress the tissue signal while increasing the detection of the contrast agents, providing a much more sensitive imaging technique. Nonlinear contrast imaging is only possible on the Vevo 2100 system using the MS200 and MS250 transducers.



Vovo2100

Study Name: Advanced Contrast
Series Name: Mouse
Image Label: Kidney, Pancreas, Spleen - untarg bolus
Frequency: 21 MHz

Cortex
Medulla



Disadvantages of CEUS

Microbubbles don't last very long in circulation.

They have low circulation residence times because they either get taken up by immune system cells or get taken up by the liver or spleen even when they are coated with PEG.

Ultrasound produces more heat as the frequency increases.

Monitoring Required



Targeting ligands can be immunogenic, since current targeting ligands used in preclinical experiments are derived from animal culture.

Low targeted microbubble **adhesion** efficiency. This is main reasons that targeted contrast-enhanced ultrasound remains in the preclinical development stages