

Introduction to Diagnostic Medical Imaging

Diagnostic Medical Imaging using Contrast-Enhanced Ultrasound System

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History of Medical Ultrasound¹:

The discovery of piezoelectricity by the Curies in 1880 using natural quartz started the chapter of using ultrasound as an energy source for many ultrasonic applications. But the applications of ultrasound in medicine did not begin until shortly after the 2nd World War. The main applications of ultrasound during this time were to develop SONAR for underwater navigation, communication and to detect other vessels. The publication by Dr. Karl Theodore Dussik in Austria in 1942 on their work on transmission ultrasound investigation of the brain was the first published medical ultrasonic application. Since then, with the development of the computer technology, ultrasound sensors technology, and the use of micro gas-bubble based contrast agents enable the resolution and quality of the ultrasound imaging to improve substantially. Coupling with less invasive nature of the ultrasound technology, inexpensive to invest the equipment than radiographic radiation technology and highly portable of the ultrasound equipment facilitate “diagnostic ultrasound” to be a preferred imaging modality in many different clinical situations. This paper will discuss, the use of contrast agents, the types of contrast agents, the advantage/disadvantage of using contrast agents and the challenges² of the medical ultrasound system in the future.

Medical Ultrasonic System:

The block diagram of a medical ultrasound system is shown in Figure 1^{3,4}.

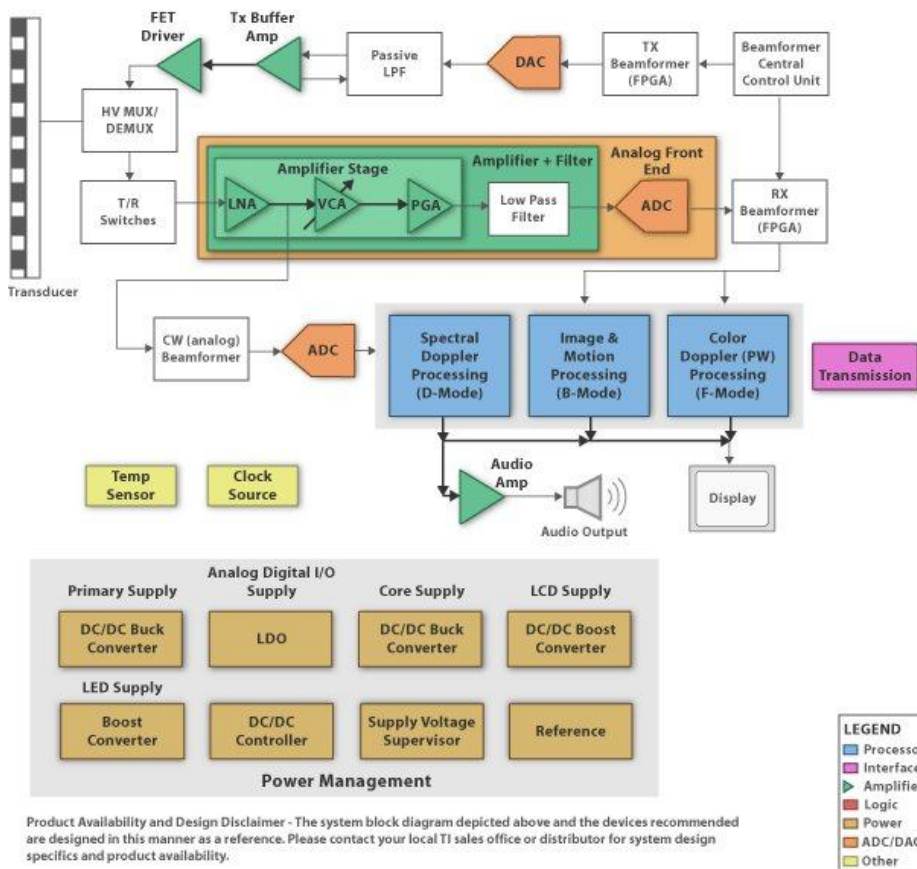


Figure 1 the block diagram of a medical ultrasonic system

The gel is usually used to prevent gap between the skin of patient diagnosed and ultrasound probe to reduce the artifacts. Diagnostic ultrasound is used mainly in two modalities on how mechanical energy applied either as continuous energy or pulsed energy. Continuous sound energy uses a

steady sound source and Doppler-effect for applications in measuring fetal heart beat as well as evaluating blood flow through different structures. Pulsed sound energy utilizes a pulse-echo effect to record different densities of tissues and their reflected sound energy levels. Through electronic processing of the returning sounds, a two-dimensional image can be created that provides information about the tissues and objects within the tissues. Combining the time dimensional and faster imaging processing speed, a 3-D real time ultrasound imaging can be created. The real-time medical ultrasonic imaging provides valuable information in the area scanned for details, texture and the shape.

Principles of Medical Ultrasonic System:

$$c = \frac{1}{\sqrt{\rho_0 K}}$$

Equation 1 speed of sound measurement.

$$Z = \rho_0 c$$

Equation 2 impedance measurement.

Where c is the speed of sound in a human tissue that depends on the average density of ρ ($\text{kg}\cdot\text{m}^3$) and the compressibility K ($\text{m}^2\cdot\text{N}^{-1}$) of the tissue. While acoustic impedance Z ($\text{kg}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$) depends on the average density of ρ ($\text{kg}\cdot\text{m}^3$) and the speed of sound of the tissue.

Object of Interest	Speed of Sound (m/s) room temp (25c)
Air	330
Fat	1450
Human tissue	1540
Brain	1541
Blood	1570
Skull bone	4080
Water	1480

Figure 2 the speed of sound on human body

These two equations and the speed of sound differences among human body shown in figure 2 illustrate the basic principles of how medical ultrasound imaging works. Since the human tissues are similar in speed of sound and compressibility, to improve the resolution of ultrasound imaging we must increase the sound energy applied (higher frequencies) and find a means to enhance the contrast among different tissues. Given that the air (micro-bubbles) has substantially lower speed of sound and higher compressibility enable it to be the main ingredient of contrast agent for diagnostic ultrasound technology.

Contrast-enhanced Medical Ultrasound System⁵:

Ultrasound contrast agents are gas-filled microbubbles that are managed intravenously to the body circulation. Microbubbles have a high degree of energy-reflection (echogenicity) from high impedance. The reflection of sound energy difference between the gas in the microbubbles and the soft tissue surroundings of the body is enormous. Because of the huge impedance differences, the

reflection of the ultrasound waves for these contrasts will produce a unique ultrasound imaging with enhanced contrast. For its usages, the contrast-enhanced ultrasound agents can be divided into two categories (1) untargeted and (2) targeted.

Untargeted microbubbles are injected intravenously into the circulation of human body for a certain period of time with ultrasound system monitoring on the area of interest. When microbubbles in the blood flow past the imaging window, the unique reflection of microbubbles would magnify the difference between microbubble and tissue echogenicity. The ultrasound system converts the strong echogenicity into a contrast-enhanced image of the area of interest. In this way, the bloodstream's echo is enhanced, thus allowing the distinguish of blood from surrounding tissues. Targeted microbubbles are the microbubbles targeted with ligands that bind certain molecular markers. These microbubbles will travel through the body and eventually find their respective targets and bind together specifically. Detection of binding microbubbles in a specific area might be the indication of disease in certain state or to identify certain cells in the area of interest.

Advantages of contrast-enhanced ultrasound⁵

- (1) Improve the resolution of traditional ultrasound system for the interface between blood flow and allowing real-time evaluation of blood flow.
- (2) It is safe to use ultrasound for molecular imaging system comparing with other radionuclide imaging system.
- (3) It is inexpensive to measurement or invest in ultrasonic system than other imaging modalities such as MRI, PET and SPECT.
- (4) Very small amount of microbubbles contrast agents are needed for measurements.
- (5) For specific application, contrast-enhanced ultrasound proved to be better than CT or other imaging modalities^{6,7}.

Disadvantages of contrast-enhanced ultrasound⁵

- (1) Microbubbles don't last very long in circulation because they are either taken up by immune system cells and/or by the liver or spleen even with specific coatings.
- (2) Higher frequency transducer is needed for higher resolution imaging but the monitoring of heat generated from transducer is required.
- (3) Microbubbles might burst at low ultrasound frequencies could cause local microvasculature and hemolysis.
- (4) More clinical study needed for selecting targeting ligands
- (5) Targeted microbubbles only adhere a small fraction of injected microbubbles bind to the area of interest.

Medical Ultrasound System Challenges^{2,8}

The use of contrast agents coupling advanced computer/transducer technologies have improved the performance of medical ultrasound system to a milestone that could outperformed some other imaging mortalities⁶ (CT.) To improve the resolutions of current medical ultrasound system to a sub-millimeter levels, the improvement needed the compounded effect from contrast agents, low-heat high frequencies transducer as well as even more advanced computer/software technology. In

the future the frequencies deployed would be from 20MHz to 100 MHz instead of 1-15 MHz used in most medical ultrasound system. The medical research on the targeted micro-bubbles with ligands will produce the contrast agent that demonstrates both efficiency and compatibility. It is also essential to manufacture the battery-powered medical ultrasound system that is both portable and powerful enough to facilitate the decision making for a doctor in real time.

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