TEHRAN UNIVERSITY OF MEDICAL SCIENCES

TUMS PRECLINICAL CORE FACILITY (TPCF)

INTRODUCTION TO IN VIVO MICRO ULTRASOUND IMAGING AND ITS APPLICATIONS

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Overview

- Introduction
- Ultrasound Physics
- Ultrasound Imaging
- Applications
- Ultrasound Contrast Agents
- Summery

Introduction
What is a Waves

- In physics, a **wave** is a disturbance that transfers energy through matter or space, with little or no associated mass transport. Waves consist of oscillations or vibrations of a physical medium or a field, around relatively fixed locations. From the perspective of mathematics, waves, as functions of time and space, are a class of signals.

Introduction
Types of Waves

- Mechanical Wave
- Electromagnetic Wave
- Matter Wave
- Gravity Wave

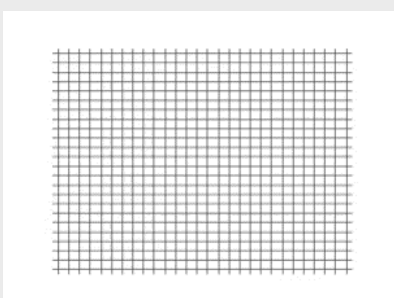
Introduction

Types of Waves

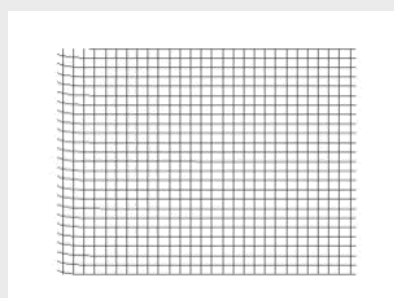
- Mechanical waves require a physical medium. The particles in the medium can move in two different ways: either perpendicular or parallel to direction of the wave itself.
- In a *longitudinal* wave, the particles in the medium move parallel to the direction of the wave.
- In a *transverse* wave, the particles in the medium move perpendicular to the direction of the wave.
- A *surface* wave is often a combination of the two. Particles typically move in circular or elliptical paths at the surface of a medium.

Introduction

Types of Waves



Longitudinal Waves



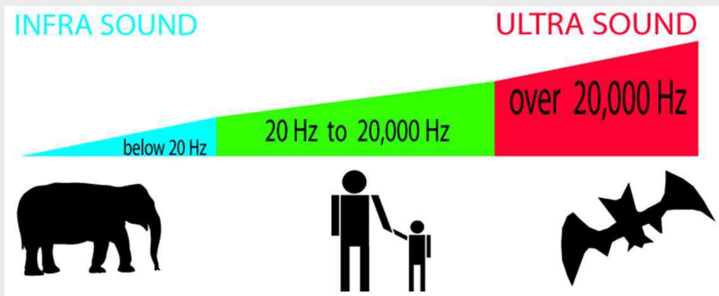
Transverse Waves

Introduction

What is "Ultra"…….sound?

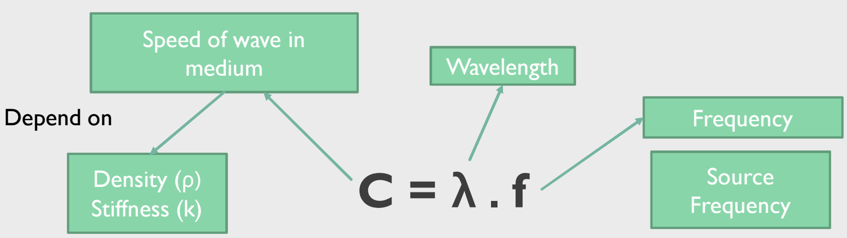
Audible range is 20 to 20,000 cycles per second

Ultrasound has frequency greater than 20,000 cycles per second



Ultrasound Physics

Frequency and Wavelength of Waves



f (MHz)	λ (mm)
2	0.77
5	0.31
10	0.15
15	0.1

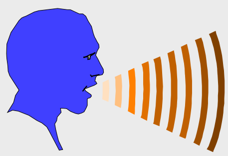
f= 3.5 MHz
C=1500 m/s
Wavelength=**?**

=1500/3.5e6=0.00043 m =0.43 mm

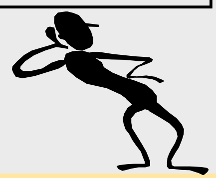
Ultrasound Physics
Ultrasound Transducer

- Acts as both speaker & microphone
  - Emits very short sound pulse
  - Listens a very long time for returning echoes
- Can only do one at a time

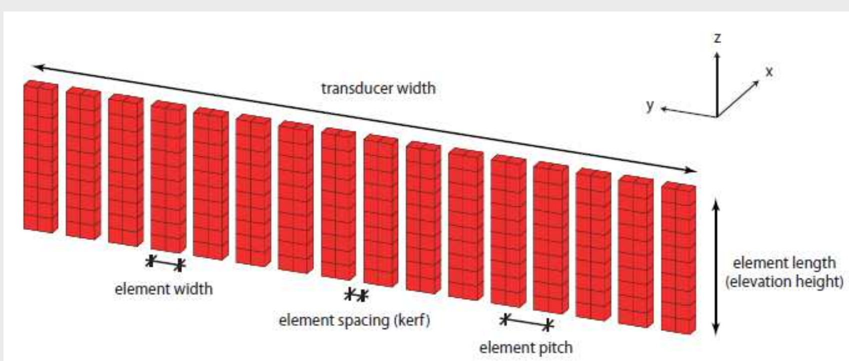
Speaker
transmits sound pulses



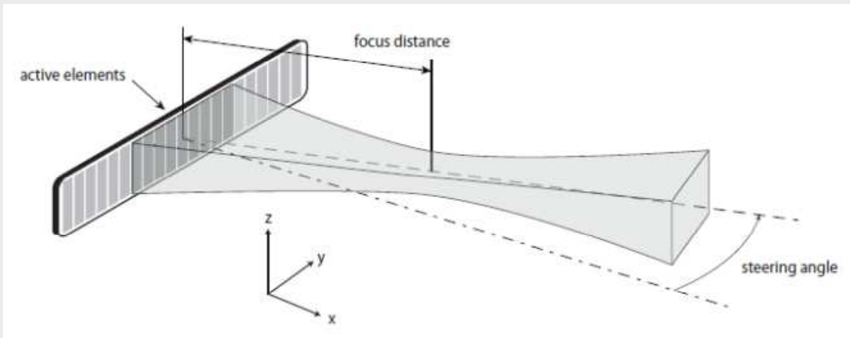
Microphone
receives echoes



Ultrasound Physics
Ultrasound Transducer

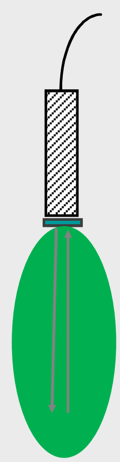


Ultrasound Physics
Ultrasound Transducer



Ultrasound Imaging
What does your scanner know about echoed sound?

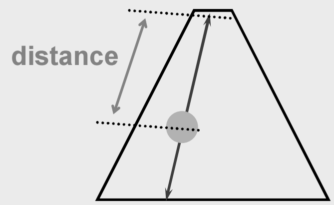
What was the time delay between sound broadcast and the echo?



Ultrasound Imaging
Distance of Echo from Transducer

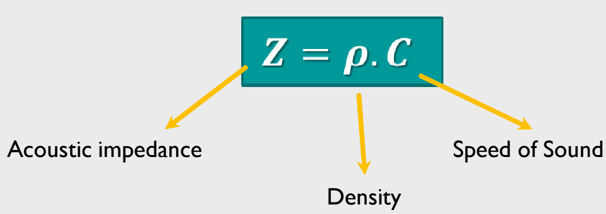
- **Time delay accurately measured by scanner**

distance = time delay X speed of sound



Ultrasound Imaging
Acoustic Impedance

Acoustic impedance of a medium: measure of the response of the particles of the medium in terms of their velocity, to a wave of given pressure



Ultrasound Imaging

Acoustic Impedance

Amplitude of returning echo is proportional to the difference in acoustic impedance between the two tissues

- Thus, when an ultrasound beam encounters two regions of very different acoustic impedances, the beam is reflected or absorbed

  So ------- Cannot penetrate

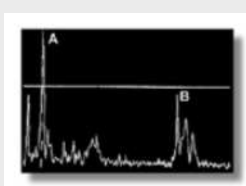
  Example: soft tissue – bone interface

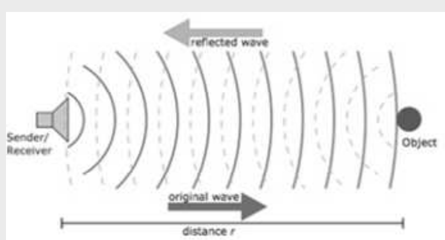
Material	Z(Kg $^{-2}$ s^{-1})
Liver	$1/66 \times 10^6$
Kidney	$1/64 \times 10^6$
Blood	$1/67 \times 10^6$
Fat	$1/33 \times 10^6$
Water	$1/48 \times 10^6$
Air	430
Bone	$6/47 \times 10^6$

Ultrasound Imaging

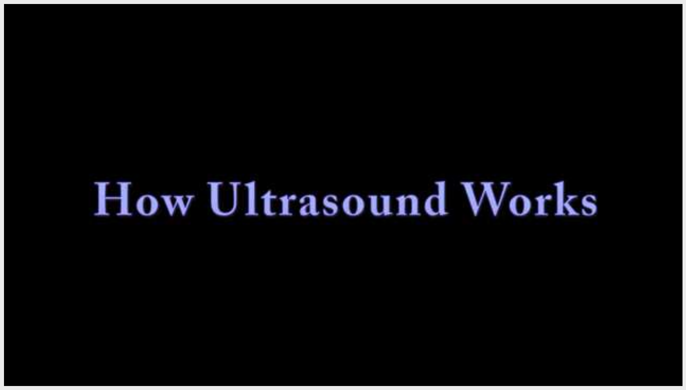
Pulse-Echo

- Pulse travels through the body tissues and encounters many interfaces and scatters which generate echoes
- After a short pulse is transmitted (Transmit mode), the transducer start listening for echoes (Receive mode)
- Echoes start returning from different depths in a continuous series (pulse–echo sequence)



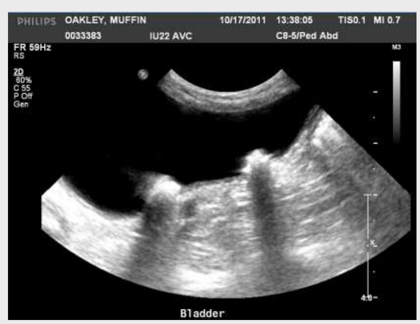


Ultrasound Imaging



Ultrasound Imaging

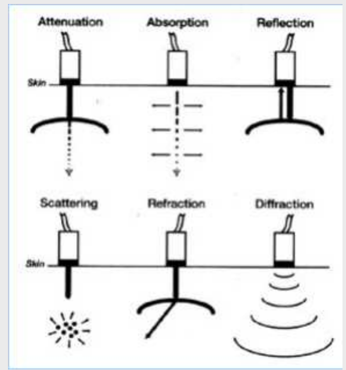
- Two regions of very different acoustic impedances, the beam is reflected or absorbed



Ultrasound Imaging
Different Interactions

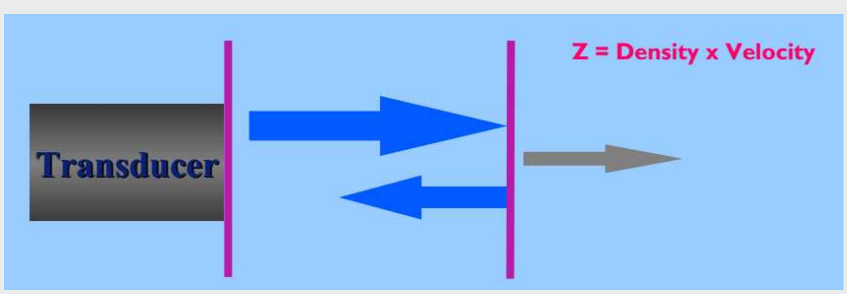
- Interactions of Ultrasound with tissue

- **Reflection**
- **Transmission**
- **Attenuation**
- **Scattering**



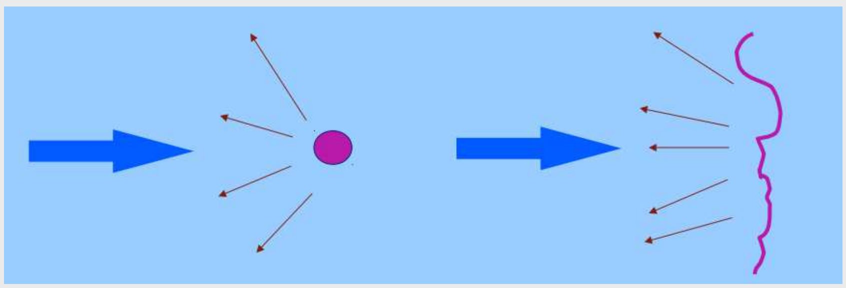
Ultrasound Imaging
Reflection

- Occurs at a boundary between 2 adjacent tissues or media
- The amount of reflection depends on differences in acoustic impedance (z) between media
- The ultrasound image is formed from reflected echoes



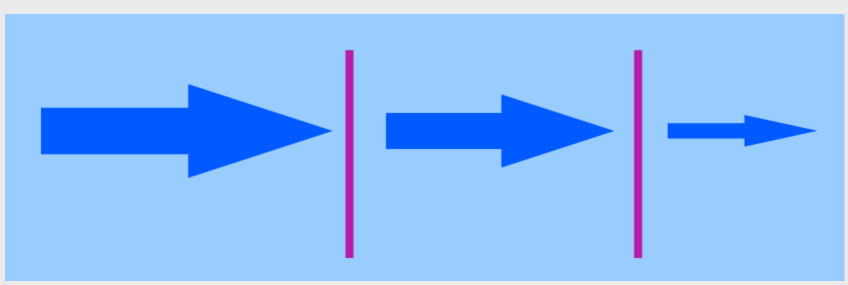
Ultrasound Imaging
Scattering

- Redirection of sound in several directions
- Caused by interaction with small reflector or rough surface
- Only portion of sound wave returns to transducer



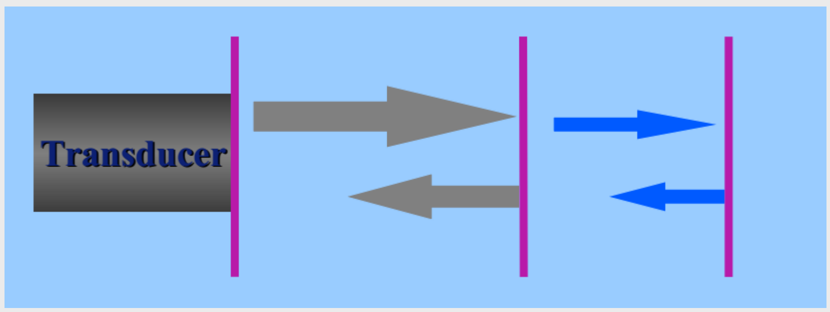
Ultrasound Imaging
Attenuation

- The deeper the wave travels in the body, the weaker it becomes
- The amplitude of the wave decreases with increasing depth

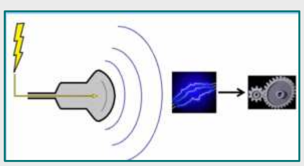


Ultrasound Imaging
Transmission

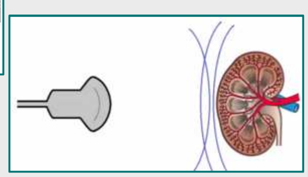
- Not all the sound wave is reflected, some continues deeper into the body
- These waves will reflect from deeper tissue structures



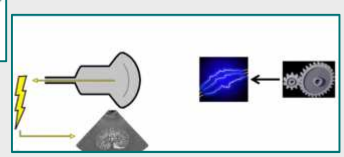
Ultrasound Imaging



1. Electrical Energy converted to Sound waves



2. The Sound waves are reflected by tissues



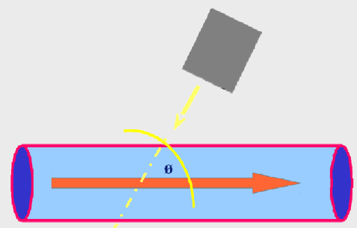
3. Reflected Sound waves are converted to electrical signals and later to Image

Ultrasound Imaging
Doppler Effect

Apparent change in received frequency due to a relative motion between a sound source and sound receiver

– Sound TOWARD receiver = frequency

– Sound AWAY from receiver = frequency



- Used to evaluate and quantify blood flow
  - Transducer is the sound source and receiver
  - Flow is in motion relative to the transducer
- Doppler produces an audible signal as well as a graphical representation of flow = Spectral Waveform

Ultrasound Imaging
Advantages and Disadvantages

Advantages

- Close to clinical translation from animal models
- High spatial and temporal translation
- Uses non-ionising radiation
- Portable and Low cost

Disadvantages

- Quality and interpretation of the image highly depends on the skill of the person doing the scan
- Other factors can affect image quality, including the presence of air and calcified areas in the body (e.g. bones, plaques and hardened arteries), and a person's body size
- Use of a special probe (e.g. for the oesophagus, rectum or vagina) is required in some ultrasounds
- Targeted imaging limited to vascular compartment

Ultrasound Imaging
Special Probes

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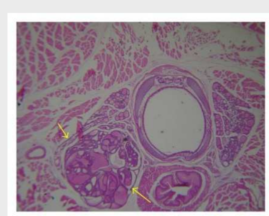
Applications: Oncology

- Micro Ultrasound imaging of thyroid in living mice
- Frequency: 35 MHz probe
- mice model: thyroid disease (TRK)

an enlarged left lobe with hypoechoic nodule (arrows)



Histopatholog y analysis shows a thyroid adenoma

Marcello Mancini and et. al, Endocrinology, Volume 150, Issue(10), 4810–4815,

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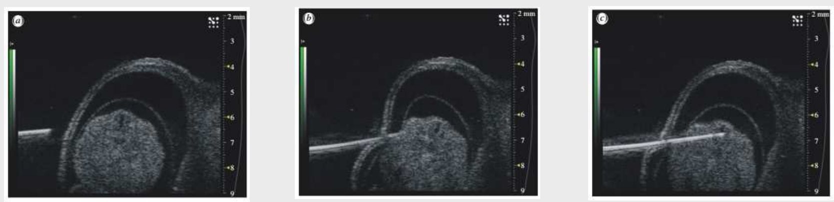
Applications: Guidance for Prenatal Interventions

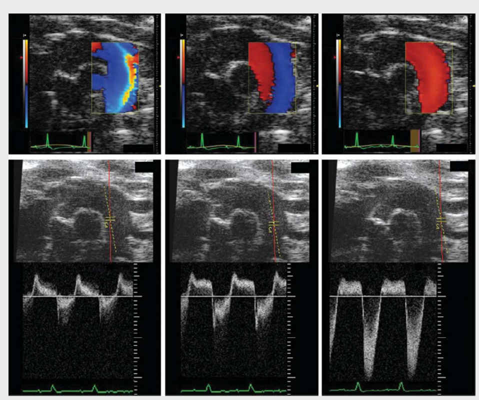
- ❑ Ultrasound guided microinjection into the spinal canal of a mouse embryo
- ❑ Frequency: 30 MHz probe
- ❑ mice model: mouse embryo



Nieman, B. J. & Turnbull, D. H., Meth. Enzymol. 476, 379–400

Applications: Cardiovascular Imaging

- Flow distribution in the aortic arch

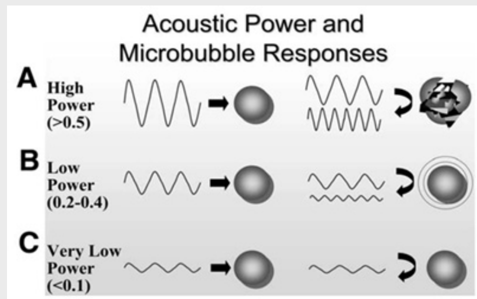


F. Stuart Foster and et. Al, Interface Focus (2011) 1, 576–601

Ultrasound contrast agents

Microbubble contrast agents

comprised of gas bubbles less than 5 mm in diameter and encapsulated by a polymer or lipid shell, represent a special kind of scattering source that is critical to the development of molecular imaging with ultrasound.



Ultrasound contrast agents

Microbubble contrast agents

There are a variety of microbubble contrast agents. Microbubbles differ in their shell makeup, gas core makeup, and whether or not they are targeted.

Microbubble shell: selection of shell material determines how easily the microbubble is taken up by the immune system

Microbubble gas core: The gas core is the most important part of the ultrasound contrast microbubble because it determines the echogenicity

Ultrasound contrast agents

How it works:

There are two forms of contrast-enhanced ultrasound, untargeted (used in the clinic today) and targeted (under preclinical development). The two methods slightly differ from each other.

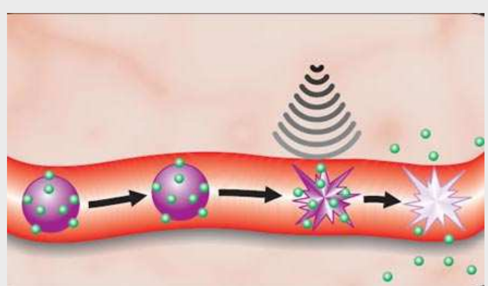
Untargeted contrast agents: The microbubbles will remain in the systemic circulation for a certain period of time. During that time, ultrasound waves are directed on the area of interest.

Targeted contrast agents: Microbubbles targeted with ligands that bind certain molecular markers that are expressed by the area of imaging interest are still injected systemically in a small bolus

Ultrasound contrast agents

- Drug delivery

the system shatters the shells of the microbubbles by means of a focused, high-energy ultrasound pulse. Once the shells are destroyed, the contents of the microbubbles spill into the surrounding area and the drugs reach the tumor directly instead of going through the whole bloodstream.



Ultrasound contrast agents

Following of Micro Bubble injection in time

tail vein injection of 80 ml Micro Marker

t = 0 *t* = 1s *t* = 5s

F. Stuart Foster and et. Al, Interface Focus (2011) 1, 576–601

Summery

- How does an US imaging system work?
- Which kind of contrast agents improve an US image?
- US Imaging applications.

Thanks for Your Attention