

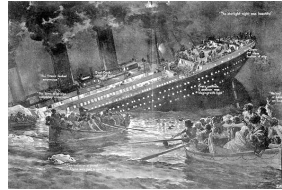
PowerPoint Slides

- ❖ Medical Imaging

1

A Smidge of Ultrasound (US) History

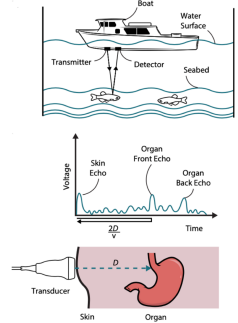
- SONAR and US development traceable to sinking of Titanic in 1912
- In 1913, a British scientist filed patents to detect icebergs based on underwater echo ranging



2

The Essence of Ultrasound (US)

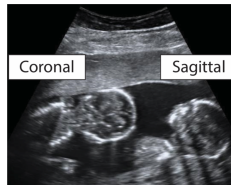
- Maps body structures based on echo detection, similar to SONAR
- Transducer generates and directs a US pulse into the body and detects US reflected or scattered by anatomic structures
 - ❖ Tissue depth is $D = v \times t_{\text{echo}}/2$, where t_{echo} is the echo time and $v = 1540 \text{ m/s}$ (US speed in soft tissue/water)
- Echo amplitude creates contrast
 - ❖ Large amplitude (stronger) echoes arise from "mismatched" interfaces, like soft tissue/bone interfaces (bright in images)
 - ❖ Small amplitude (weaker) echoes arise from "similar" interfaces, like different soft tissues interfaces (lighter, variable shades of gray in images)



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Medical Applications

- Applications
 - ❖ Technique of choice for fetal imaging – high-resolution, real-time, with no risk
 - ❖ Powerful method of monitoring blood flow
 - ❖ Organ imaging
- Strengths & Weaknesses
 - ❖ Low risk, real-time imaging
 - ❖ Inexpensive and portable
 - ❖ Not suited for bone, limited ability to see deep in larger patients



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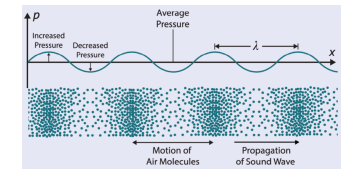
Some Key Attributes of Waves

- Properties of a wave
 - ❖ λ = wavelength (distance between adjacent crests) in units of "m"
 - ❖ T = period (cycle time) in "s"
 - ❖ ν = frequency (cycles/s) = $1/T$ in "Hz"
 - ❖ v = propagation speed = $\lambda \nu$ in "m/s"
 - ❖ A = amplitude (wave height/determines energy) in "m"

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Some Key Attributes of US

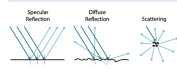
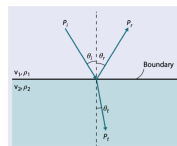
- US is a sound wave of high frequency
 - ❖ US frequencies in the range from 2 MHz - 10 MHz (megahertz)
 - ❖ Humans hear from ~20 Hz – 20 kHz
- Sound waves are compression waves
 - ❖ Propagate in media (not a vacuum)
 - ❖ Speed in tissue 1540 m/s
 - ❖ Compression waves occur in elastic media when molecules shifted by an applied force
 - ❖ Molecules displaced along the direction of wave propagation \Rightarrow longitudinal wave
 - ❖ <https://www.youtube.com/watch?v=7GdAY7Kq3E>



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Wave Behavior at an Interface – The Essence of US

- A wave is partially reflected and transmitted at a smooth boundary between media in which the wave speed differs
 - ❖ Reflected wave propagates in reverse direction (for normal incidence)
 - ❖ Transmitted wave propagates in original direction
- Specular reflection contributes to echoes – the signal in US imaging
- Diffuse reflection from irregular structures and scattering also contribute to echoes
- Transmission generates echoes from deeper structures



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Intensity of Reflection

- In the absence of a boundary there is no reflection
- Intensity of specular reflection is determined by the mismatch at the boundary
 - ❖ Small mismatch \rightarrow small reflection
 - ❖ Big mismatch \rightarrow big reflection

	Fat	Muscle	Skin	Brain	Liver	Blood	Cerebral Bone
Water	0.047	0.02	0.029	0.097	0.005	0.087	0.07
Fat		0.02	0.024	0.049	0.047	0.01	0.01
Muscle			0.009	0.013	0.012	0.02	0.04
Skin				0.022	0.04	0.029	0.06
Brain					0.029	0.01	0.07
Liver						0.029	0.01
Blood							0.07

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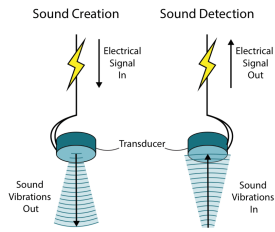
US is Generated Via Energy Transformation

- US generated and detected using a transducer
- Transducer = device that converts energy from one form to another
- Examples
 - ❖ Speaker – electrical into mechanical
 - ❖ Ear – mechanical into electrical
 - ❖ Light bulb – electrical into light and heat
 - ❖ Your brain – mechanical (e.g., stimuli) into electrical

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Transducers – The Mouth and Ears of US Machines

- Key component of US transducer is a piezoelectric crystal
 - Electrical potential \leftrightarrow mechanical deformation
- Generation of US by transducer
 - Short electrical pulse at frequency ν causes mechanical vibration of crystal that generates US at same frequency ν
 - Crystal thickness determines ν
- Detection of US echo by transducer
 - Mechanical vibrations of wave cause crystal vibration that generates an electrical signal
- Tutorial/Animation
 - <http://www.olympus-ims.com/en/ndt-tutorials/transducers/characteristics/>



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Basic Physics of US Imaging – Part I

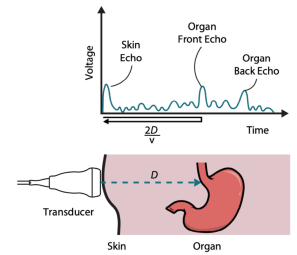
- Body tissue generates an interface where US reflects and transmits
- Acoustic impedance (Z)
 - Z is a measure of resistance to sound passing through medium
 - Reflection and transmission occur at an interface with ΔZ
 - Light similarly undergoes reflection and transmission at an interface with Δn
- Very large ΔZ (e.g., air/skin interface) is bad \rightarrow all US reflected
 - Coupling medium used to match impedance of crystal and skin
 - Body layers have similar impedances \rightarrow $< 1\%$ reflected
 - Good enough for detection and leaves enough US to continue on and undergo further reflection

Tissue	Acoustic Impedance (rayl = kg/(m ² s))
Air	0.0004×10^6
Lung	0.18×10^6
Fat	1.34×10^6
Water	1.48×10^6
Skin	1.6×10^6
Kidney	1.63×10^6
Blood	1.65×10^6
Liver	1.65×10^6
Muscle	1.71×10^6
Bone	7.8×10^6

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Basic Physics of US Imaging – Part II

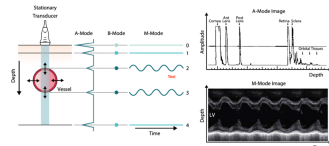
- Reflection/echo sent back to transducer, which generates a voltage that is recorded and converted into an image
 - Amplitude determined by echo strength
 - Arrival time determined by tissue depth
- Amplitude increases as ΔZ increases – quantify later
- Time increases as depth increases
 - Time = distance/speed = $2D/\nu$



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From Echo into Static One-Dimensional Image

- Two 1D imaging modes – A & M
- A (amplitude) mode simple & instructive
 - Echoes collected along one line within body
 - Echoes from various depths shown as spikes along a line
 - Spike height reflects echo amplitude
 - Spike position reflects echo time
 - https://folk.ntnu.no/stoylen/strainrate/basic_ultrasound
- A mode is useful for biometry of the eye – measurement of eye dimensions
 - Used to determine the power of intraocular lens used in cataract surgery
 - <https://www.youtube.com/watch?v=4W0m9jIMt>



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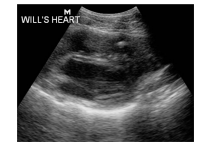
From Echo into Dynamic One-Dimensional Image

- M (motion) mode adds motion to A mode
 - Depth plotted along vertical axis
 - Echoes shown as points with brightness determined by echo strength
 - Dots for a given depth (structure) plotted versus time revealing structure motion
 - Popular in cardiology to study valve motion
 - https://folk.ntnu.no/stoylen/strainrate/basic_ultrasound

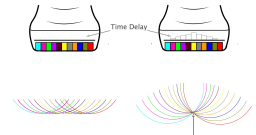
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From Echo into Two-Dimensional Real-Time Image

- Two-dimensional B (brightness) mode generates an image resembling cross-sectional slice
 - Each line in B scan is like an A scan
 - For each line scan, record echo time (structure position) as dots along vertical
 - Also record echo intensity as dot brightness – generates contrast
 - http://folk.ntnu.no/stoylen/strainrate/basic_ultrasound#B2D
- Multiple line scans received by transducer with multiple crystals
 - Beam typically scanned, steered, and focused using timed crystal activation
 - https://en.wikipedia.org/wiki/Phased_array
 - <http://www.cdm.ca.ca/crcch/bora/yvuka/rlb/sem2006/ondrgh30tbl/P4ar/inside.php.htm>
- Motion monitored in real time
 - Images generated quickly (30 frames per second)



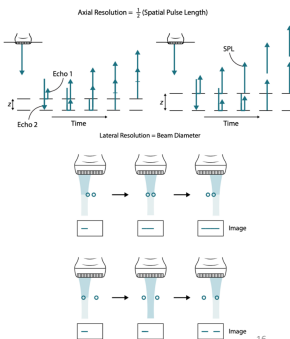
if hover over image to play movie



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Factors that Affect Imaging – Resolution

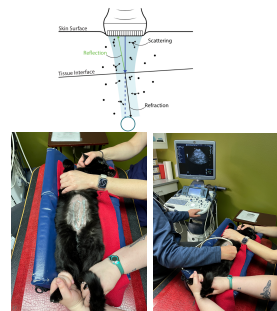
- Resolution
 - Axial
 - Lateral
- Axial – ability to discriminate structures on axis with beam
 - Objects resolved if $SPL < 2z$
 - SPL typically $\sim 3\lambda \rightarrow$ resolution improves with increasing ν
 - Penetration decreases with increasing ν
- Lateral – ability to discriminate structures side by side within beam in image plane
 - Objects resolved if beam diameter $<$ object separation (like LSCM)
 - Resolution changes with depth due to beam spread
 - Focus to ensure best resolution for structure of interest



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Factors that Affect Imaging – Reflection, Refraction, and Scattering

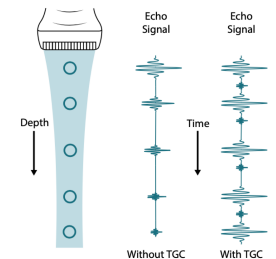
- Reflection and refraction of light at an interface
 - Fresnel Equations for normal incidence $\rightarrow R = (n_2 - n_1)^2 / (n_2 + n_1)^2$
 - Air/glass interface $R = 4\%$ and $T = 96\%$
- Reflection and refraction of ultrasound at a smooth interface
 - $R = (Z_2 - Z_1)^2 / (Z_2 + Z_1)^2$
 - No reflection/echoes without impedance mismatch
 - Excessive impedance mismatch (e.g., air/tissue) \rightarrow too much reflection
 - Coupling gel used to eliminate air between transducer and skin
 - Bone generates only surface image
- Small structures like RBCs generate a (back) scatter signal



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Factors that Affect Imaging – Intensity and Attenuation

- Intensity and attenuation
 - US loses intensity with depth
 - Eventually no echoes
- Causes of attenuation
 - Absorption
 - Scattering
- Attenuation increases with ν
 - At higher ν , molecules move faster (rub more), generating thermal energy more quickly
 - Half-depth obeys $L_{1/2} = \theta/\nu$
- Scanners compensate for attenuation using time gain compensation

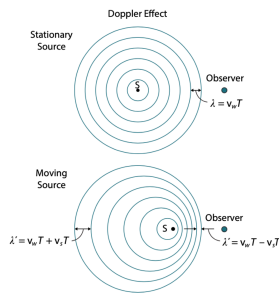


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Imaging and Measuring Blood Flow with US

Doppler Effect is the basis of blood flow measurement

- Perceived frequency depends on relative motion of source and observer
- Moving **source** – λ changes because crest spacing altered
- Moving **receiver** – ν changes because rate of crest interception altered

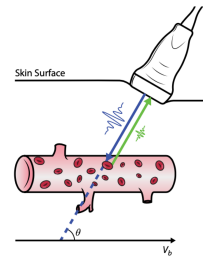


- Tutorial**
- <http://www.ton-capo.org/~mmp/apollist/doppler/d.htm>
- <https://www.einstein-online.info/en/spotlight/doppler/>

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Doppler Ultrasound

- US sent out by transducer at v_0 and encounters RBC
- Two Doppler shifts**
 - One shift – RBC is a moving receiver of US from transducer
 - Another shift – US reflects off RBC, which then is a moving source of US detected by transducer
- Transducer detects $\Delta v = v_{\text{echo}} - v_0$**
 - $\Delta v = 2v_0 \cos \theta v_{\text{blood}} / v$
 - θ is the angle between beam and direction of flow
 - Valid if $v_{\text{blood}} \ll v = 1540$ m/s
 - Magnitude of Δv determines speed
 - Sign of Δv determines direction (e.g., $+$ → blood moving toward transducer)



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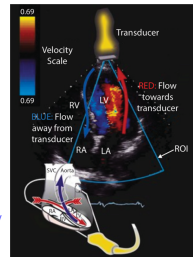
Common Medical Applications of US

- Fetal heart rate and gestational age**
 - ~80-100 bpm at 5 weeks
 - Accelerates until week 9 and then decelerates and stabilizes at 120-160 bpm
 - <http://www.youtube.com/watch?v=y-KwV1q2VW>
- Carotid intima media thickness US exam**
 - Two carotid arteries, one on each side of neck, deliver blood from heart to brain
 - US can reveal blockage and ease of blood flow in carotid artery and is used to screen for risk of stroke
 - <https://www.youtube.com/watch?v=W-SJxeMnDM>

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Color Flow Doppler Images

- Superimposes Doppler blood flow data on B mode image
- To generate B mode image, measure time for echo return and echo amplitude
- To generate flow data
 - Determine if echo frequency is shifted
 - If so, magnitude and direction of blood flow superimposed on image
 - Common mapping format – BART (blue away, red towards)
 - Yellow or green – flow without defined direction (e.g., turbulent)
 - Brightness – magnitude of velocity
- Applications**
 - Faulty valves
 - Leaky blood vessels
 - Variation in flow due to plaque



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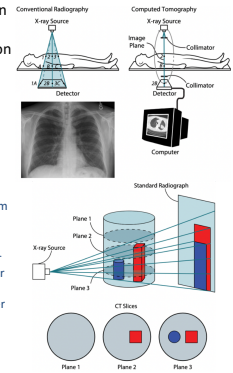
Summary – US

- Advantages**
 - Noninvasive – body not opened and nothing inserted
 - Quick, inexpensive, and convenient
 - Not harmful
 - Good for soft tissue
- Disadvantages**
 - Strong reflection at tissue/gas interface – not good for lungs, digestive system
 - Does not pass well through bone – not good for fractures

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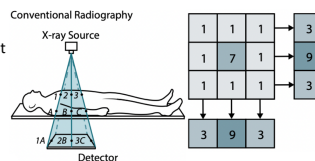
The Essence of Radiography

- X-ray beam traverses a patient positioned between source and detector
- Beam attenuation, along each ray path, depends on the anatomical structures encountered
- Projection (conventional) radiography**
 - Transmitted beam generates a signal that is the summed attenuation along the various ray trajectories
 - Image is a projection of radiopaque structures along the beam path
- Computed tomography (CT)**
 - Source and detector rotate around the patient, and reconstruction methods convert projections obtained from many angles into cross-sectional slices
- Strengths & Weaknesses**
 - Projection radiography – high resolution, high contrast for structures like bone, relatively inexpensive, rapid, good for broken bones, breast cancer screening
 - CT – images preserve structure depth and are much better at revealing soft tissues, good for trauma assessment, tumor staging
 - Main negative – ionizing radiation



An Introduction to Medical X-Ray Imaging

- Images (radiographs) = shadows (projections) created when part of X-ray beam absorbed by object along beam path



- X-rays assumed to travel along straight paths
- No depth information
- Unfocused shadows created
- Reduced contrast

Radiograph

- Dark = more transmission
- White = less transmission



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Why Not Use an X-Ray Microscope?

- Focusing lenses for visible radiation are "easily" fabricated**
 - $n_{\text{glass}} \sim 1.5$ in the visible
 - Visible radiation refracts significantly and is not strongly absorbed
 - Light slows in glass → lenses are convex/bulge at center
- Focusing lenses for X-rays are difficult to fabricate**
 - $n \sim 1$
 - X-rays do not refract much
 - Lenses are concave (like acoustic lenses)

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Interactions between X-rays and Body

- Photons used in diagnostic imaging**
 - $\lambda < 10$ nm and 15 KeV $< E < 150$ KeV
- Diagnostic X-rays**
 - Absorbed via Photoelectric (PE) Effect
 - Scattered by Compton Effect
 - Transmitted

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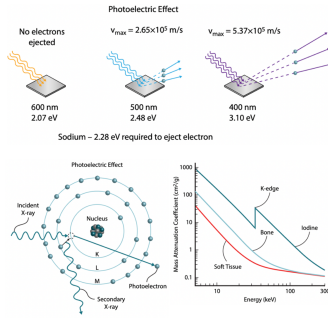
PE Effect – The Primary Source of Contrast

- If $E < 25$ KeV, PE effect dominates absorption

- X-ray interacts with tightly bound electron in a shell of C, O, H, N
- If $E_{\text{photon}} >$ binding energy of shell, X-ray absorbed and electron escapes
- Vacant orbital refilled by an electron and characteristic X-ray produced/scattered

- Probability $\propto \rho Z^3 / E^3$

- Z dependence gives contrast – bone with large Z = 20 (Ca²⁺) gives big PE effect for diagnostic X-rays
- Probability falls with X-ray energy
- Absorption edge exception – PE effect for a particular shell increases discontinuously when $E_{\text{photon}} >$ binding energy



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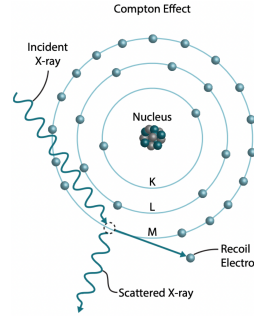
Compton Effect – The Source of Background Fog

- X-ray interacts with outer shell electron

- Electron ejected
- X-ray changes energy and direction consistent with conservation of energy and momentum

- Probability

- Z independent
- As ρ increases, Compton increases
- Compton less affected by changes in anatomy than PE
- No absorption edge effects



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Transmitted X-rays

- Transmitted X-rays make radiograph
 - PE provides diagnostic information, revealing anatomical structures with high absorption
 - Compton provides no useful information because trajectory is not linear → creates fog
- Radiograph reveals differential absorption
- For monoenergetic X-rays
 - μ is attenuation coefficient
 - After rays travel $1/\mu$, 37% left $I_{\text{trans}} = I_0 e^{-\mu x}$
 - μ decreases with E so high-energy rays travel farther → used for thick samples

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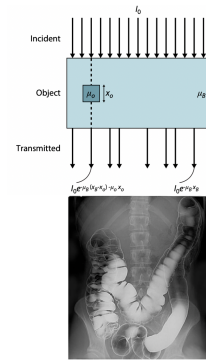
Attributes of Images

- Quality determinants
 - Contrast, resolution, noise
- Balance with dose determinants
 - Absorption, scattering
- Contrast – analyze in some detail
- Resolution ~ 0.1 mm
 - Detector properties (e.g., pixel size)
 - Properties of source and imaging geometry
 - Movement during exposure
 - Quantification – measure PSF using tiny hole that does not absorb
- Quantum noise: signal does not exactly reproduce transmission profile
 - Minimize with efficient detector, increased exposures and intensity
 - Latter increase dose

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Image Formation – Contrast

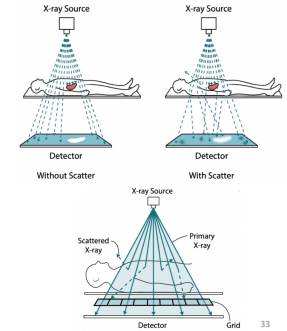
- Local contrast $C_{\text{local}} = (I_B - I_o) / I_o$
- Contrast good if μ 's very different or absorber large
- Blood vessel in soft tissue
 - $C_{\text{local}} \sim 0.02$
- Contrast media – nontoxic liquids
 - High Z element (barium, iodine) that increases absorption due to PE effect and absorption edges
 - Vessel in soft tissue → $C_{\text{local}} \sim 0.15$



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Image Formation – Energy & Scattering

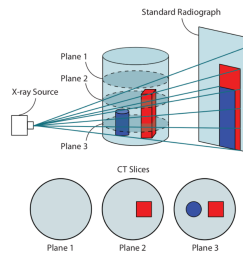
- Energy
 - Low energy (E) improves contrast
 - High E required for transmission through thick body parts
 - Low E okay for thin body parts
- Scattering
 - Scattering destroys information about photon path
 - For a typical abdominal radiograph, 50-90% of photons are scattered
 - Scattered photons distinguishable due to lower E and direction offset
- Reduction of Scattering
 - Decrease irradiated area
 - Use a grid that selectively absorbs scattered rays



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Computed Tomography (CT)

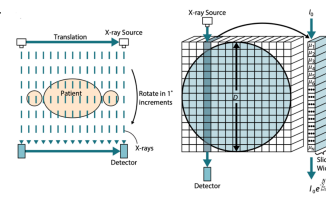
- Tomography = picture of a plane
 - Convert a series of X-ray views into a cross-sectional image
- Cross-section versus projection
 - Cross-section = analog of slice of fruit cake showing location of nuts and fruit
 - Projection = analog of cake flattened by steam roller



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Essence of Implementation

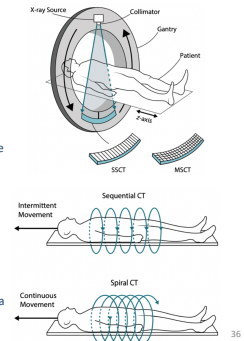
- Consider first generation scanner
 - Irradiate thin slice in patient
 - Collect ~160 transmission measurements (a "view") by translating source and detector on opposite sides in synchrony
 - Collect 180 views by rotating source/detector in increments of 1°
 - Reconstruct matrix of attenuation values from $160 \times 180 = 28,800$ data points
 - Encode attenuation matrix as a grayscale



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Modern Scanners – Rotation Replaces Slow Translation

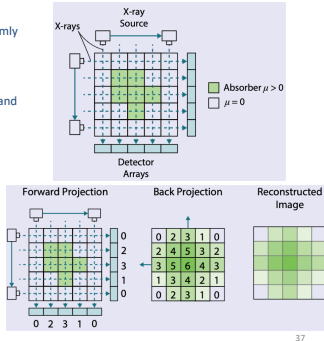
- Most common modern scanner
 - Rotate-Rotate
 - Large fan beam encompasses patient
 - ~750 detectors along x/y fan beam
 - Detector and X-ray tube rotate through 360° together
 - 300-1000 views in 1° increments in a few seconds
 - Translate patient to collect data for another slice
- Latest innovations – spiral (helical) & multi-slice scanners
 - Continuous movement of patient though scanner
 - Faster scanning useful for severe trauma (auto accident)
 - No gaps between slices
 - Detectors with two-dimensional arrays
 - Collect 64 high-resolution slices at a time using a beam of width 40 mm = 64×0.625 mm
 - Massive increase in speed



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Reconstruction Algorithms

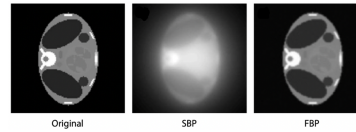
- **Simple Back Projection (SBP)**
 - ❖ Assume attenuation occurs uniformly along ray path
- **SBP Example**
 - ❖ Two views of object generated
 - ❖ Spread each view back uniformly and add
 - ❖ Reconstruction shows more absorption in center but blurred



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Filtered Back Projection

- Filtering before back projection removes blur
- Reconstruction exact if collect infinite # of views and # of points/view
- Alternatives
 - ❖ Systems of linear equations
 - ❖ Iterative approaches



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High-Contrast Biological Imaging in the Water Window

- X-rays falling within the K absorption edge of C and O fall in H₂O window
 - ❖ Soft X-rays in H₂O window yield high-contrast biological images without staining
 - ❖ Water absorbs poorly
 - ❖ Protein absorbs well
- X-ray tomographic imaging of cellular architecture exploits the water window

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Imaging Cellular Architecture Using CT

- Soft X-ray tomography of cells is very similar to medical CT
 - ❖ Soft rays ($E < 540$ eV; $\lambda \sim 2-5$ nm) well suited to study of organic specimens
 - ❖ Imaging in the water window yields good penetration (up to $10 \mu\text{m}$ of water/ice) \rightarrow good for cells
 - ❖ High contrast between protein and water obtained without staining
- Structures overlap in "thick" objects \rightarrow need tomography
 - ❖ Collect many projects \rightarrow radiation dose is high
 - ❖ Specimen frozen to reduce radiation damage
 - ❖ Use filtered back-projection (or similar approaches) to reconstruct cellular structure in 3D
 - ❖ Resolution ~ 30 nm
 - ❖ <http://ww2.kqed.org/guest/2012/09/11/x-ray-microscope-seeing-cells-in-3-d/>

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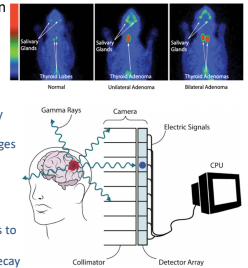
Summary – X-ray

- Advantages
 - ❖ Fast, cheap
 - ❖ Excellent images of the skeleton
 - ❖ Excellent soft tissue images using CT
 - ❖ <https://www.youtube.com/watch?v=HWn-pG4B-M>
 - ❖ Anyone can have a CT scan but not an MRI (later)
 - ❖ Less sensitive to movement than MRI
- Disadvantages
 - ❖ Ionizing radiation \rightarrow cell damage
 - ❖ μ not the most sensitive measure of anatomy and not a measure of function

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The Essence of Radionuclide Imaging

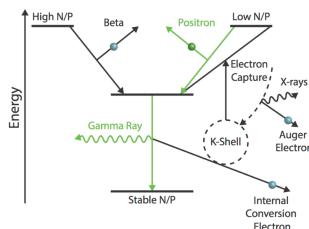
- Emission/functional analog of X-ray transmission imaging
 - ❖ Most rapidly growing modality due to thrust towards personalized medicine based on emission imaging
- Transmission and emission imaging used together to improve diagnosis/treatment
 - ❖ X-ray techniques assay for structural changes caused by trauma or disease
 - ❖ Emission techniques assay for disease-associated changes in function (e.g., visible as altered distribution of a radioactive tracer)
- Basis of projection and tomographic emission imaging
 - ❖ Patient exposed to a radiopharmaceutical that localizes to a particular site (e.g., a tumor)
 - ❖ Site emits gamma-ray photons generated by nuclear decay
 - ❖ Gamma rays produce a spatially varying "count profile"
- Strengths & Weaknesses
 - ❖ High-contrast method of mapping function, such as brain activity in normal and impaired patients
 - ❖ Main negatives – ionizing radiation and poor resolution



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Overview of Unstable Nuclei – Part I

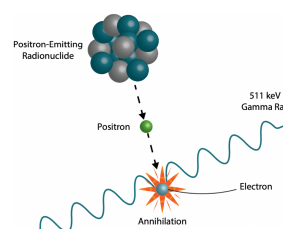
- Many decay schemes whereby an unstable "parent" nucleus will undergo a spontaneous transition to generate a more stable "daughter"
- Medicine relies on decay processes that lead to gamma ray photons that can escape body
- Isomeric transitions
 - ❖ Radioactive decay produces a daughter in an excited nuclear state
 - ❖ Occasionally daughter metastable (somewhat long-lived)
 - ❖ Tc-99m has a characteristic decay time (a half-life) of ~ 6 hours.
 - ❖ Tc-99m emits photons with an energy of ~ 140 keV



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Overview of Unstable Nuclei – Part II

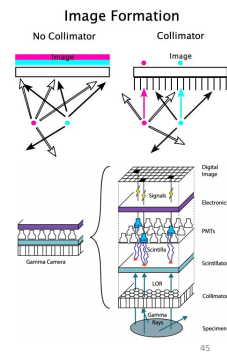
- Positron emission
 - ❖ Decay process involves release of a positron (β^+), which is the positively charged analog of the electron
 - ❖ Reflects a shortage of neutrons and reduces the shortage by converting a proton into a neutron
 - ❖ Outcome is downstream production of two, 511-keV "annihilation" photons, which are emitted in anti-parallel directions
 - ❖ Important positron emitter is fluorine-18, ^{18}F
- Useful characteristic decay times
 - ❖ Several hours to few days
 - ❖ Long enough to permit image production and short enough to minimize harm and get strong signal
 - ❖ Decay of unstable nuclei is exponential



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Detectors

- Most common is Anger gamma scintillation camera
 - ❖ Key components = collimator, large continuous scintillation crystal, PMTs
- Collimator is novel
 - ❖ Need one-to-one correspondence between ray trajectory and line of origin
 - ❖ Collimator needed because gamma emission is isotropic
 - ❖ Collimator functions like a straw and limits detected photons to those along a particular line of response
 - ❖ Collimator a major determinant of resolution and signal strength



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Image Quality – Part I

- **Big take-home message**
 - ❖ Contrast in nuclear images relatively good
 - ❖ Resolution relatively poor
- **Contrast determinants**
 - ❖ Attributes of radiopharmaceutical (e.g., specificity of binding)
 - ❖ Background radioactivity caused by over- and underlying structures (mostly a problem in projections)
 - ❖ Background caused by scatter
 - ❖ Noise
- **Scatter reduction**
 - ❖ Energy discrimination is used
 - ❖ Scattered have lower energy

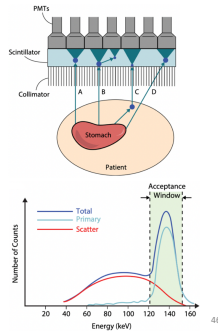


Image Quality – Part II

- **Resolution**
 - ❖ Major determinant is the collimator resolution, R_c
 - ❖ Calculate FWHM of the image of a point source of radioactivity at a distance z from a collimator
 - ❖ $R_c = D \left(1 + \frac{z+c}{L}\right)$
- **Implications**
 - ❖ Resolution degrades with increasing distance between source and collimator
 - ❖ Resolution degrades with increasing collimator hole diameter and scintillator thickness
 - ❖ Resolution improves with increasing collimator length
 - ❖ Typical collimator resolution for a source that is 10 cm deep is ~5 mm, and a typical overall resolution at 10 cm is ~6–7 mm

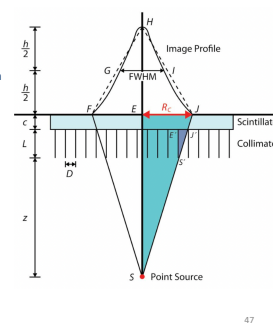
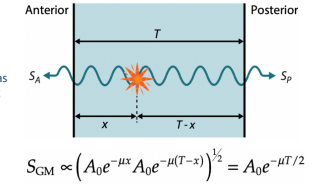


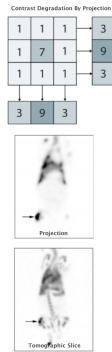
Image Quantification

- **Complicated by depth-dependent resolution and attenuation**
 - ❖ Deeper structures appear less labeled due to depth-dependent attenuation
 - ❖ Experimental remedy – keep detector as close as possible (e.g., body contouring cameras)
 - ❖ Theoretical remedy – compute geometric mean of anterior and posterior views to get depth-independent signal
 - ❖ State-of-the-art = combine emission tomography with CT



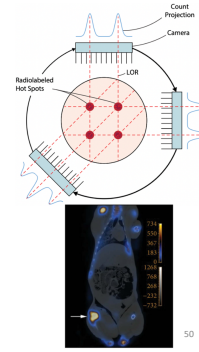
Emission Tomography – Reconstructing Radionuclide Distribution

- **Advantages over projections**
 - ❖ No structural superposition
 - ❖ Better contrast
 - ❖ Better localization
 - ❖ Better suited for quantification
- **Disadvantages**
 - ❖ Sometimes poorer resolution – source farther from detector and smoothing during reconstruction
 - ❖ Increased dose
- **Two approaches**
 - ❖ Single-photon emission computed tomography (SPECT)
 - ❖ Positron emission tomography (PET)



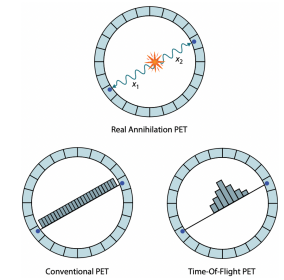
SPECT

- **Implementation**
 - ❖ Use radiopharmaceuticals, commonly labeled with Tc-99m, that generate a single photon per decay
 - ❖ Collect 64 – 128 views (projections)
 - ❖ View = set of data points representing sums of activities along lines
 - ❖ Generate different views by rotating the camera around the patient
 - ❖ Reconstruct
 - ❖ <http://www.people.vcu.edu/~mhcrosthwait/cirs322/spectpart1.htm>
- **Data correction and state-of-the-art dual-mode imaging systems**
 - ❖ Attenuation of gamma rays leads to artificially reduced counts from deeper structures
 - ❖ Correction – combine CT with SPECT (or PET) and use CT to map attenuation coefficients for correction
 - ❖ Dual-mode systems also produce aligned anatomical and functional images
 - ❖ <https://www.umassmed.edu/saic/pestctimages/>



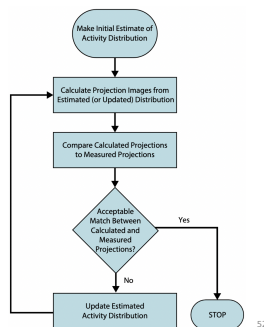
PET

- **Implementation**
 - ❖ Use radiopharmaceuticals, commonly labeled with ^{18}F , that decay and generate a positron
 - ❖ Two anti-parallel annihilation photons arrive, nearly simultaneously, at two detectors
 - ❖ “Coincidence” event is recorded
 - ❖ Coincidence detection eliminates need for collimators → two to three orders of magnitude better sensitivity
- **Time-of-flight (TOF) detection**
 - ❖ Difference in arrival time, Δt , used to refine the location of decay event along the line between detectors
 - ❖ Accurate TOF → reconstruction unnecessary
 - ❖ Currently TOF can only develop a probability distribution for the decay event, but a significant improvement



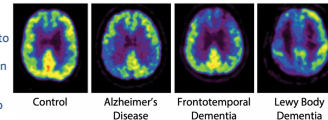
Reconstruction

- **Similar to reconstruction in CT**
 - ❖ Both FBP and iterative approaches used
 - ❖ Iterative preferred – reconstructions less noisy, fewer artifacts
- **Essence of iterative reconstruction**
 - ❖ Use current estimate to compute projection data
 - ❖ Compare calculated and measured projection data and use “difference” to update estimate
 - ❖ If calculated projections are too high, lower estimates, etc.
 - ❖ Similar to iterative deconvolution of fluorescence images



Applications

- **Brain disease**
 - ❖ Reduced uptake of ^{18}F fluoro-deoxyglucose (FDG) used to identify metabolically inactive, degenerating regions of the brain
- **Cancer screening**
 - ❖ Enhanced uptake of FDG used to identify metabolically active cancer cells
 - ❖ <https://www.youtube.com/watch?v=GHL6Cv1r0k>
 - ❖ <https://www.youtube.com/watch?v=rk3j5mgh1ag>
- **Bone screening**
 - ❖ Enhanced uptake of methylene diphosphonate used to identify bone turnover that accompanies fractures, infections, and cancer
- **Developing a personalized approach to treatment and prevention**

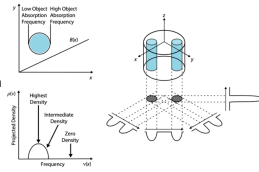


Summary of Radionuclide Imaging

- Emission analog of transmission-based X-ray imaging
- Functional complement to anatomical X-ray-based imaging
- Planar and tomographic images generated
 - ❖ Good contrast
 - ❖ Low resolution
- State-of-the-art systems combine anatomical X-ray imaging with functional nuclear imaging

An Introduction to Magnetic Resonance Imaging (MRI)

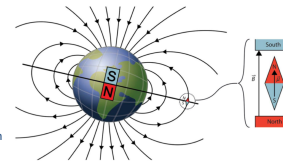
- MRI noninvasive and exquisite soft tissue contrast with relatively high resolution
 - Wounded joint, brain, beating heart
 - Functional and anatomical information
- MRI based on detecting transitions between quantized nuclear energy levels created in the presence of a magnetic field
- Unusual features of MRI
 - Signal frequency used to encode location
 - Many parameters (density, relaxation times, among others) used to generate contrast
 - <https://nationalmaglab.org/magnet-academy/watch-play/interactive-tutorials/magnetic-resonance-imaging-mri/>



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Quantum Mechanics and MRI

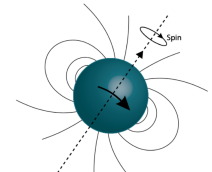
- Understanding magnetically active nuclei
 - Nuclei with an odd # of protons and/or neutrons are magnetically active and possess a magnetic moment, $\vec{\mu}$
 - Like a compass needle, these nuclei experience a torque in a magnetic field and have a preferred orientation in the field



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Origins & Attributes of Nuclear Magnetism

- Classical view
 - Charge in motion (e.g., current in a wire loop) is magnetic
 - Proton = small charge that spins fast → magnetic
- Quantum view
 - Proton, neutron, and electron have an intrinsic magnetic moment that is related to intrinsic spin angular momentum
- Hydrogen has a large magnetic moment and is abundant
 - Most commonly used to generate images via MRI



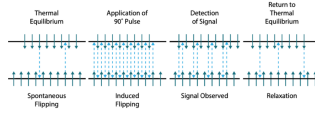
Key Attributes of Magnetically Active Nuclei

Nucleus	Spin	Gyromagnetic Ratio (MHz/T)		Relative Sensitivity	Abundance %
		Ratio	Ratio		
¹ H	1/2	42.58	1.000	99.99	
³ He	1/2	-32.83	0.442	0.0001	
¹³ C	1/2	10.71	0.016	1.108	
¹⁹ F	1/2	40.06	0.833	100.0	
²³ Na	3/2	11.26	0.083	100.0	
³¹ P	1/2	17.24	0.066	100.0	

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MRI Essentials – Part 1

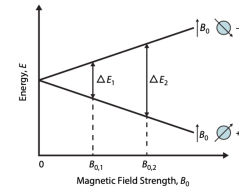
- Magnetic field strength measured in Teslas (T)
 - Main MRI field ~3 T oriented along z
- Magnetic strength of a nucleus
 - Determined by magnetic moment
 - $\mu_N = 1.41 \times 10^{-26} \text{ J/T}$
 - Two quantized energy states $\pm \mu_N B$
 - μ_N along B = lower (-) energy state
- Effects of static B field
 - Two energy states accessible with energy difference small relative to thermal energies
 - Very small (~0.001%) net alignment of protons along B
- Qualitative attributes of signal generation
 - Nuclei absorb radiation with E_{photon} equal to the energy difference between the two quantum states
 - Signal = radio-frequency waveform generated by the excited population



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MRI Essentials – Part 2

- Quantifying signal
 - $E_{\text{photon}} = h\nu = \Delta E$
 - $\Delta E = E_{\text{nucleus, high}} - E_{\text{nucleus, low}}$
 - $E_{\text{high/low}} = \pm \mu_N B = \pm (1.41 \times 10^{-26}) B$
 - $\Delta E = (2.82 \times 10^{-26}) B$
 - For H nucleus, $\nu = 42.58 \text{ MHz}$ if $B = 1 \text{ T}$
 - Radio frequency part of EM spectrum
- Essential Concept!
 - Frequency is proportional to field strength
 - $\nu = \Delta E/h = (2.82 \times 10^{-26}) B/h = (42.58 \times 10^6) B$
 - ν is called the Larmor/resonance frequency
 - This is the basis for making signal depend on location within body



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Proton Density MRI in Action

- Tutorial
 - <http://phet.colorado.edu/en/simulation/mri>
- Questions for Simplified MRI Tutorial
 - What ν will be absorbed by H nucleus when $B = 1 \text{ T}$?
 - What is ν for 2 T?
 - With $B = 1 \text{ T}$, $\nu = 42.58 \text{ MHz}$, and no gradient, where does signal arise in head?
 - With $B = 1 \text{ T}$, $\nu = 42.58 \text{ MHz}$, and a maximal vertical gradient, where does signal arise in head?
 - What frequency localizes the tumor in a gradient?
- Take home message – gradient localizes the signal!

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Generating an Image

- Review of ultrasound imaging
 - Signal consists of echo time and echo strength
 - Time identifies position (depth)
 - Strength generates contrast
- MRI
 - Signal (RF radiation) has a frequency and an amplitude
 - Frequency and phase identify position
 - Amplitude (really relaxation times) generates contrast

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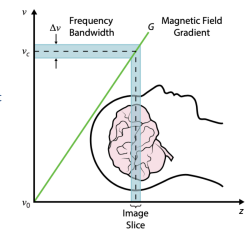
Main Issues to Overcome in MRI

- To localize signal – signal must depend on position (x,y,z)
 - Field gradients must be applied
- To generate contrast – signal must reflect a tissue variable parameter
 - Density is a relatively poor choice
 - Tissue-specific relaxation times are a better choice
 - Tissue-specific relaxation masked by effects of main field inhomogeneity without clever tricks
- We will tackle localization then contrast

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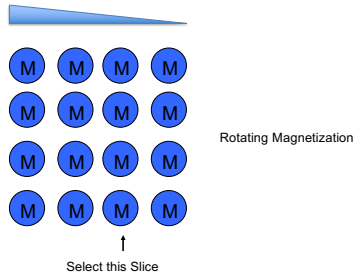
Imaging – Selecting a Slice

- Something to get excited about – selecting your slice (image plane)
 - Create a field gradient along z axis
 - Simultaneously excite with an RF pulse containing a band of ν 's that excites one slice
 - Selected slice is orthogonal to applied gradient (z gradient → transaxial (transverse) slice)
 - <https://www.cis.rut.edu/htbooks/mri/chap-5/15-3.htm>

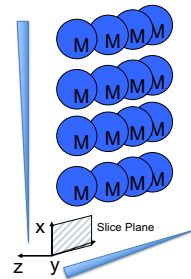


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Animation – Selecting a Slice

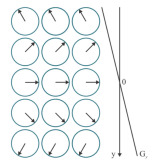


Animation – Mapping Within Slice

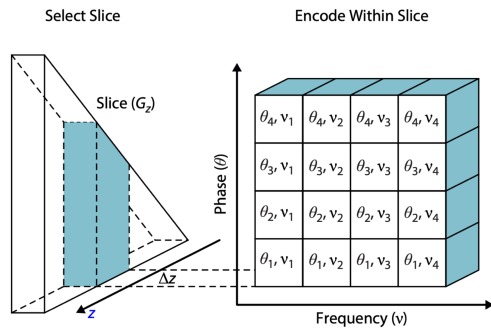


A Summary of Image Encoding

- 3D mapping in MRI involves slice selection followed by phase and frequency encoding
 - ❖ Apply slice selection gradient – this defines image plane
 - ❖ Apply and turn off y gradient
 - ❖ Gradient along y is off during signal measurement → cannot detect differences in frequency along y so detect differences in phase (how much spins out of sync)
 - ❖ Apply an x gradient and readout signal → detect differences in resonance frequencies along x
- Phase encoding – an example using simple numbers
 - ❖ Spin in high part of gradient rotates at 200 rad/s for 5 ms
 - ❖ Spin in low part of gradient rotates at 100 rad/s for 5 ms
 - ❖ Phase angles are 1.0 rad and 0.5 rad
 - ❖ Different spin locations encoded in different phases/angles



Encoding Summary

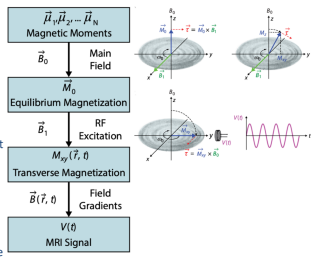


Using Relaxation Times To Create Contrast

- Proton densities (ρ) are similar for different soft tissues
 - ❖ ρ is a poor way to encode contrast
- MRI typically relies on more variable parameters
- Tissues return to equilibrium after excitation by the RF pulse
 - ❖ Relaxation times that govern the return to equilibrium vary much more for soft tissues than ρ
 - ❖ Use relaxation times to encode contrast!
 - ❖ https://www.radiologymasterclass.co.uk/tutorials/mri/t1_and_t2_images

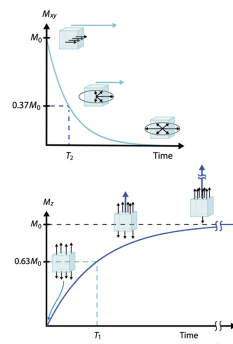
A Classical Analysis of Signal Generation and Relaxation

- MRI monitors changes in net magnetization in voxels
 - ❖ Generating a detectable signal in MRI requires measurement of net magnetization of many nuclei
 - ❖ Changes in net magnetization can be described classically
- Changes in net magnetization
 - ❖ Rotate net magnetization away from z so it varies with time
 - ❖ 90° RF pulse at Larmor frequency rotates magnetization into xy plane
 - ❖ After pulse, magnetization returns to equilibrium via interactions with environment
 - ❖ M_{xy} varies with time and generates voltage at Larmor frequency in nearby coil



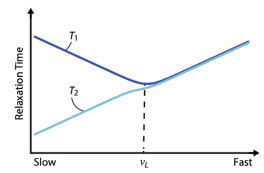
Relaxation Times Govern Return to Equilibrium

- Transverse magnetization M_{xy} created by a perturbing (e.g., by 90°) pulse of radiation is the source of the MRI signal
- Decay of M_{xy} back to zero (the equilibrium value) in the absence of extrinsic field inhomogeneity
 - ❖ $M_{xy} = M_0 e^{-t/T_2}$
- Decay of M_{xy} is accompanied by increase of M_z from 0 (after 90° pulse) to its equilibrium value
 - ❖ $M_z = M_0 (1 - e^{-t/T_1})$
 - ❖ https://www.radiologymasterclass.co.uk/tutorials/mri/t1_and_t2_images
- Three relaxation times influence the return of magnetization to equilibrium



Attributes of Relaxation Times

- Transverse relaxation times
 - ❖ T_2^* – incorporates extrinsic field inhomogeneity, weak variation with tissue type
 - ❖ T_2 (spin-spin) – involves energy exchange between nuclei, driven by motion at low ν , strong variation with tissue type
- Transverse (spin-lattice) relaxation time
 - ❖ T_1 – involves energy exchange between nuclei and environment, driven by motion at Larmor ν , strong variation with tissue type
- Most tissues $T_2 \ll T_1$

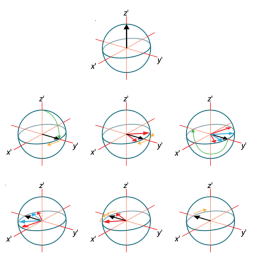


Relaxation Time and Proton Density Data for Brain Tissue and Blood

Field Strength (T)	Tissue	T_1 (ms)	T_2 (ms)	T_2^* (ms)	Proton Density (gm/cm ³)
1.5	White matter	510	67	n.a.	0.61
	Gray matter	760	77	69	0.69
	Arterial blood	1441	290	55	0.72
	CSF	2630	280	n.a.	1.0
3.0	White matter	1080	70	50	0.61
	Gray matter	1820	100	50	0.69
	Arterial blood	1932	275	46	0.72
	CSF	3817	1442	n.a.	1.0

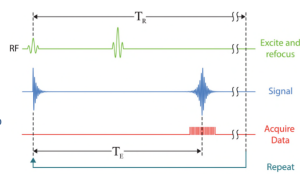
Recovering T_2

- Relaxation usually dominated by T_2^* (static variations in main field)
 - ❖ Pulse sequences needed to tease out anatomy-dependent relaxation (T_1 and T_2)
- Pulse to extract T_2 (Spin Echo)
 - ❖ After 90° RF pulse → spins lose coherence due to field variations, and M_{xy} decays rapidly
 - ❖ Apply a 180° RF pulse at $TE/2$ that reverses spins → they recombine, and M_{xy} grows
 - ❖ Measure signal (echo) at time TE
 - ❖ http://en.wikipedia.org/wiki/File:HahnEcho_GWM.gif
 - ❖ Change in signal strength between initial signal and echo determined by T_2



The Spin Echo Pulse Sequence

- Pulse sequences needed to tease out anatomy-dependent relaxation times and achieve weighting based on relaxation times
- The simplified 2D Spin Echo pulse sequence (suppressing gradients)
 - ❖ 90° degree RF pulse tips magnetization into transverse plane
 - ❖ 180° pulse reverses loss of synchrony and creates a spin echo at TE where data are sampled
 - ❖ Repeat this cycle of pulses at intervals TR
 - ❖ Signal amplitude and thus contrast determined by manipulating TR and TE



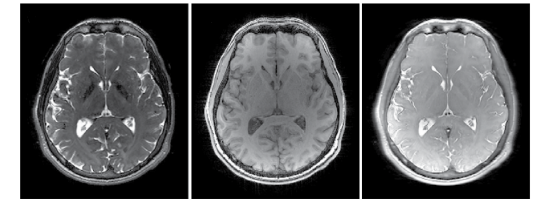
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Deciphering Signal Weighting

- Amplitude $(x, y) \propto \rho(x, y)(1 - e^{-TR/T_1})e^{-TE/T_2}$
- ρ -weighted
 - ❖ Relaxation terms $\sim 1 \rightarrow TE$ short and TR long
- T_2 -weighted
 - ❖ (T_1 effect $\sim 1 \rightarrow TR$ long
 - ❖ TE relatively long so tissues with short T_2 give no signal (dark) but those with long T_2 do (bright)
- T_1 -weighted
 - ❖ (T_2 effect $\sim 1 \rightarrow TE$ short
 - ❖ TR relatively short so tissues with short T_1 have big M_z to flip and give strong signal (bright) but those with long T_1 do not (dark)
 - ❖ <https://www.nibib.nih.gov/science-education/science-topics/magnetic-resonance-imaging-mri>

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Examples of Weighting and Image Contrast



T_2 Weighting

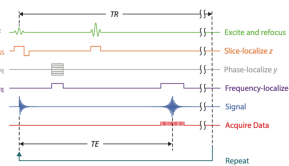
T_1 Weighting

ρ Weighting

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The Full Spin Echo Pulse Sequence

1. The patient is placed in a strong, static, external magnetic field.
2. A pulse of RF radiation with narrow bandwidth is applied together with a slice-selection gradient. Protons in a small slice are excited, M_z and transverse magnetization is generated.
3. A phase-encoding gradient is applied transiently. This introduces a phase difference between the protons along the y direction, which will generate data that fill in one "row" of the data matrix (Fig. 13.11).
4. A rephasing (echo) pulse is applied at time $TE/2$, together with the slice-selection gradient, to regenerate proton synchrony and enhance the MRI signal.
5. A frequency-encoding gradient is applied along x in conjunction with data acquisition during echo evolution and decay, which occurs at time TE .
6. Data are collected for multiple repetition times, TR . For each TR , the phase-encoding gradient is altered to yield new phase data and thereby fill out the data matrix.
7. The image is computed via Fourier transformation of the MRI signal, with the choice of TR and TE determining the signal amplitude and thus image contrast.
8. Steps 2 – 7 can be repeated for additional slices.



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Summary – MRI

- Advantages
 - ❖ Very low-energy radiation and no reported hazards
 - ❖ High-contrast submillimeter resolution of soft tissue
 - ❖ Different brain tissues resolvable \rightarrow tumors, dementia detectable
 - ❖ Functional MRI allows noninvasive, high resolution mapping of neural activity based on a signal from deoxyhemoglobin
 - ❖ <https://www.sciencelearn.org.nz/videos/523-functional-mri-looking-at-the-brain-over-time>
- Disadvantages
 - ❖ Oscillating fields cause ion movement (current) in body that can lead to heating
 - ❖ Fields can cause metal implants to move and can affect pacemakers \rightarrow not everyone can have an MRI
 - ❖ MRI equipment expensive
 - ❖ Image formation complex

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