Introduction to the Course and the Techniques

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Rationale for the Course
Translational Clinical Science Cycle
Translational Clinical Science Cycle

Discovery of new approaches to image human anatomy and physiology (basic science bench to bedside)

Using imaging to discover new information about human disease

Use of imaging to make clinical trials of drugs or devices more scientifically valid (imaging biomarkers) or less expensive (surrogate endpoints)

Routine clinical use of imaging (diagnosis and treatment response assessment)

Clinical trials that test the diagnostic power of imaging
Course Components

• Discovery of new approaches to image human anatomy and physiology
  – Nader Pouratian, MD
  – Danny JJ Wang, PhD

• Using imaging to discover new information about human disease
  – Katherine Narr, PhD
  – Paul M. Vespa, MD

• Use of multimodal imaging in clinical trials
  – David S. Liebeskind, MD
  – Nancy L. Sicotte, MD
  – Benjamin M. Ellingson, PhD
MRI 101 Laboratory

- Friday April 11 at 11 AM
  - Meet at the entrance to the Ahmanson-Lovelace Brain Mapping Center (660 CE Young Drive South)

- Content
  - MRI Safety
  - The ‘look and feel’ of MRI
    - For patients and investigators
Medical Imaging

- Medical Imaging is based on the interaction between electromagnetic radiation and living tissue
- The brain is surrounded by bone
  - Ultrasonography does not play a major role in brain imaging
- Neuroimaging is equally based on interaction between
  - Electromagnetic radiation and bone
  - Electromagnetic radiation and brain
Neuroimaging Requirements

• Brain imaging requires electromagnetic radiation that
  – is safe
  – penetrates bone
  – interacts with brain to produce contrast to anatomy/function/physiology
Brain Components

- Water
- Salts
- Metabolites
- Neurotransmitters
- Protein
- Lipids
- Membranes
- Cells
- Blood vessels
- Hemoglobin
Electromagnetic radiation is composed of oscillating electric and magnetic fields.

(wave frequency is inversely proportional to wavelength)
MRI Near Infrared Brain Imaging Poor Bone Penetration Computed tomography (CT) Positron Emission tomography (PET)

EcoG/EEG MRI Near Infrared Brain Imaging Optical Brain Imaging Molecular Damage
Bone penetration

• Bone excludes
  – Infrared Light
  – Visible Light
  – Ultraviolet Light

• Bone is penetrated by
  – High intensity X-rays
    • Computed Tomography
    • X-ray Angiography
  – Radio frequency waves
    • Magnetic Resonance Imaging
  – Microwaves
  – Gamma rays
    • Positron Emission Tomography
Microwave Imaging?
Imaging with Microwaves?

• Microwave-based imaging is impractical due to
  – Tissue heating
  – Poor penetration

• Small charged particles (Na\(^+\), K\(^+\), Cl\(^-\)) in tissue can move in resonance with the applied microwave field
  – Friction between the moving ions and medium produces heat.

• Beginning to be a factor for MRI because newest MRI frequencies approach the microwave region of the electromagnetic spectrum
Electric Field

The electric field from an isolated positive charge

The electric field from an isolated negative charge
EcoG/EEG

(very low frequency electric field imaging)
Electrocortigraphy
Electrocortigraphy (EcoG)

• Uses electrodes placed on the brain cortex to detect time varying electric fields produced by neural activity
  – A functional brain imaging technique
  – Very low frequency
• Detection of E-fields is much enhanced if electrodes are placed directly on the brain surface
  – Bone is an electric insulator
  – Electric field strength decays rapidly with distance
• Safety
  – Requires neurosurgery
  – Applicable only to specific patient populations
Electroencephalographic Imaging
Magnetic Fields
Magnetic Fields

• Movement of electric charge (electric current) produces a dipole magnetic field
• Movement of a magnetic field produces electric current
• Magnetic fields always have two or more poles
  – All magnetism is fundamentally due to electric current
Magnetic Resonance Imaging
(low frequency magnetic field imaging)
Magnetic Resonance Imaging

- MRI utilizes the magnetic resonance signal produced by the protons (¹H) of tissue water.

- MRI has become the “method of choice” for nondestructive visualization of brain anatomy
  - Anatomic contrast depends on microscopic biophysical properties of tissue that (mostly) influence how fast water molecules can move

- Functional MRI techniques ‘trick’ the proton MR signal to depend on brain function
  - Usually indirect detection of blood flow or oxygenation changes that accompany neural activity
One volume element from the imaged tissue section

Proton spin magnets oriented parallel or antiparallel to the applied magnetic field and precessing about it
MRI Magnetic Fields

• $B_0$ penetrates bony structures allowing the brain to be “seen” through bone
  – $B_0$ is typically 1.5 Tesla or greater (30,000 times the strength of the earth’s magnetic field)

• Nuclear magnets rotate around $B_0$ at a characteristic frequency in the radio frequency region of the electromagnetic spectrum
  – 63 Mhz at 1.5 T

• Addition of an oscillating magnetic field ($B_1$) interacts with the nuclear magnets causing them to produce a signal

• Addition of spatial variation in $B_0$ (magnetic field gradients) supports imaging
Magnetic Field Gradient(s) and Imaging

• A magnetic field gradient is a smooth variation in $B_0$ from one position to another position
  – Anterior-to-posterior variation
  – Superior-to-inferior variation
  – Left-to-right variation

• Gradients are purposefully applied as part of the imaging process
Frequency bandwidth of selective excitation MRI of the selected slice

B₀ in presence of S/I magnetic field gradient

MR signal frequency

MRI of the selected slice
The Image

• “Signal” discussed thus far is depicted as gray level of each element in the image
  – White = greater signal
  – Gray = less signal
  – Black = no signal

• MR Images usually have no absolute calibration
MRI Contrast

• Signal/image creation in MRI uses a complex set of pulses of the oscillating $B_1$ magnetic field
  – A pulse sequence
• Adjustment of pulse sequence timing parameters can be used to create different types of signal contrast to cellular composition
• T1-weighted imaging: Gray matter, white matter and cerebrospinal fluid give unique signal intensities
  – Often used for brain morphometry studies
• T2-weighted imaging: Fluid produces prominent signals
  – Often used for evaluating different types of lesions
T2-weighted Imaging
T1 weighted imaging (with contrast)
MRI Contrast Agents

- Typical contrast agents are chelates of metals ions (e.g. gadolinium) having unpaired electron spins.
- Water molecules must “touch” the agent to enhance signal.
- Typical contrast reagents are designed to not pass the blood brain barrier.
- Signal is enhanced only where blood brain barrier is damaged.
Computed Tomography
Computed Tomography Technique
CT Contrast
CT contrast

• Intrinsic CT contrast is within brain is limited
  – Gray matter, white matter and CSF can be distinguished, but not as effectively as with MRI

• CT neuroimaging often uses intravenous contrast agent (iodinated materials) to create vascular contrast

• CT angiography (CTA)
  – Visualization of larger blood vessels (usually arteries)

• CT perfusion (CTP)
  – Dynamic measurement of contrast passage to measure/image microvascular perfusion
CT Safety

• Xrays strip electrons from molecules
  – Ionizing radiation
  – Damages molecules
• In neuroimaging large xray intensity is used to overcome absorption by calcium in bone
• Xray exposure is sometimes a limiting factor
  – Dynamic studies such as CTP
  – Multiple studies on the same patient
• Allergic reaction to contrast agent
• Renal insufficiency that results in poor clearance of contrast agent
Positron Emission Tomography
Positron Emission Tomography

• Based on the existence of a subatomic particle called a positron (a positive electron)

• Certain unstable nuclear isotopes emit positrons
  – Requires an onsite cyclotron

• Emitted positrons move a small distance before encountering a negative electron causing decay to two gamma rays
PET Technique
PET Imaging
PET Tracers

- $^{18}$Fluorodeoxyglucose (FDG) is a tracer of glucose metabolism
  - Injected into vascular system
  - Transported into cells by glucose transporters
  - FDG metabolism reaches a ‘dead end’ after phosphorylation
  - tracer of glucose metabolism
- $^{15}$O
  - Injected into the vascular system
  - Penetrates all membranes
  - Washout rate depends on cerebral blood flow
- $^{15}$O$_2$
  - Delivered by inhalation
  - Tracer converted to CO$_2$ by respiration and washed out by blood flow
  - Analysis of time course can be used to determine the rate of oxygen metabolism if a CBF measurement is also done
- Many other PET tracers are in development
  - The basis of ‘molecular imaging’
PET Safety Issues

• Gamma ray exposure

• Chemical safety
  – Positron emitters tend to have short half lives
  – Tracer molecules must be synthesized immediately before use

• Pharmacological effects of the tracer
  – Many PET tracers are analogs of drugs or neurotransmitters
Image Processing/Interpretation
(be critical)
What property is shown by the image?

- Gray scale and color are used to convey information about tissue properties
  - ‘The image looks cool but what is being shown?’
- Is the image quantitative or only approximate
  - MRI and CT data are often approximate
  - PET images are often quantitative
- What post-acquisition image manipulations have occurred?
Learning Points

• Neuroimaging techniques can be described at a basic level without using complex physics
• All techniques use some form of electromagnetic radiation that can pass through bone
• Contrast depends on interaction between radiation in brain
Learning Points

- **EcoG**
  - Functional contrast
  - Requires neurosurgery
- **MRI**
  - Uses radio waves and magnetic fields
  - Anatomic, vascular and functional contrast
  - Extensive use of contrast agents
- **PET**
  - Primarily uses tracers that emit positrons and gamma rays
  - Ionizing radiation
  - Requires cyclotron and chemistry
- **CT**
  - Uses x-rays
  - Ionizing radiation
  - Anatomic and vascular contrast