Magnetic Resonance Spectroscopy of Breast and Prostate Cancer

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Objectives

- Brief outline of Magnetic Resonance Imaging (MRI)
- Difference between MRI and Magnetic Resonance Spectroscopy
- Magnetic Resonance Spectroscopy (MRS) Sequences
- MRS in Breast
- MRS in Prostate
- Future Directions

Background MRI

- Recall that the magnetization vector M is described by the Bloch equation:

\[
dM/dt = M \times \gamma B - M_{1}^j + M_{2}^{ij} - (M_{1} - M_{2})k - fM_a - \lambda M_b
\]

M,longitudinal magnetization per gram of brain tissue; M,a = longitudinal magnetization per ml of arterial blood; T₂ = transverse relaxation time; T₁ = spin–lattice relaxation time; f = brain blood flow (ml/g/sec); λ = brain blood partition coefficient (0.9 ml/g)

Larmor Frequency

- The Larmor frequency is defined as:

\[
\omega_0 = \gamma B_0 / 2\pi
\]

Where \(\omega_0\) = Larmor frequency, \(\gamma\) = gyromagnetic constant (42.6 MHz/T), and \(B_0\) is the Magnetic Field
Background MRI

- Localization of MR signal
  - Fields
    - $B_0$ Main Magnetic Field
    - $B_1$ Radiofrequency Field
  - Gradients
    - $x, y, z$

Gradient Vector Definition:
\[
\mathbf{G} = \frac{\partial B_1}{\partial x} \mathbf{x} + \frac{\partial B_1}{\partial y} \mathbf{y} + \frac{\partial B_1}{\partial z} \mathbf{z} \equiv \mathbf{G} = G_x \mathbf{x} + G_y \mathbf{y} + G_z \mathbf{z}
\]

- $G_x$, $G_y$, and $G_z$ are generated by three different coils.
- Gradients are measured in Tesla per meter (T/m) or Gauss per cm (G/cm), where $0.01\text{mT/m}=1\text{G/cm}$
- Typical values range from 20 up to 80mT/m

The magnetic field is linearly dependent on the location within the magnet:
\[
\mathbf{B}_i = B_0 + \mathbf{G} \otimes r_i
\]

- Where $B_0$ is magnetic field at $r_i$ and $\mathbf{G}$ is the total gradient vector
- For example, in the $x$-direction
  \[
  \mathbf{B}_x = B_0 + \mathbf{G} \otimes x
  \]

The Larmor frequency is defined as:
\[
\omega_i = \gamma B_0 / 2\pi
\]

- The variation in Larmor frequency is defined as:
  \[
  \omega_i = \omega_0 + \gamma \mathbf{G} \otimes r_i
  \]
  Where $\gamma$ is the gyromagnetic constant (42 MHz/T), and $\mathbf{G}$ is the total gradient vector
- For example, in the $x$-direction
  \[
  \omega_x = \omega_0 + \gamma \mathbf{G} \otimes x
  \]
Proton Spectroscopy

- Chemical Shift
  - Nuclei are "shielded" from the magnetic field, this shielding is called chemical shift and defined as
    \[ B_i = B_0 (1 - \sigma) \]
  - Where \( B_0 \) is the magnetic field, \( \sigma \) is the shielding (depends on the chemical environment)

- Thus, resonance condition is
  \[ \omega = \frac{\gamma}{2\pi} B_0 (1 - \sigma) \]

Proton Spectroscopy

- Chemical shift measurements
  - Parts per Million (ppm)
    \[ \delta = \frac{(\omega - \omega_{def})}{\omega_{def}} \]
    - Independent of magnetic field strength
    - Increases when measured in Hz

- Example:
  - Water is 4.7ppm and Lipids (Fat) is 1.3ppm
  - At 1.5T, what is the chemical shift?
    - (4.7-1.3) \sim 3.4
    - \[ \delta = \frac{(\omega - \omega_{def})}{\omega_{def}} \]
    - \[ 3.4 \text{ppm} \times \omega_{def} = 3.4 \text{ppm} \times 63.8\text{MHz} = (\omega - \omega_{def}) \]
    - \[ (\omega - \omega_{def}) = 217 \text{ Hz} \approx 220 \text{ Hz} \]
  - At 3T, \sim 440 Hz
  - Implies greater spectral resolution
Proton Spectroscopy

- Spin-Spin Coupling (J or scalar coupling)
  - Molecular interaction between adjacent protons
  - Causes additional splitting of the spectra
  - Need high magnetic field

- J constant
  - Measured in Hz
  - Independent of magnetic field strength

Overview

Spectroscopy Sequences

- PRESS

- STEAM

- ISIS

- LASER
Spectroscopy Sequences
STEAM (Stimulated Echo Acquisition Mode)

RF Pulses

90° 90° 90°

Gradients (phase)

Localization by Adiabatic Selective Refocusing (LASER) Spectroscopy Sequence

- AFP = Adiabatic Full Passage pulses
- AM = amplitude modulation
- FM = frequency modulation

What are the differences in the RF pulses in PRESS and STEAM spectroscopy sequences?

25% The number and type of RF pulses and duration of pulses
25% b. 90-90-180
25% c. 90-90-90
25% d. 90-180-180

Spectroscopy Metabolites

- Water = 4.7 ppm
- Lipids = 1.3 ppm
- Choline (Cho) = 3.2 ppm
- Creatine (Cr) = 3.0 ppm
- Citrate (Ci) = 2.6 ppm
Spectroscopy Metabolites

- **Choline (Cho)**
  - 3.2 ppm
  - Membrane turn over and breakdown
  - Increased in cancer
  - Decreased in stroke
- **Creatine (Cr and PCR)**
  - 3.0 ppm
  - 3.94 ppm (if >3T and good water suppression)
  - Energy buffer
- **Citrate (Ci)**
  - 2.6 ppm
  - Intermediate compound of the citrate acid cycle
  - It produced by a unique testosterone-induced pathway

Background - Breast Cancer

- Breast cancer is the most frequently diagnosed cancer in women
  - Breast cancer is the second leading cause of death
- Current detection methods include:
  - Clinical breast exam
  - Mammography
  - Ultrasound
- Magnetic Resonance Imaging (MRI) provides additional information in patients with occult breast cancer or equivocal findings on the other common detection methods.

By using MRS as an adjunct, the chemical and molecular environment of a breast tumor can be examined.

Data Acquisition: MRS

- T1 FSPGR (TR/TE = 250/4.2)
- Fat Suppressed T2 FSE (TR/TE = 5700/102)
- 3D FSPGR, pre/post 0.1 mM/kg Gd
  - 3.5 min, (TR/TE = 20/4) (2 x 0.4 x 1.1mm³)

**Spectroscopy**

- PRESS CSI: single slice 10mm, TR/TE = 2000/272 ms
- Manual Shimming on lesion
- Lipid Suppression using STIR pulses (TI = 171 ms)

Single Voxel Applications

- **Spectroscopy (1.5T)**
  - PRESS, TR/TE = 2000/272 ms, 356 512 points
  - Auto or Manual Shimming on lesion
  - Lipid Suppression using STIR pulses (TI = 171 ms)
  - After lesion localization
What are the major metabolites and parts per million (ppm) in cancerous breast tissue at 1.5T or 3T and long echo times:

- 33% a. Taurine (3.4ppm)
- 33% b. Water (4.7ppm), lipid (1.2ppm) and choline (3.2ppm)
- 33% c. Water (4.7ppm), lipid (1.2ppm) and myo-inositol (3.6ppm)

What are the possible lesions/conditions that might lead to increased metabolites (i.e., choline, etc.) in benign conditions:

- 25% a. Fibrocystic changes
- 25% b. Lactating women, fibroadenoma, BPH, and high membrane turnover
- 25% c. Invasive ductal carcinoma
- 25% d. BPH
Why Prostate MRS

- Current detection methods include:
  - Digital Rectal Exam and/or clinical symptoms
  - Prostate-specific antigen (PSA)
  - Transrectal ultrasonography (TRUS) with biopsy
  - MRI/MRSI

- Magnetic Resonance Imaging (MRI) and Spectroscopy (MRSI) is being used more frequently for diagnosing and monitoring prostate cancer in men.

- Prostate MRSI provides additional information in patients with occult prostate cancer or equivocal findings on the other common detection methods.

Reference:

Background: MRI/MRS Data Acquisition

- Pelvic Coil:
  - Axial T1-weighted images (TR/TE = 600-700/12 ms)
  - Axial T2-weighted (TR/TE = 4000-6000/90-120 ms)
  - Diffusion weighted EPI (TR/TE = 10,000/99 msec, b=0,500,1000)
  - T1-weighted fast low angle contrast-enhanced GRE (TR/TE = 50/4.4 ms).

- Endorectal coil
  - T2 FSE: Axial and Coronal (TR/TE = 4000-6000/90-120 ms)
  - 3D MRSI (TR/TE = 1000 ms; 144 ms; phase encoding steps = 16 x 8 x 8; FOV = 110 x 55 x 55 mm³)

T₂WI Criteria for Prostate Cancer

On T2-weighted image a discrete, focal nodule-like dark signal.

MRSI Criteria

- Choline (Ch) and ↓ citrate (Ci)

 Normal Spectrum: 
\[\text{Ch} + \text{Cr/Ci} = 0.57\]

 Excess Spectrum: 
\[\text{Ch} + \text{Cr/Ci} > 0.57\]
Localizers

MRSI localizers and protocol

- Full coverage with 3DCSI (VOI: 45 mm x 45 mm x 45 mm)
- TR = 750 ms
- TE = 145 ms
- 8 averages
- 8 saturation slabs
- Spectral water and fat suppression within VOI
- Spatial resolution: 5 mm x 5 mm x 5 mm
- TA = 12 minutes
What are the major metabolites in cancerous prostrate tissue at 1.5T or 3T and long echo times?

33% a. Taurine
33% b. Water (4.7ppm), lipid (1.2ppm), choline (3.2ppm) and NAA (2.2ppm)
33% c. Water (4.7ppm), lipid (1.2ppm), choline (3.2ppm), creatine (3.0ppm), and citrate (2.6ppm)

Why is spectroscopy used in breast or prostrate imaging?

25% a. Diagnosis of the lesion
25% b. Classification of the lesion
25% c. Adjunct for diagnosis and research for detecting abnormal metabolites
25% d. Detection of hypertrophy

Future Directions

- 3D MRS
- SENSE MRS
- High Field (7T)
  - Brain
  - Breast
3D Spectroscopy

- 3D PRESS CSI: 8 slices, 10mm, TR/TE = 1010/280 ms
- 1500 Hz bandwidth, 1024 data points, acquisition window 882 msec (echo position 20%),
- CHESS water and lipid suppression (3 pulses, flip angles 161°, 83°, 89°),
- one signal average (NEX 1), scan time = 12 min 6 secs.

3D MRSI of Breast Phantom

T1 weighted images

3D MRSI

a) T1WI   b) Water

c) Lipids   d) Choline
SENSE MRSI

Phase and Sensitivity data best obtained by B1 field mapping using MRI

Raw MRSI Data, N Channels → Spatial Filter, 2D FFT (X,Y) → B1 Sensitivity Profiles Degraded to MRSI Resolution (i.e., 32x24 or 32x16) → Body Coil + Phased Array Images

\[
n(t, x, y) = \sum_{m=1}^{N} \exp(-i \text{arg}(a_n(x, y))) \times b_n(t, x, y) / \sum_{m=1}^{N} a_n(x, y)
\]

SENSE MRSI

MRSI signal coil 1
\[ b_1 = a_{11}x_1 + a_{12}x_2 \]

MRSI signal coil 2
\[ b_2 = a_{21}x_1 + a_{22}x_2 \]

([\text{sensitivity of nth coil at point m}]

\[ b = Ax \]

\[ x = A^{-1}b \]

SENSE MRSI

RF coil sensitivity → B1 Maps
SENSE-MRSI 3.0T

Scan Time 10 minutes: SNR improvements compared to volume coil @ 1.5T

PBM 4321

7T “Braino” Phantom

7T MRSI Human Brain - Selected Spectra

7T MRSI: Metabolic Images

PBM 4321

PBM 4321

PBM 4321
Conclusions

- MRS of breast and prostate has tremendous potential
- Imaging at high spatial resolution and high magnetic field strength ex-vivo improves detail of morphology and MRS results
- These MRS methods will be useful for therapeutic monitoring
- Future trends will lead to faster imaging time and improved spectral resolution

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