MR Spectroscopy
Potential Uses Beyond the Brain in Veterinary Medicine

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In vivo MR Spectroscopy

• First reported in the brain in animal models in late 1970s
  o Phosphorus-31 ($^{31}$P)
  o Measured metabolism
    ▪ Adenosine triphosphate (ATP)
    ▪ Phosphocreatine (PCr)
    ▪ Inorganic Phosphate (Pi)

• First in vivo $^{31}$P MRS in humans reported in 1981
  o Primary focus for MRS during the 1980s was on $^{31}$P
  o Clinical applications limited
    ▪ Low spatial resolution and SNR
    ▪ Requires large voxel volume (>30 cm³)

Barker PB, et al., 2010.
$^1$H-MR Spectroscopy

- 1983 – first $^1$H-MRS in rat brain (8.5T)
- 1985 – first $^1$H-MRS in human brain (1.5T)
- Advantages over $^{31}$P
  - High natural abundance
  - Higher SNR and spatial resolution
  - Uses same hardware as conventional MRI
  - Smaller voxel volumes (1-8 cm$^3$ at 1.5T)
- Primary MRS technique for human brain metabolism since mid-1980s

Barker PB, et al., 2010.
Spectrum Acquisition

- Define voxel in tissue of interest
  - Single voxel
  - Multi-voxel
- Proton signal of metabolites within voxel used to produce the image
- Chemical shift (resonance frequency) plotted on x-axis (ppm)
- Relative metabolite concentrations within voxel plotted on y-axis
Normal Brain Spectrum

Prostate Spectroscopy

- Relatively low sensitivity and specificity of prostate cancer diagnosis with conventional imaging (US, MRI) in human medicine
  - Various prostate pathologies can mimic cancer
    - Chronic prostatitis
    - Scar tissue
    - Hemorrhage
- Studies report increased sensitivity and specificity with addition of MRS to US, MRI, biopsy, and/or protein-specific antigen (PSA) test
- Coil options
  - Endorectal coil
  - External phased-array coil

Barker PB, et al., 2010.
Normal Prostate Spectrum

- Normal prostate contains high levels of citrate (Cit)
  - Strong peak at 2.6 ppm (usually coupled)
- Other prominent peaks
  - Creatine (Cr) at 3.0 ppm
  - Choline (Cho) at 3.2 ppm
  - Myo-Inositol (Ino) at 3.6 ppm
    - Marker for altered membrane metabolism
  - +/- Polyamine (spermine) at 3.1 ppm
- Metabolite ratio
  - Based on peak area
  - Cho + Cr / Cit (CC/C) or Cho/Cit
  - Normal CC/C = 0.22 +/- 0.013 (Jung JA, et al., 2004)


Barker PB, et al., 2010.
Abnormal Prostate Spectroscopy

- **Benign Prostatic Hyperplasia (BPH)\(^1\)**
  - Increased citrate production by secretory epithelial cells
  - ↑ Cit peak, therefore ↓ CC/C ratio
  - Spectrum can look very similar to normal prostate

- **Prostatitis**
  - Disagreement between studies
  - ↑ Cit, which decreases to normal following treatment\(^2\)

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\(^1\)Garcia-Segura JM, et al., 1999.

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    - ↓ Cit, to the point of mimicking prostate cancer

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Abnormal Prostate Spectroscopy

- Prostatic adenocarcinoma
  - Normal glandular epithelial cells replaced by cancer = ↓ Cit
  - Increased cell membrane turnover = ↑ Cho
  - ↑ CC/C ratio, corresponding to degree of malignancy
  - May also see ↑ Ino
    - Should be < Cr peak in normal and BPH
    - Cr/Ino ratio < 1.0 reported as secondary indicator to discriminate between BPH and carcinoma

1 Barker PB, et al., 2010.
2 Garcia-Segura JM, et al., 1999.
Grading Scale for Malignancy

Jung JA, et al., 2004
Potential Use in Veterinary Medicine?

- Possible
  - Prostate size – age and breed variation
    - Volume averaging with surrounding fat
  - Castrated vs. intact
  - Lower citrate concentrations vs. humans¹
  - Cost
    - MRI not routine to evaluate prostate
  - Accessibility of prostate for imaging and FNA/biopsy
    - More difficult in humans (intrapelvic)
  - Questionable differentiation between prostatitis and cancer
  - Needs further investigation

Breast Spectroscopy

- Third-most common clinical use of MRS in human medicine
- Characterize breast lesions and determine malignancy
  - Added specificity to conventional MRI in defining malignant lesions
- Hallmark peak is Cho at 3.2 ppm
  - Increasing Cho peak height correlates with increased malignancy
  - Elevated Cho more frequently seen in malignant than benign lesions

Weinstein S, et al., 2010.

Image from Bartella L, et al., 2007.
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Potential Use in Veterinary Medicine?

- Doubtful
  - Size and periphery of mammary glands
    - Volume averaging with surrounding fat
  - Periphery of palpable masses/nodules conducive to FNA or biopsy without imaging guidance
  - Cost
  - Potential for identification of metastasis?
    - ↑ Cho peak not specific for mammary carcinoma
    - No metabolite peak specific to mammary-origin cells
Musculoskeletal Spectroscopy

• Relatively new procedure in human medicine
  o Limited reports in the literature
  o First report ~ 2000
• Mainly utilized in research at this time
• Choline and creatine peaks are present in metabolically active muscle
• High lipid and water peaks, which may obscure smaller adjacent peaks
• ↑ Cho peak with active tumors
  o Malignant >>> Benign
  o Active benign lesions – neurofibroma and stress fractures – can show Cho peak
  o Can see discrete Cho peak and increased Cr peak post-operatively
• Multi-voxel can be used to assess margins for extent/infiltration of mass

Musculoskeletal Spectroscopy

“Normal” muscle spectrum - myocutaneous flap post- tumor resection

Musculoskeletal Spectroscopy


Low-grade sarcoma
Musculoskeletal Spectroscopy

Potential Use in Veterinary Medicine?

- Possible
  - Size
    - Larger muscles – accommodate voxel
    - Smaller muscles – volume averaging
  - Determine malignancy of musculoskeletal masses (↑ Cho)
  - Differentiate recurrence of tumor vs. treatment effects
  - Needs further investigation
Liver Spectroscopy

- Relatively new MRS technique in human medicine
- Characterize diffuse liver disease
- Quantify lipid content in the liver
- Diagnose malignancy (↑ Cho)
- High water and lipid peaks may obscure smaller peaks
- Technical limitations
  - Motion (primarily respiratory)
  - Low SNR
  - Volume averaging

Motion Artifacts

- Diffuse liver disease
  - Quality may not be as affected
  - Specific voxel location not as important
  - Avoid large vessels and edges of liver lobes

- Focal liver disease
  - Large masses – majority of sampling may be representative
  - Small masses/nodules – volume averaging

- Motion correction
  - Manual/automatic post-processing
    - Cannot correct for inclusion of different tissues
  - Respiratory gating
    - ↓ SNR due to shorter sequence
    - Slightly different sample volume with each breath

Diffuse Liver Disease

- Hepatic Steatosis (Fatty Liver)
  - Multiple lipid peaks in liver
    - Methyl (-CH$_3$) at 0.9-1.1 ppm
    - Methylene (-CH$_2$) at 1.3-1.6 ppm
  - Total lipid/water ratio increases with steatosis grade (0 to 3)
- Metabolite changes indicative of inflammation or fibrosis have not been clearly established

Hepatic Steatosis (Fatty Liver)

Focal Liver Disease

- Hepatocellular Carcinoma
  - ↑ Cho relative to lipids
- Ability to distinguish benign and malignant tumors from normal liver parenchyma has not been established
- Relatively large amounts of choline-containing compounds may occur in normal liver
- More susceptible to motion artifact

Potential Use in Veterinary Medicine?

- Possible
  - Hepatic lipidosis
    - Different fat content in animal liver vs. human liver?
    - Varying “baseline” fat content- lean vs. obese? dog vs. cat? breed differences?
  - Diffuse liver diseases
  - Regenerative nodules vs. malignant tumors
  - Cost
  - Anesthetic drug effects on liver MRS?
  - Liver size
  - Motion artifacts
Summary

• Human medicine
  o MRS routinely used as a diagnostic tool with conventional MRI
  o Decades of research and experience
  o Higher strength MRI units allow ↑ SNR and resolution

• Veterinary Medicine
  o Virtually no MRS data to this point
  o Technically challenging due to small patient size
  o Cost
  o Potential areas of benefit
  o Improving technology and availability of higher strength MRI
References


References


Questions?