Perfusion MRI and MRE for Sarcomas: A novel imaging quest for surgical planning, radiation therapy planning and treatment response assessment

Kay Pepin, Sarah James, Matt Howe, Doris Wenger, Matthew Frick, Michael Herman, Nadia Laack, Deanna Pafundi
It takes a team…

- Michael Herman, Ph.D.
- Deanna Pafundi, Ph.D.
- Radiation Oncology
  - Nadia Laack, M.D.
  - Sarah James, M.D., Ph.D.
- Radiology:
  - Matt Howe, M.D.
  - Doris Wenger, M.D.
  - Matthew Frick, M.D.
- Surgery: Peter Rose, M.D.
- Pathology: Karen Fritchie, M.D.
- Kiaran McGee, Ph.D.
- MRE Group
  - Richard Ehman, M.D.
  - Roger Grimm
  - Tom Hulshizer
- Study Coordinators
- MRI Staff
- Funding
  - Varian
  - Mattenson Funds
  - NIH R01 EB001981
Soft Tissue Sarcomas

- Rare, heterogeneous group of malignancies
  - ~12,000 cases per year
- > 50 different subtypes
- 50 % mortality rate

Why is Sarcoma Research Important?

- Sarcoma is curable by surgery = 20% of the time
- Sarcoma is curable by surgery and chemo and/or radiation = 30% of the time
- Sarcoma is not curable by previously listed approaches = 50% of the time

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**Purpose:** Determine efficacy of Magnetic Resonance Elastography (MRE) and Perfusion MRI for the early assessment of response to therapy and correlate with standard clinical response metrics
Modify chemotherapy and/or RT

Evaluate novel therapies
Perfusion MRI and MRE for Sarcomas

Background on Magnetic Resonance Elastography & Perfusion MRI

Technical Development

Initial Response Assessment
Perfusion MRI and MRE for Sarcomas

Background on Magnetic Resonance Elastography & Perfusion MRI

Technical Development

Initial Response Assessment
Perfusion MRI and MRE for Sarcomas

Magnetic Resonance Elastography

- Quantify tissue mechanical properties in vivo
- Noninvasive
- Applications in Oncology:
  - Detection
  - Characterization (Malignant vs. Benign)
  - Response assessment
MR Elastography (MRE)

1. Induce Deformation
2. Observe Deformation
3. Calculate Stiffness

Gel phantom with stiff inclusions

Wave Images → Elastogram
MRE: Characterizing Liver Cancer

MRE: Surgical Planning of Meningiomas

Murphy et al. (2013) J Neurosurg
MRE: Chemotherapy Response Assessment; Lymphoma

Baseline

2 weeks

Shear Stiffness (kPa)

Baseline: 3.72 kPa

2 weeks: 6.85 kPa

3.72 kPa
Perfusion MRI and MRE for Sarcomas

Perfusion MRI

- Quantify physiologic parameters related to blood flow and tissue perfusion
- Applications in Oncology:
  - Detection
  - Characterization (Malignant vs. Benign)
  - Response assessment
Perfusion MRI

- Method: Dynamic Contrast-Enhanced MRI (DCE-MRI)
- Measures parameters related to:
  - Arterial Enhancement $\rightarrow$ Tissue Microvasculature
  - Wash-in Rates
- Quantitative analysis
  - $K_{\text{trans}}$: the transfer constant (blood plasma $\rightarrow$ extracellular space)
  - $k_{\text{ep}}$: the rate constant (extracellular space $\rightarrow$ blood plasma)
  - $V_e$: the fractional volume of the extravascular-extracellular space
  - $k_{\text{ep}} = K_{\text{trans}}/V_e$
Perfusion MRI

- Determine quantitative values of $K_{\text{trans}}$ and $k_{\text{ep}}$ from a time series of 3D images showing the transit of a contrast agent.
Perfusion MRI and MRE for Sarcomas

Background on Magnetic Resonance Elastography & Perfusion MRI

Technical Development

Initial Response Assessment
Technical Development

• Optimize DCE-MRI
  • MRI coil selection
  • Pulse sequence parameters
  • # time frames

• Optimize MRE
  • Driving frequency
    • 60-120 Hz
  • Driver & amplitude
  • Pulse sequence parameters
Pilot Study: Patient Demographics & Diagnosis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Location</th>
<th>Histology</th>
<th>Sex, Age (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chest Wall</td>
<td>Liposarcoma</td>
<td>M, 37</td>
</tr>
<tr>
<td>2</td>
<td>Tricep</td>
<td>Pleomorphic sarcoma</td>
<td>F, 55</td>
</tr>
<tr>
<td>3</td>
<td>Thigh</td>
<td>Pleomorphic sarcoma</td>
<td>M, 64</td>
</tr>
<tr>
<td>4</td>
<td>Proximal Tibia</td>
<td>Fibrosarcoma</td>
<td>F, 69</td>
</tr>
<tr>
<td>5</td>
<td>Ankle</td>
<td>Liposarcoma</td>
<td>M, 52</td>
</tr>
<tr>
<td>6</td>
<td>Tricep</td>
<td>Ewing’s sarcoma</td>
<td>M, 55</td>
</tr>
</tbody>
</table>
Perfusion MRI in Sarcoma: Methods

• Image acquisition
  • 3D time-resolved DCE-MRI
    • Cartesian Acquisition with Projection-Reconstruction-like sampling (pCAPR)\(^1\)
  • Acquisition time: 3-5 minutes
  • Frame time: 6.6 seconds

• Image reconstruction
  • Iterative sparse reconstruction method\(^2\)
  • Robust, efficient numerical optimization strategy
  • Nonlinear least squares estimates of \(K_{\text{trans}}\) and \(k_{\text{ep}}\)

1. Froemming A, et al. ISMRM #1169. 2015
Chest Wall Sarcoma
Quantitative DCE-MRI: $K^{\text{trans}}$ & $k_{\text{ep}}$
MRE in Sarcoma: Methods

• Image acquisition
  • 3D Gradient-echo MRE
  • Motion frequency: 60 Hz
  • MRE driving apparatus: variable

• Image reconstruction
  • Stiffness quantification:
    • 3D Local frequency estimation

Manduca A et al. Med Imag Anal 2001; 5(4)
MRE: Example Results in Chest Wall

- MRE Magnitude Image
- MRE Phase (Wave) Image
- Elastogram (Stiffness Map)

Shear Stiffness (kPa)
Chest Wall Sarcoma: Imaging Summary

Conventional Imaging

Axial T1
Axial Post-contrast T2
Sagittal T1
Sagittal Post-contrast T2

Advanced Imaging

Perfusion

Ktrans
Kep
MRE

Shear Stiffness (kPa)

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Goal: Identify Early Response to Therapy

- **Morphologic Imaging**
  - $K_{\text{trans}}$
  - $k_{\text{ep}}$
  - Volume

- **Pathology**
  - % necrosis
  - ↓ proliferation
  - ↑ apoptosis

- **DCE-MRI**
  - ↓ $K_{\text{trans}}$
  - ↓ $k_{\text{ep}}$

- **MRE**
  - ↓ stiffness
  - Tissue adhesion

- **Metabolic Imaging**
  - ↓ $^{18}$F-FDG PET activity
Example Imaging Timeline

Conventional MRI

MRE

Perfusion MRI

Radiation Therapy

Transit to

Conventional MRI

MRE

Perfusion MRI

Base of Timeline: Radiation Therapy

Transit to

Chemotherapy

MRE

Surgery

Pathology
Response Assessment: Patient Demographics & Diagnosis

<table>
<thead>
<tr>
<th>#</th>
<th>Location</th>
<th>Histology</th>
<th>Sex, Age (yrs)</th>
<th>Chemo?</th>
<th>RT?</th>
<th>Surgery?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Paraspinal</td>
<td>Spindle Cell sarcoma</td>
<td>M 83</td>
<td>No</td>
<td>Protons, 7000 cGy</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Distal Thigh</td>
<td>Myxoid Liposarcoma</td>
<td>F 55</td>
<td>No</td>
<td>Photons, 5000 cGy</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Calf</td>
<td>Myxoid Liposarcoma</td>
<td>F 62</td>
<td>Yes</td>
<td>Photons, 5000 cGy</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Thigh Liposarcoma: Stiffness Change with RT

Baseline

Pre-Surgery

Whole Tumor Stiffness

3.58 kPa

2.53 kPa

Shear Stiffness (kPa)
Thigh Liposarcoma: Stiffness Change with RT

Shear Stiffness (kPa)

Baseline Pre-Surgery

Whole Tumor

3.58 kPa

2.53 kPa
Thigh Liposarcoma: Perfusion Change with Radiation Therapy

Baseline

Pre-Surgery
Correlation with Pathology

- Regional changes
  - 50% viable tumor remaining
  - 50% necrosis
- Qualitative stiffness comparison
- Defined future workflow
Perfusion MRI and MRE for Sarcoma: Summary

• 1) Defined MRE and Perfusion MRI protocols for sarcoma

• 2) Performed an initial response assessment
  • Tumor stiffness
  • Perfusion
  • Regional changes

• 3) Future work
  • Establish reproducible comparison techniques
  • Determine correlation of imaging findings and outcomes
    • Local recurrence, event-free survival, etc.
Clinical Impact

- Individualize local and systemic therapy decisions and treatment volumes based on chemotherapy response.
  - Reduce treatment volumes in good responders
  - Modify therapy in poor or late responders
- Early, predictive response assessment
  - Improve patient care
  - Efficiently evaluate novel targeted therapies.