Whole Body Venography in the Post-Ablavar Era

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Department of Medical Imaging
Disclosures

- Institutional research agreement with Siemens Healthineers
- NHLBI-RO1HL115828 grant support, Co-PI
- Describing pulse sequences as generically as possible
- Off-label contrast use
  - Trade names for contrast agents
Whole body venography in the post-Ablavar era

Goals

- Discuss MRV techniques
- Incorporating contrast agents into MRV
- MRV body imaging examples
  - Chest
  - Abdomen, pelvis
  - Extremities
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<th>Pros</th>
<th>Cons</th>
<th>Breathhold</th>
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<td><strong>Time-resolved dynamic contrast-enhanced MRV</strong></td>
<td>High temporal resolution (1-3 sec/frame) displaying dynamic passage of contrast No timing issues</td>
<td>Balance between temporal/spatial resolution Difficult to obtain isotropic pixels Not ECG-gated</td>
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<td><strong>Contrast-enhanced standard MRV</strong></td>
<td>High spatial resolution vascular images at a single time point in contrast bolus</td>
<td>Sensitive to bolus arrival time Not ideal for portal venous eval Not ECG-gated*</td>
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<td><strong>Contrast enhanced 3D GRE/bSSFP IR T1, T2 prep, VIBE</strong></td>
<td>High spatial resolution Venous imaging ideal</td>
<td>Relies on contrast No artery/vein separation Long imaging time (6-10 min) ECG-gated*</td>
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<td><strong>Time-resolved dynamic contrast-enhanced MRV</strong></td>
<td>High temporal resolution imaging (&lt;1 to &gt;10 sec/frame) Displaying dynamic passage of contrast Allows evaluation of vascular hemodynamics Venous collaterals No timing issues</td>
<td>Balance between temporal/spatial resolution Difficult to obtain isotropic voxels Not ECG-gated</td>
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<td><strong>Contrast-enhanced standard MRV</strong></td>
<td>High spatial resolution vascular images at single time point in contrast bolus Can subtract arterial from venous phases</td>
<td>Sensitive to bolus arrival time Not ideal for portal venous eval if imperfect timing Not ECG-gated*</td>
<td>Ideal if chest, abdomen</td>
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## MRV techniques

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<td><strong>Contrast-enhanced standard MRV</strong></td>
<td>High spatial resolution vascular images at single time point in contrast injection</td>
<td>Sensitive to bolus arrival time Direct contrast injection</td>
<td>Ideal if chest, abdomen</td>
</tr>
<tr>
<td>Direct injection</td>
<td></td>
<td></td>
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| **Contrast enhanced 3D GRE/bSSFP T2 prep, IR T1** | High spatial resolution  
Venous imaging ideal                                                      | Relies on contrast  
No artery and vein separation  
Long imaging time (6-10 min)  
ECG-gated                              | Respiratory navigator if chest, abdomen                               |
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<tr>
<td><strong>Contrast enhanced GRE VIBE</strong></td>
<td>High spatial resolution  Can achieve isotropic resolution  15-30 sec acquisition  Multiphase imaging</td>
<td>Relies on contrast Parenchymal and vascular information  Not ECG gated</td>
<td>Yes  Radial 90-120 sec acquisition  No multiphase</td>
</tr>
<tr>
<td>Volumetric interpolated single breath-hold examination LAVA, THRIVE</td>
<td></td>
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![Time-resolved CE-MRA](image1)

![VIBE post-contrast](image2)
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<tr>
<td>Non-contrast</td>
<td>Flowing blood appears bright</td>
<td>2D</td>
<td>No</td>
</tr>
<tr>
<td>Time-of-flight</td>
<td></td>
<td>Relies on blood inflow</td>
<td></td>
</tr>
<tr>
<td>TOF</td>
<td></td>
<td>Flow must be perpendicular</td>
<td></td>
</tr>
<tr>
<td>Historical</td>
<td></td>
<td>Cannot scan in coronal plane</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inplane saturation, lack of inflow effects can yield nondiagnostic</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>images</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Long imaging times</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Motion artifact</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High signal intensity acute</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>thrombus can mimic flow</td>
<td></td>
</tr>
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http://www.konez.com/Vaka005_e.htm
# MRV techniques

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<tr>
<td>Non-contrast Quiescent-Interval Single-Shot (QISS) MRA/V</td>
<td>High spatial resolution imaging Can saturate veins/arteries if unidirectional flow</td>
<td>2D Relies on blood inflow Long imaging time (10-15 min) Not for systemic venous/portal venous ECG-gated</td>
<td>Yes if scanning chest/abdomen</td>
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</tbody>
</table>

![Arterial and venous images](image)

Courtesy of Dr Bob Edelman and Siemens
## MRV techniques

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T2 prep GRE (Fast low-angle shot) FLASH

- T2 magnetization preparation pulse
  - Duration 40 msec
  - Decrease in background signal
  - Intrinsic increase in blood signal over background
  - Given lack of blood pool contrast, increase in blood signal desirable

- Post-contrast

Non-contrast T2 prep GRE
T2 prep GRE (Fast low-angle shot) FLASH

- Fat saturated
- Segmented acquisition with centric ordering phase encoding
- Respiratory navigator triggered
- Thought to be best pulse sequence compromise for MRV in the post-Ablavar era

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<th>Pediatric</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOV (mm²)</td>
<td>200 × 190</td>
<td>300 × 280</td>
<td>360 × 340</td>
</tr>
<tr>
<td>Matrix</td>
<td>176 × 166</td>
<td>224 × 212</td>
<td>240 × 226</td>
</tr>
<tr>
<td>In-plane resolution (mm²)</td>
<td>1.1 × 1.1</td>
<td>1.3 × 1.3</td>
<td>1.5 × 1.5</td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>1.2</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>1.31</td>
<td>1.21</td>
<td>1.19</td>
</tr>
<tr>
<td>Flip angle (°)</td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td># of segments</td>
<td>22</td>
<td>27</td>
<td>30</td>
</tr>
<tr>
<td>Acceleration factor</td>
<td>2</td>
<td>2</td>
<td>2</td>
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## Contrast agents

<table>
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<tr>
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<th>Extracellular</th>
<th>Blood Pool</th>
<th>USPIO</th>
</tr>
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<tbody>
<tr>
<td><strong>Properties</strong></td>
<td>Low molecular weight</td>
<td>Higher/high molecular weight prevents passage through vascular epithelium and leakage into interstitial space</td>
<td>High molecular weight prevents passage through vascular epithelium and leakage into interstitial space</td>
</tr>
<tr>
<td></td>
<td>Diffuse from and equilibrate between the intravascular interstitial spaces</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Products</strong></td>
<td>Most gadolinium based contrast agents</td>
<td>Albumin binding MultiHance Ablavar</td>
<td>ferumoxytol</td>
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</tbody>
</table>
| **Relaxivity plasma** | $r_1 = 3.6-5.2$  
  $r_2 = 4.3-6.1$ | $r_1 = 6.3-19$  
  $r_2 = 8.7-34$ | $r_1 = 15$  
  $r_2 = 100.4$ |
| **1.5T, 37°**       | (L mmol$^{-1}$sec$^{-1}$)                          |                                                             |                                                             |
| **Plasma T1/2, hrs** | 1-1.5                                              | 2-3                                                         | 14-15                                                        |
| **Image**           | Immediately                                       | Up to 1-2 hours                                             | Up to 3 days                                                |

Contrast agent issues

- March, 2015 ferumoxytol FDA black box warning
  - Serious potentially life-threatening allergic reactions
- July, 2015 FDA safety alert
  - Gadolinium based contrast agent (GBCA)
  - Brain deposition of gadolinium
- May, 2017 FDA update
  - No adverse health effects from gadolinium brain deposition
  - Unchanged recommendations regarding use of GBCA
  - Limit GBCA to circumstances which contrast is necessary; assess need for repetitive administration
- September, 2017
  - FDA votes to recommend that GBCAs include a label warning about gadolinium retention in certain organs and tissues with greater risk in children and pregnant women
- September, 2016 Ablavar removed from market
  - Large void in contrast for MRA/V
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Contrast agents

• Extracellular contrast
  – Macrocyclic
    • Least potential for brain and tissue deposition
  – High relaxivity agent
    • Allows single dose (0.1 mmol/kg) MRV
    • Add 0.5x dose (0.05 mmol/kg) for scanning two anatomic regions

• Ferumoxytol
Extracellular contrast administration

- **FLASH acquisition**
  - Ideally contrast present through majority of acquisition
- **Time-resolved MRA (2/3 of total GBCA dose)**
  - Loads vasculature with contrast
  - Allows evaluation of vascular hemodynamics
- **Slow infusion (1/3 of total GBCA dose) at injection rate of 0.05 ml/sec**
  - Keeps some contrast in blood pool
- **Dilute contrast to minimum of 5 mL**
- **Slow saline flush 0.05 ml/sec after contrast**
Slow infusion T2 prep FLASH evaluation

- 42 patients undergoing clinically indicated MRA/V
  - 4 months - 37 years (13.6 ± 7.6 years)
  - 1.5T Magnetom Aera (Siemens Medical Solutions)
- T2 prep FLASH imaging
  - Extracellular contrast injection protocol
- Image quality of thoracic vasculature evaluated
  - **Qualitative scoring criteria**
    - 0 – Excellent vessel delineation without significant artifacts
    - 1 – Good vessel delineation, but with artifacts
    - 2 – Insufficient or non-diagnostic vessel delineation

Presented at SPR 2017
Slow infusion T2 prep FLASH image quality

- **Imaging time**
  - $9:25 \pm 4:34$ (min:sec, mean +/- SD)
  - Varied by patient size, respiratory rate, cooperation

- **Diagnostic image quality for all vessels evaluated**

- **Inhomogeneity artifacts in most vessels**
  - Pulmonary veins most common 83%, right greater than left
  - No direct comparison, but more artifacts than IR T1 FLASH Ablavar

![Image Quality Score (0-2)](image)

0 – Excellent vessel delineation without significant artifacts
1 – Good vessel delineation, but with artifacts
2 – Insufficient or non-diagnostic vessel delineation
10 yo with D-TGA s/p arterial switch

Signal inhomogeneity in pulmonary veins
3 yo with PAPVR to SVC

Significant signal inhomogeneity in pulmonary veins and descending Ao
5 yo with aortic dilatation

Significant signal inhomogeneity in descending Ao Veins well imaged
Slow infusion FLASH

Conclusions

• Slow infusion T2 prep FLASH technique yields diagnostic image quality MRA/V
• Inhomogeneity artifacts observed in multiple vessels, particularly pulmonary veins and in high velocity flow regions
• Potential causes of artifacts
  – Turbulent flow experiences $90^\circ$ excitation but not $180^\circ$ refocusing during T2 preparation
  – T2 prep sensitive to local field inhomogeneity especially near air/tissue interfaces
  – Right pulmonary veins near navigator saturation band
• Try IR T1 FLASH
IR T1 FLASH

- Nonselective 180° inversion preparation pulse
  - Background suppression
- Blood signal entirely from contrast, less SNR than T2 prep
  - Blood pool contrast
    - TI 260 msec at 1.5T
  - Extracellular
    - TI 300 msec at 1.5T
      - Longer inversion time allows for more T1 recovery to account for lower relaxivity of extracellular contrast

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<td>TR (msec)</td>
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14 yo with Marfan syndrome
5 yo with PHACES
Delayed IR T1 FLASH

Delayed IR FLASH due to patient motion limiting navigator efficiency

T2 prep FLASH following additional 0.05 mmol/kg contrast
IR T1 FLASH

- Better option for chest, abdomen and pelvis
  - Better performance c/w T2 prep FLASH with decreased artifacts
  - Must image quickly
  - Delay leads to decreased vascular contrast enhancement

- Consider ferumoxytol
Ferumoxytol

- 55 patients as of 9/1/2017
- Initial indications
  - Complex CHD
    - Fontan
  - Abdomen/pelvis MRV
    - Rex shunt, Abernethy, thrombus
  - Upper/lower dedicated extremity MRV
    - Not vascular malformation
  - Renal failure
- Broadened indications
  - Body venous examination
    - Pulmonary, systemic, or portal/splanchnic
Ferumoxytol

- Dose
  - 3 mg/kg, 1.5T

- Administer over 15 min via syringe pump in prep area
  - If no precontrast imaging

- Administer via power injector
  - If precontrast imaging

- Dilute to 60 ml in power injector syringe and inject over 15 min
  - Injection rate 0.07 ml/sec
  - Followed by normal saline flush

- BP monitored q 1 min during infusion

- Patient monitored at least 30 min after infusion complete
Ferumoxytol

- 250+ pediatric patients as MRI contrast
  - Mild adverse reactions reported
    - Nausea, transient hypotension
  - No serious adverse reactions in children
  - Serious adverse reactions in adult patients
- UCLA FeraSafe Multi-center Registry
- Image with IR T1 FLASH post contrast
  - Blood pool contrast
    - Flip angle 18°, TI 260 msec at 1.5T
  - Ferumoxytol
    - Flip angle 16°, TI 300 msec at 1.5T
    - To decrease T2* effects and allow more T1 relaxation

Muehe. Invest Radiol 2016; 51:221.
Ning. MRM 2016; 34: 152.
Vasanawala. JMRI 2016; 75: 2107.
7-year old meso-Rex bypass and enlarging spleen
3-year old metastatic Wilms tumor, LPV thrombosis, and enlarging spleen

Liver lesion/vascular evaluation protocol
Eovist followed by ferumoxytol
5 yo with intermittent leg swelling
Evaluate for vascular abnormality
Whole body venography in the post-Ablavar era

- IR T1 FLASH
- VIBE
  - Shorter acquisition
- T2 prep FLASH
  - Delayed imaging
- Extracellular contrast
  - High relaxivity
  - Slow infusion
- Ferumoxytol
  - If venous detail required
  - Pulmonary veins, splanchnic, thrombus, combined arterial and venous, Fontan
- Further development of non-contrast sequences
Thank you for your attention