MRI assessment of fetal cardiac physiology

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The Circulation of the Fetus in Utero

METHODS FOR STUDYING DISTRIBUTION OF BLOOD FLOW, CARDIAC OUTPUT AND ORGAN BLOOD FLOW

By Abraham M. Rudolph, M.D., and Michael A. Heymann, M.B., B.Ch.

ABSTRACT

Techniques are described for insertion of vinyl catheters into the umbilical and limb vessels of the fetus of the sheep or the goat through small uterine incisions, with the ewes under spinal analgesia. The catheters are exteriorized and the fetus can be studied in its normal intrauterine environment. During constant infusion of antipyrine into a fetal limb vein, placental arteriovenous difference of antipyrine was measured, and fetal umbilical blood flow was calculated by the Fick method. “Carbonized” microspheres (50-μ diameter) labeled with various nuclides were injected into different venous sites in the fetus. The distribution pattern of the microspheres was used to determine the relative distribution of blood flow. Experimental evidence is provided that (1) there is no significant recirculation of microspheres, (2) the distribution of spheres is proportional to flow, and (3) circulatory physiology is not altered by injection of spheres. Quantitative data on the distribution of umbilical venous and superior and inferior vena caval return were obtained. It was possible to determine the actual blood flow to each of the fetal organs by relating the proportions of nuclide in each organ to that in the placenta. Total cardiac output was then calculable, taking into consideration the hemodynamic arrangement of the fetal circulation.
stationary spins
stationary spins
stationary spins

$G_x$ time
stationary spins
stationary spins

$G_x$ vs time

no net phase shift
moving spins

\[ G_x \]

\[ \text{time} \]
moving spins

$G_x$

time
moving spins

G_x

time
moving spins

$G_x$

time

---

*Figure: Diagram showing a plot of $G_x$ versus time with arrows indicating the movement of spins.*
moving spins

$G_x$

time

$\uparrow \downarrow \uparrow \downarrow$
moving spins
moving spins

\[ G_x \]

\begin{align*}
\text{time} & \\
\end{align*}

phase shift \sim \text{blood flow velocity}
Cine phase contrast imaging

Flow (ml/s)

0  25  50  75  100

-10  0  10  20  30  40  50
Cardiac gating
Metric optimized gating (MOG)
Metric optimized gating (MOG)
Cine phase contrast MRI
Phase contrast with MOG vs conventional gating (adult neck vessels during exercise)
Fetal PC MRI – reproducibility and internal validation

Prsa et al. Circ Cardiovasc Imag 2012
MRI and US flows (AAo and MPA)

$r = 0.77$

$p < 0.0001$

Average MR & US Flow measurement

Prsa et al. *Circ Cardiovasc Imag* 2012
MPA/AAo flow (MRI) vs RVED/LVED (US)

$r = 0.54$
$p = 0.0003$

Prsa et al. *Circ Cardiovasc Imag* 2012
Slice prescriptions

- **Main Pulmonary Artery (MPA)**
- **Descending Aorta (DAo)**
- **Ductus Arteriosus (DA)**
- **Superior Vena Cava (SVC)**
- **Main Pulmonary Artery (MPA)**
- **Right Pulmonary Artery (RPA)**
- **Left Pulmonary Artery (LPA)**
- **Umbilical Vein (UV)**

Flow (mL/s) vs. Time (% Cardiac Phase): MPA, RPA, LPA, UV
Distribution of blood flow in the normal late gestation human fetus (n=40)

PC MR Flow (ml/min/kg)

% of CVO

Prsa et al. Circ Cardiovasc Imag 2014
Relaxation time: $T_1$ and $T_2$
Fetal MR oximetry with T2 mapping

T2 preparation time (ms)

Signal intensity

T2 = 100 ± 3.6 ms
SO2 ≈ 60% ± 1.3%
Fetal cardiovascular physiology by T2 mapping
T2 oximetry vs conventional blood gases in children with CHD

\[ y = 0.7871x + 12.435 \]

\[ R = 0.825, \ P < 0.001 \]
T2 mapping in the cardiac ventricles of fetal lambs

Wedergartner et al. MRM 2010
MR oximetry vs conventional blood gases in fetal lambs
Adult blood *in vitro* - T2 versus SaO$_2$

\[
\frac{1}{T_2} = \frac{1}{0.285} + 12.10\left(1 - \frac{SaO_2}{100}\right) + 4.98\left(1 - \frac{SaO_2}{100}\right)^2
\]
Reproducibility of fetal T2 mapping

\[ Y = 1.029X - 3.969 \]

\[ R^2 = 0.98, P < 0.0001 \]
Interobserver variability – fetal vessel T2 and PC measurements
T1 and hematocrit *in vitro* (7T)

\[ R_{1,\text{blood}}(\text{Hct}, Y = 0.6) = \frac{0.305 + 0.275 \cdot \text{Hct}}{0.95 - 0.25 \cdot \text{Hct}} \]
Combined T1 and T2 measurement for non-invasive evaluation of blood oxygen saturation and hematocrit

Portnoy et al. ISMRM 2015
SaO₂ and Hct by T1 and T2 mapping versus conventional laboratory measures in vitro

Portnoy et al. ISMRM 2015
Normal fetal SaO₂ (%) by MRI versus lamb reference (n=20)

<table>
<thead>
<tr>
<th>Vessel</th>
<th>UV</th>
<th>AAo</th>
<th>MPA</th>
<th>SVC</th>
<th>DAo</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI (mean±SD)</td>
<td>88±4</td>
<td>67±7</td>
<td>56±9</td>
<td>46±10</td>
<td>58±8</td>
</tr>
<tr>
<td>Lamb reference</td>
<td>80</td>
<td>65</td>
<td>55</td>
<td>40</td>
<td>60</td>
</tr>
</tbody>
</table>
Normal fetal hemodynamics by MRI (n=20)
Measuring human fetal oxygen delivery and consumption by MRI

1. Measure hemoglobin concentration
   • Fetal [Hb] at 37 weeks GA = 15 g/dL*

2. Measure vessel T2 and flow (Q)
   • UV T2
   • DAo T2
   • $Q_{uv}$

3. Convert T2 to SaO$_2$

\[
\frac{1}{T2} = \frac{1}{T2o} + K \cdot \left(1 - \frac{SaO2}{100}\right)^2
\]

4. Calculate oxygen content, oxygen delivery and oxygen consumption

\[
DO_2 = Q_{uv} \times C_{uv}O_2
\]

and

\[
VO_2 = Q_{uv} \times (C_{uv}O_2 - C_{ua}O_2)
\]

where

\[
O_2 \text{ content} = [Hb] \times SaO_2 \times 1.36
\]

* Nicolaides et al. *Lancet* 1988;331;1073-1075

δ Wright et al. *JMRI* 1991;1:275-283
### Fetal oxygen delivery and uptake (ml/min/kg) by MRI (n=20)

<table>
<thead>
<tr>
<th></th>
<th>Fetal lamb(^\pi)</th>
<th>Human at term delivery(^*)</th>
<th>Late gestation human by MRI (^\delta)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DO2</strong></td>
<td>~20</td>
<td>13.4</td>
<td>20.4</td>
</tr>
<tr>
<td><strong>VO2</strong></td>
<td>7-8</td>
<td>6.58</td>
<td>6.9</td>
</tr>
<tr>
<td>Cerebral DO2</td>
<td></td>
<td></td>
<td>12.0</td>
</tr>
<tr>
<td>Cerebral VO2</td>
<td></td>
<td></td>
<td>4.0</td>
</tr>
</tbody>
</table>

\(^\pi\) Rudoph AM. *Congenital Diseases of the Heart* 2009  
\(^*\) Acharya G. *Acta Obstetricia et Gynecologica* 2009  
\(^\delta\) Seed & Macgowan. *Magnetom Flash* 2014
Pulmonary blood flow and foramen ovale shunt

\[ r = -0.64 \]
\[ P < 0.0001 \]
Main pulmonary artery T2 versus pulmonary blood flow

\[ r = 0.43 \]
\[ P = 0.02 \]
Umbilical vein T2 versus descending aorta T2 – AVΔO₂

- **r = 0.53**
- **P = 0.002**
AVΔO₂ versus umbilical vein flow

UV T2 - DAo T2 (ms) vs. UV flow (mL/min/kg)

D

$r = -0.2$

$P = 0.2$
Oxygen delivery versus oxygen consumption

![Graph showing the relationship between DO₂ and VO₂.](image-url)
Fetal hemodynamic adaptation to acute hypoxia

Jensen A J Dev Phys 1991
14 IUGR fetuses versus 26 normals at 35 weeks GA: vessel flows
14 IUGR fetuses versus 26 normals at 35 weeks GA: vessel T2s

Zhou et al. ISMRM 2015
Fetal oxygen delivery and consumption

*P=0.02

*P=0.0001

VO2

DO2

ml/min/kg

ml/min/kg

Non-IUGR

IUGR

Zhou et al. ISMRM 2015
Receiver operator curves for MRI and ultrasound parameters of late onset IUGR
Serial measurements in a case of late onset IUGR – pulsitility index

Middle cerebral artery

Umbilical artery

Zhou et al. *SCMR* 2015
Serial late gestational Individual vessel flows by MRI

Zhou et al. SCMR 2015
UV T2, fetal DO$_2$ and VO$_2$

Zhou et al. SCMR 2015
Placental histology

• Placental weight: 396g (10\textsuperscript{th}-25\textsuperscript{th} centile)

• Mild overcoiling of the umbilical cord

• Mild dysmaturity of chorionic villi

Zhou et al. SCMR 2015
Normalization of flow distribution in chronic hypoxia with fall in fetal VO₂

Yaffe et al J Dev Physiol 1987

Rurak et al Am J Physiol 1990
Hemodynamics of chronic lamb placental insufficiency

<table>
<thead>
<tr>
<th></th>
<th>SaO₂ (%)</th>
<th>Placental weight (g)</th>
<th>Fetal weight (kg)</th>
<th>Brain-to-liver ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>68.7±4</td>
<td>441±24</td>
<td>3.9±0.2</td>
<td>0.48±0.04</td>
</tr>
<tr>
<td>Placental restriction</td>
<td>38.9±1*</td>
<td>157±21*</td>
<td>2.6±0.2*</td>
<td>0.93±0.12*</td>
</tr>
</tbody>
</table>

*Poudel et al. AJP 2014

![Graph showing blood flow (ml/min/100g) for different organs: Brain, Heart, Adrenal, Liver, Lung, Kidney, Spleen, Thymus, Pancreas.](image-url)
Hypoxia and the fetal cerebral circulation – summary of the animal literature

Pearce J Appl Physiol 2006
Brain weight, placental weight and SVC flow

- Brain weight and placental weight: $R^2 = 0.36, p < 0.01$
- Brain weight and SVC flow: $R^2 = 0.3, p = 0.0002$