醫用磁振學 MR MRM
磁振對比劑
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本週課程內容 http://www.ym.edu.tw/~cflu
- 磁振對比劑原理與安全性
- Gd對比劑應用

- MRI The Basics (3rd edition)
  - Chapter --
- MRI in Practice, (4th edition)
  - Chapter 11: Contrast Agent in MRI

Image Contrast Parameters
- Intrinsic contrast parameters
  - T1 relaxation time
  - T2 relaxation time
  - Relative proton density
- Extrinsic contrast parameters (can be controlled)
  - TR (repetition time)
  - TE (echo time)
  - TI (inversion time)
  - Flip angle

Contrast agent (with varying magnetic susceptibility) can affect local magnetic field and hence T1 and T2 relaxation times.
Gadolinium (Gd) 釓

• The most commonly used MR contrast agents are Gadolinium based.
• As an element, Gd is ferromagnetic and highly toxic.
• Metal ions (Gd^{3+}) with free electrons tend to accumulate in tissues with a natural affinity for metals (compete with Ca^{2+}).
  - Membranes
  - Transport proteins
  - Enzymes
  - Osseous matrix
  - Reticuloendothelial system: lungs, liver, spleen, and bone

Gadolinium Chelates

• Chelates have a high affinity for metal ions.
• Gd chelates are paramagnetic and relatively safe.
  - Shorten T1 and T2* relaxation time
• In a patient with normal renal function, the biological half-life of Gd chelates is 2 hours.
• Majorly excreted by the renal system.

Magnetic Susceptibility

• Diamagnetic substances
  - Mild negative effects on the local magnetic field
  - Gold, silver, and oxyhemoglobin
• Paramagnetic substances
  - Low but positive effect on the local magnetic field
  - Gd chelate, deoxyhemoglobin
• Superparamagnetic substances
  - Higher positive susceptibility, create large disruptive changes in local magnetic field
  - Iron oxide
• Ferromagnetic substances
  - Very high positive susceptibility
  - Iron

Effects of Contrast agents

axial T1WI  axal T2WI
axal T1WI – post Gd  FLAIR
Edema  Cyst  Tumor
The first chelate that proved effective for MR contrast media was diethylene triaminepentaacetic acid (DTPA).

**Development of Contrast Agent**

<table>
<thead>
<tr>
<th>Generation</th>
<th>Linear Ionic</th>
<th>Linear Nonionic</th>
<th>Macroyclic Ionic/Nonionic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Generation</td>
<td>Linear Ionic</td>
<td>Products: Magnevist (Gd-DTPA)</td>
<td>Products: Omniscan (Gd-DTPA-BMA)</td>
</tr>
<tr>
<td>2nd Generation</td>
<td>Linear Nonionic</td>
<td>Products: DOTAren (Gd-DOTA)</td>
<td>Products: ProHance (Gd-HP-DO3A)</td>
</tr>
<tr>
<td>3rd Generation</td>
<td>Macroyclic Ionic/Nonionic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Products:
- Magnevist (Gd-DTPA)
- Omniscan (Gd-DTPA-BMA)
- Dotarem (Gd-DOTA)
- ProHance (Gd-HP-DO3A)

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**European group recommends to stop using 4 linear GBCAs**

March 10, 2017 – A committee of the European Medicines Agency (EMA) has recommended the suspension of the marketing authorizations for four linear gadolinium-based contrast agents (GBCAs) used for MRI scans because of concerns about small amounts of gadolinium from administered GBCAs being deposited in the brain.

At the completion of its year-long review of GBCAs, the EMA’s Pharmacovigilance and Risk Assessment Committee (PRAC) “found convincing evidence of accumulation of gadolinium in the brain from studies directly measuring gadolinium in brain tissues and some of increased signal intensity seen on MRI scan images many months after the last injection of a gadolinium contrast agent”.

Linear agents recommended for suspension by the PRAC are:
- Gadobenate, marketed as MultiHance by Bracco Diagnostics Inc.
- Gadodiamide, marketed as Omniscan by GE Healthcare
- Gadopenetic acid, marketed as Magnevist by Bayer HealthCare Pharmaceuticals
- Gadoversetamide, marketed as OutMARK by Mallinckrodt Inc.
Ionicity (renal safety and adverse reactions)

- **Osmolality**: The number of dissolved particles per kg of water.
- **Ionicity** is closely related to osmolality.
- A close tracking between ionicity and high osmolality is noted (may affected by the manufacturer's decision).

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Ionicity</th>
<th>Osmolality (mOs/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnevist®</td>
<td>ionic</td>
<td>1960</td>
</tr>
<tr>
<td>MultiHance®</td>
<td>ionic</td>
<td>1970</td>
</tr>
<tr>
<td>Omniscan™</td>
<td>non-ionic</td>
<td>799</td>
</tr>
<tr>
<td>Optiomark™</td>
<td>non-ionic</td>
<td>1110</td>
</tr>
<tr>
<td>Dotarem®</td>
<td>ionic</td>
<td>1350</td>
</tr>
<tr>
<td>ProHance®</td>
<td>ionic</td>
<td>630</td>
</tr>
<tr>
<td>Gadavist®</td>
<td>non-ionic</td>
<td>1603</td>
</tr>
<tr>
<td>Eovist®</td>
<td>ionic</td>
<td>688</td>
</tr>
<tr>
<td>Ablavar®</td>
<td>ionic</td>
<td>825</td>
</tr>
</tbody>
</table>

Gd Deposition

- Gd contrast agent
  - Has seven unpaired electrons and the ability to allow rapid exchange of bulk water.
  - Unpaired electrons have a magnetic moment that is 500,000 times that of a hydrogen proton.
  - This large magnetic moment creates fluctuations in the local magnetic fields.

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Relaxivity

- The effect of a substance on relaxation rate is known as its relaxivity.

\[ \frac{1}{T_1_{\text{observed}}} = P \frac{1}{T_1_{\text{enhanced}}} + (1 - P) \frac{1}{T_1_{\text{bulk water}}} \]

Gadolinium Administration/Dose

- The recommended dosage of gadolinium is 0.1 millimoles per kilogram (mmol/kg) of body weight, (0.2 ml/kg).

- The lethal dose, \( \text{LD}_{50} \) – the dose required to kill half of the study population) determined in rat studies is between 6 and 20 mmol/kg.

- As dose increases (to a point), the ability to visualize structures and lesions also increases. With standard gadolinium the optimal dose is weight-based.

A standard (fix) dose of contrast agent is unacceptable!

Dose effects

ACR White Paper on MRI Safety

- The ACR approves of the injection of contrast material and diagnostic levels of radiopharmaceuticals by certified and/or licensed radiologic technologists and radiologic nurses under the direction of a radiologist or his or her physician designee who is personally and immediately available, if the practice is in compliance with institutional and state regulations.

ACR: American College of Radiology.
Clinical Consideration

- Three clinical scenarios must be considered...
  - subcutaneous extravasation of contrast
    - slightly better performance of low osmolar/non-ionic agents
  - potential nephrotoxicity
    - the difference between ionic and nonionic formulations is minimal.
  - problems related to acute increase in serum osmolality
    - The osmolar effect of a contrast agent is determined by its concentration in the blood.

Contrast media (by IV injection) has circulated through the heart and aorta, its concentration has been significantly diluted.

Nephrogenic Systemic Fibrosis

- Nephrogenic systemic fibrosis (NSF): patients who suffered from renal insufficiency.
- Normally, approximately 80% of gadolinium is excreted by the kidneys in 3 h and 98% is recovered by feces and urine in one week.
- But it may take longer for patients with NSF.
- Gadolinium is a contraindication and a relative precaution for patients in renal failure.

Other T1 agents

- Manganese
  - For liver imaging
  - Be taken up by the Kupffer cells in the liver.
- Hyperpolarized helium gas
  - For inhalation imaging for the lungs
- Superparamagnetic iron oxide (SPIO) agents

Gd對比劑應用

Applications of Gd contrast agents
Clinical Applications

- Tumors pre- and post-operation
- Pre- and post-radiotherapy
- Infection
- Infarction
- Inflammation
- Post-traumatic lesions
- Post-operation lumbar disc
- Contrast-enhanced MRA

Lumbar Spine with bone metastases

Timing for abdominal imaging

Enhancement and phase
Abdominal vessels

Arterial phase

Intermediate phase

THE END

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