Session II: Challenges in Diagnostic Imaging

Contrast-enhanced US

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Outline

• Introduction

• Main part
  1. US contrast
  2. Dx of HCC on CEUS
  3. HCC histologic grade on CEUS
  4. Cost-Efficiency of CEUS
  5. Perfusion Study of CEUS

• Summary
Introduction

- **PRACTICE GUIDELINE EASL 2005**

![Flowchart]

- Normal
  - Repeat US Every 3-6 mos

- Positive
  - Nodule < 1 cm
  - Nodule 1-2 cm
  - Nodule > 2 cm

  - 2 Exams* Biopsy
  - 1 Exam* Biopsy

* : CEUS, CT, MR
HAP: Hypervascularity
EP : Wash-out
Introduction

- 2009 간세포암종 진료 가이드라인

Liver Mass

위험인자 -

위험인자 +

Biopsy

Atypical E

AFP < 200 ng/ml

AFP > 200 ng/ml

Nodule > 2 cm

2 Exams*

CT or MR

* : CT, MR, Angio
HAP: Hypervascularity
EP : Wash-out
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• Summary
1. US Contrast Agents

- **SonoVue** (Bracco, Milan, Italy): available in Korea

- **Gas**: SF6 (sulfur hexafluoride)
- **Phospholipid shell**: 2.5 μm

- **Maximum backscattering**: about 3 MHz
- **Elimination half-life**: 6 min
- **80%**: via the lungs in 11 min
- **Continuous scanning** after injection
- **Vascular phase**: up to 5 min after injection
US Contrast Agents

- Sonazoid (Daiichi Sankyo, Tokyo, Japan)

- Gas: Perfluorobutane
- Lipid (not disclosed)

- Vascular phase (up to 5 min)
- Post-vascular phase (10 min to 1 hr): Kupffer cell uptake
- Possible combination of arterial phase and post-vascular phase
- Defect Reperfusion imaging
Conclusive Dx Rate: 80%
## 2. Dx of HCC on CEUS

Ability to detect arterial hypervascularity in HCCs in cirrhosis

<table>
<thead>
<tr>
<th>Author</th>
<th>No. Lesions</th>
<th>Lesion size (cm)</th>
<th>Detection rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CEUS (%)</td>
</tr>
<tr>
<td>Gaiani 2004</td>
<td>103</td>
<td>2.8 ±1.3</td>
<td>91</td>
</tr>
<tr>
<td>Bolondi 2005</td>
<td>41</td>
<td>1-2</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>2-3</td>
<td>97</td>
</tr>
<tr>
<td>Forner 2008</td>
<td>60</td>
<td>0.5-2</td>
<td>78</td>
</tr>
<tr>
<td>Maruyama 2011</td>
<td>16</td>
<td>1.4 ± 0.4</td>
<td>44</td>
</tr>
<tr>
<td>Mandai 2011</td>
<td>92</td>
<td>2.0 ± 1.7</td>
<td>77</td>
</tr>
<tr>
<td>Giorgio 2004</td>
<td>28</td>
<td>1.6 (0.9-2)</td>
<td>53.6</td>
</tr>
<tr>
<td></td>
<td>46</td>
<td>3.5 (2.1-6.5)</td>
<td>91.3</td>
</tr>
</tbody>
</table>
F/66

S/P RFA due to HCCs
M/53
Liver cirrhosis
Arterial phase

Portal V phase

Delayed phase
Early arterial phase
Portal Venous Phase
Enhancement pattern summary

Arterial phase
Dx of HCC on CEUS

- Excellent for depiction of arterial hypervascularity
  - Giorgio 2007
    - HCCs $< \text{ or } = 10$ mm : MR $>$ CEUS
    - HCCs $> 10$ mm : CEUS $>$ MR
- Useful in the cases with suspicious hypervascularity on CT/MR
- Hepatic lesions in pts with renal dysfunction
  - No hazard for liver and kidneys
- Sono-guided targeting
  - Hyper/Hypo vascular nodules
3. HCC histologic grade on CEUS

- Proportion of hypervascular tumors
  - W/D: 66%
  - M/D and P/D: 80%

- Proportion of hypoechoic tumor on post-vascular phase
  - W/D: 54%
  - M/D and P/D: 92%

Arterial enhancement vs. Pathologic Differentiation

Jang HJ. Radiology 2007;244:898
Washout Time vs. Pathologic Differentiation

**CEUS**

<table>
<thead>
<tr>
<th></th>
<th>&lt;90s</th>
<th>90-180s</th>
<th>180-300s</th>
<th>No washout</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=14</td>
<td>7 (50%)</td>
<td>4 (29%)</td>
<td>1 (7%)</td>
<td>2 (14%)</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=80</td>
<td>2 (3%)</td>
<td>24 (30%)</td>
<td>35 (44%)</td>
<td>7 (70%)</td>
</tr>
<tr>
<td>Poor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=10</td>
<td>1 (10%)</td>
<td>2 (20%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Jang HJ. Radiology 2007;244:898
## 4. Cost-efficiency of CEUS

Prospective studies for all hepatic nodules not characterized by US or CT

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>No. Lesions</th>
<th>Performance</th>
<th>Cost Efficiency</th>
<th>Concordance Rate</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>France 2009</td>
<td>733</td>
<td>Sen &gt; 80% Spf &gt; 90%</td>
<td>CEUS &gt; CT or MR</td>
<td>84.5 % with CT/MR</td>
<td>CT (191 Euro) MR (322 Euro) US (155 Euro)</td>
<td></td>
</tr>
<tr>
<td>Germany 2010</td>
<td>269</td>
<td></td>
<td></td>
<td>85.8 % with MR</td>
<td>Hemangiomas (50%) FNH (18%)</td>
<td></td>
</tr>
<tr>
<td>Romania 2011</td>
<td>316</td>
<td>Conclusvie Dx rate 79.1 %</td>
<td>CEUS &gt; CT or MR</td>
<td></td>
<td>CT price 1.6 x CEUS MR price 3.6 x CEUS</td>
<td></td>
</tr>
<tr>
<td>Korea ?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CT price ? x CEUS MR price ? x CEUS</td>
<td></td>
</tr>
</tbody>
</table>
5. Perfusion study with CEUS

- **Advantage of CEUS**
  - Real time observation of pure vascular perfusion
  - Easily repeatable
  - No hazard to patients

- **Disadvantage of CEUS**
  - Anatomical limit
  - Motion limit → Time/effort are needed for correction

- **Perfusion studies with antiangiogenic drug**
  - Change of tumor vascularization within 1-2 wks
  - Significantly correlated with PFS and OS

Perfusion study with CEUS

- **A Mouse Hepatoma Model**
  - Mice bearing H22 hepatoma
  - Cisplatin vs placebo
  - CEUS on day 8
  - Cisplatin group: significant decrease in perfusion index and maximum intensity

Summary

1. **US contrast**
   - SonoVue: Vascular phase, > 80% thru lung
   - Sonazoid: Post-vascular phase (Kupffer cell uptake)
     : Defect reperfusion imaging

2. **Dx of HCC on CEUS**
   - Hypervascularity on AP: CEUS > CT
     CEUS > MR (> 1cm nodule)

3. **HCC histologic grade on CEUS**
   - Possible prediction of HCC differentiation

4. **Cost-Efficiency of CEUS**
   - Cost efficient in some countries but ? in Korea

5. **Perfusion Study of CEUS**
   - Promising and of clinical impact due to advantages of CEUS
Thank You for your attention