Gd-EOB-DTPA-Enhanced MR Imaging of Hepatocellular Adenomas: A Radiogenomics Approach

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Disclosures

• Justin Tse is a recipient of the Bayer Medical Care Investigator Initiated Research and the RSNA Research Medical Student Grant, both of which helped fund this project.
The objectives of this poster are to answer:

• What is the pathophysiology of HCAs, and how does this affect prognosis?

• What are the MR imaging findings of HCAs?

• Can Gd-EOB-DTPA-enhanced MR help further subtype HCAs?

• How do HCA MR imaging findings correlate with molecular expression?

Target Audience: Practicing abdominal radiologists and trainees
What is the pathophysiology of HCA subtypes, and how does this affect prognosis?
Introduction

- HCAs are benign liver tumors most commonly found in obese women with a history of OCP use.

- Other risk factors include: anabolic steroid use, MODY3, and glycogen storage diseases.

- Recently, they were reclassified into different subtypes based on molecular expression.

- Each subtype has variable malignant potential and therefore different management.
Reclassification into Genotypic Subtypes

**Risk Factors**

- **Inflammatory: 50%**
  - Female
  - Obesity
  - OCP use

- **HNF-1α: 30%**
  - Female
  - OCP use
  - Familial adenomatosis
  - MODY 3

- **β-Catenin: 10%**
  - Male
  - Anabolic steroids
  - Glycogen storage disease

**Molecular pathogenesis**

- JAK-STAT Activation
- Inactivation of HNFα

**Note:** remaining 10% of HCAs are unclassified and do not yet have established risk factors, molecular pathogenesis, or prognosis.
Importance of HCA Subclassification

- Prognosis and management depends on HCA subtype

**Inflammatory:**
- Risk of rupture
- Slight HCC risk
- Resected
- OCP cessation

**HNF-1α:**
- Least aggressive
- Surveillance
- OCP cessation

**β-Catenin:**
- ++ HCC risk (5-10%)
- Resected
- OCP cessation
What are the MR imaging findings of HCAs?
Inflammatory HCAs

<table>
<thead>
<tr>
<th>T2-weighted</th>
<th>Arterial Hyper-vascularity</th>
<th>Hepatobiliary Phase</th>
<th>Additional Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperintense</td>
<td>Marked</td>
<td>Hypointense</td>
<td>Atoll sign</td>
</tr>
</tbody>
</table>

- 49 year old female T2-weighted
- 24 year old female Arterial phase Atoll sign present
- 26 year old female Hepatobiliary phase Atoll sign present
**HNF-1α Inactivated HCAs**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Iso- to hyperintense</td>
<td>Mild</td>
<td>Hypointense</td>
<td>Signal dropout on out-of-phase</td>
</tr>
</tbody>
</table>

In-Phase

Out-of-Phase

59 year old female

## β-Catenin HCAs

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</tr>
</thead>
<tbody>
<tr>
<td>Hyperintense</td>
<td>Mild to moderate</td>
<td>Variable</td>
<td>Intralesional scar</td>
</tr>
</tbody>
</table>

**26 year old male bodybuilder (testosterone use)**  
β-Catenin HCA with HCC
Unclassified HCAs

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</thead>
<tbody>
<tr>
<td>Hyperintense</td>
<td>Mild to moderate</td>
<td>Hypointense</td>
<td>N/A</td>
</tr>
</tbody>
</table>

37 year old female

Pre-Contrast Phase

Arterial Phase

Hepatobiliary phase
Can Gd-EOB-DTPA-enhanced MR help further subtype HCAs?
Gd-EOB-DTPA Enhanced MR Imaging of HCAs

<table>
<thead>
<tr>
<th>HNF-1α</th>
<th>Inflammatory</th>
<th>β-Catenin</th>
<th>Unclassified</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.jpg" alt="Image" /></td>
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<td><img src="image7.jpg" alt="Image" /></td>
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</tbody>
</table>

- All HCA subtypes visually appear to lack Gd-EOB-DTPA uptake
- Do certain subtypes lack more Gd-EOB-DTPA uptake than others?
Gd-EOB-DTPA Enhanced MR Imaging of HCAs

59 year old female with multifocal HNF-1α; hepatobiliary phase

- HNF-1α visually seems to lack more uptake than that of other subtypes
Gd-EOB-DTPA Enhanced MR Imaging of HCAs


- Ratio of HCA signal intensity (SI) to liver signal intensity confirms decreased Gd-EOB-DTPA uptake in all subtypes.
- HCA subtypes demonstrate different Gd-EOB-DTPA uptake kinetics, with HNF-1α having the lowest uptake and SI.
How do HCA MR imaging findings correlate with molecular expression?
Gd-EOB-DTPA Enhanced MR Imaging: Correlation with Molecular Expression

- HNF-1α lesions are the most hypointense, consistent with reduced OATP1B1/3 expression.
- Unclassified lesions show absent OATP1B1/3 expression. Perhaps other transporters play a role in Gd-EOB-DTPA uptake/excretion.
- The atoll sign corresponds to a circumferential band of OATP1B1/3 over-expression.
Using ImageJ, OATP stained regions in the HCA and liver can be quantified.

OATP expression seems to correlate with hepatobiliary phase signal intensity ratio using linear regression (unpublished data).

*Our unpublished data

Gd-EOB-DTPA Enhanced MR Imaging: Correlation with Molecular Expression
In normal hepatocytes, Gd-EOB-DTPA is thought to be taken up by OATP1B1/3 on sinusoidal membranes and then excreted via multidrug resistant proteins (MRP).

In HCAs, decreased OATP1B1/3 expression in part explains their decreased Gd-EOB-DTPA uptake.
Proposed Mechanistic Explanations (HNF-1α)

Risk Factors

Molecular pathogenesis

MRI correlate

Biallelic inactivation of HNF-1α gene

- Intracellular fat accumulation
- Hepatocellular proliferation
- Downregulation of L-FABP1 protein

OCPs

MODY3, familial adenomatosis

- Downregulation of OATP
- Decreased Gd-EOB-DTPA uptake
- Marked hypointensity relative to liver on hepatobiliary phase imaging

Signal loss on out-of-phase imaging
Conclusions

- HCAs have been recently re-categorized based on their genotype, which is important in guiding clinical management and prognosis.

- OATP expression plays an important role in Gd-EOB-DTPA uptake and can determine the enhancement features on hepatobiliary phase for HCA subtypes.

- Recent advancements in both our understanding of HCA pathophysiology and the pharmacokinetics of Gd-EOB-DTPA have improved MR-imaging based diagnosis of HCA subtypes.
References


If further questions, please send your correspondence to Justin Tse at jrtse@stanford.edu