Objectives

- Common liver lesions seen in women on imaging
- Describe key findings on imaging
- Focal nodular hyperplasia and hepatocellular adenoma
- Provide practical tips and pointers
### Focal Liver Lesions

#### Common (~90%)

<table>
<thead>
<tr>
<th>Context</th>
<th>Common (~90%)</th>
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<tbody>
<tr>
<td>Non-cirrhotic</td>
<td>Cyst</td>
</tr>
<tr>
<td></td>
<td>Hemangioma</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>HCC</td>
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#### Uncommon Differentials (~9%)

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<tr>
<td>Non-cirrhotic</td>
<td>Cyst</td>
<td>Abscess, cystadenoma, hydatid cyst</td>
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<tr>
<td></td>
<td>Hemangioma</td>
<td>Hemangioma mimics</td>
</tr>
<tr>
<td></td>
<td>FNH</td>
<td>adenoma</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>HCC</td>
<td>Dysplastic nodule, pseudotumors</td>
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</table>
Cross-sectional modalities

- CT: Main modality for lesion detection and characterization

- US: Cystic versus solid, vessels
Cross-sectional modalities

- CT: Main modality for lesion detection and characterization
- US: Cystic versus solid, vessels
- MRI: Problem solving, additional characterization

Grouping by density

- Hypovascular: Less dense than adjacent liver parenchyma in arterial and portal venous phases
  - Cyst
  - Metastasis
  - Cholangiocarcinoma
Grouping by density

- **Hypervascular**: Denser than adjacent liver parenchyma in arterial or venous phases
  - Hemangioma
  - FNH
  - Adenoma
  - HCC
  - Hypervascular metastasis

**Hemangioma**

- Most common benign tumor of the liver
- Up to 7-10% of population (at autopsy)
- Females, 3rd-5th decade
- Multicentric in up to 30%
- Asymptomatic
- Giant hemangiomas (>10 cm) may cause systemic features of inflammation such as fever, weight loss, and anemia
Hemangioma

- Characteristic enhancement pattern:
  - Peripheral nodular-globular or flame-shaped & Delayed centripetal fill-in
  - 88% sensitive, 84-100% specific
- T2 hyperintense on MRI
  - 100% sensitivity, 92% specificity

Benign Hepatocellular Tumors

- Normal liver
- Female
- Focal Nodular Hyperplasia 90%
- No complication

- Hepatocellular Adenoma 10%
- 27%
- Bleeding

- Hepatocellular carcinoma
- 4.2%
Focal Nodular Hyperplasia (FNH)

Clinical features

- Female predominance: Female/Male = 8/1
- High prevalence: 1 to 5/1,000
- Oral contraception plays a limited role in FNH development
- No bleeding, no malignant transformation

Edmondson et al. 1958; Mathieu et al. 1998; Heinemann et al. 1998

Focal Nodular Hyperplasia (FNH)

- Benign tumor-like nodule:
  - Central scar of vascular channels in fibrous tissue
  - May be due to liver hyperplasia around arterial malformation
- Imaging characteristics:
  - Hypervascular enhancement of lesion
  - Delayed enhancement of central scar
  - T2: Mildly hyperintense, with bright central scar

Rad Clin N Am 1997; 5: 255-257
Focal Nodular Hyperplasia (FNH)

Arterial phase CECT  
Delayed phase CECT  

Focal Nodular Hyperplasia (FNH)

T2  
Early post-gad  
Delayed post-gad
Focal Nodular Hyperplasia (FNH) 
Implication for diagnosis

- Contrast-enhanced MRI, CT scan or CESU

**Diagnosis of FNH at MRI**
1. Isosignal or faint hyposignal in T1
2. Diffuse enhancement at the arterial phase
3. Central scar in hypersignal in T2 and enhancement during late phase

**Suspicion of FNH at imaging but absence of all typical criteria using at least 2 radiological exams**
- Tumor biopsy

**Firm diagnosis of FNH**
- No Treatment

Adopted from Nault et al, Gastroenterology, 2013

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Hepatocellular Adenoma (HCA)

- Female predominance (F:M=8:1)
- Oral contraception association: possible tumor regression after stopping oral contraception
- Adenomas may increase in size during pregnancy requiring close monitoring
Diagnosis of Adenoma (HCA)

- Discovered mainly following abdominal pain and incidentally on imaging
- Liver enzyme levels are often normal
- All tumor markers routinely tested are normal

Adenoma

- Homogeneous hypervascular enhancement (90%)
- *Pseudocapsule (17-30%)
- *T1: Often bright or heterogeneous due to micro or macroscopic fat
- T2: Mildly hyperintense
- *No central scar
**FHN versus adenoma**

Sulfur colloid scan: Taken up by Kupffer cells in FHN, no uptake in adenoma - but only positive in 55% of cases

*AJR 1981; 137:983-990*

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**Hepatocellular Adenomas (HCA)**

**Molecular Classification**
Hepatocellular Adenomas (HCA)
Molecular Classification

1. HNF1A Inactivation 30-40%
2. Inflammatory 40-50%
3. β-catenin activation 12-19%
4. Unclassified 10%

Risk Factors for Adenoma (HCA)

Common risk factors (> 95% of all HCA)
- HNF1A inactivation 30-40%
- Inflammatory 40-50%
- β-catenin activation 10-15%
- Unclassified 10%
- Germline mutation of CYP1B1
- Obesity
- Alcohol
- Androgen
- Male
- Oral contraception

Female

ACG Western Regional Postgraduate Course - Las Vegas, NV
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Risk Factors for Adenoma (HCA)

Rare genetic syndrome
(<5% of all HCA)

<table>
<thead>
<tr>
<th>Predisposing genetic alterations</th>
<th>Related disease</th>
<th>Molecular classification</th>
<th>Specific of molecular subgroups</th>
<th>Common to all subgroups</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNF1A germline mutation</td>
<td>MODY 3 diabetes</td>
<td>HNF1A inactivation 30%-40%</td>
<td>Germline mutation of CYP1B1</td>
<td>Oral contraception</td>
</tr>
<tr>
<td>GNAS somatic mosaic mutation</td>
<td>McCune Albright Syndrome</td>
<td>Inflammatory 40%-50%</td>
<td>Obesity Alcohol</td>
<td></td>
</tr>
<tr>
<td>Germline G6PC mutation</td>
<td>Glycogenosis type 1a</td>
<td>β-catenin activation 10%-15%</td>
<td>Androgen Male</td>
<td></td>
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Common risk factors
(>95% of all HCA)


Hepatocellular Adenomas (HCA)
Molecular Classification

1. HNF1A Inactivation 30-40%

2. Inflammatory 40-50%
   - Peripheral inflammatory syndrome, fever, inflammatory anemia that regress after tumor resection: “paraneoplastic like syndrome”

3. β-catenin activation 12-19%

4. Unclassified 10%

Hepatocellular Adenomas (HCA) Molecular Classification

1. HNF1A Inactivation 30-40%
2. Inflammatory 40-50%
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- Obesity
- Alcohol Intake
- Increasing number of inflammatory adenomas
- Male 38%
- • Androgen therapy
- • Anabolic intake

Possible regression after stopping Androgen
At risk of malignant transformation

Zucman-Rossi, Hepatology, 2006; Paradis, Hepatology 2007; Bioulac Sage, Hepatology 2007

Factors associated with bleeding

Systematic review of hemorrhage and rupture of hepatocellular adenomas

S.M. van Aalten¹, R.A. de Man², J.N.M. Ijzermans¹ and T. Terkivatan¹
British Journal of Surgery 2012; 99:911-916

- 1176 analyzed patients
- 27% with hemorrhage at diagnosis
- More frequent in large HCA (>5cm)
- No confirmed association with molecular subtype

What is the risk of malignant transformation?

Malignant transformation of hepatocellular adenomas into hepatocellular carcinomas: a systematic review including more than 1600 adenoma cases

Jan H.M.B. Stroot, Robert J.S. Coelen, Mechteld C et al. HPB 2010, 12, 509-522

- 1635 patients, 4.2% of malignant transformation
- Large HCA, almost all > 5cm
Summary

- Most of the focal liver lesion in women are benign
- FNH is more common than adenoma and no treatment needed
- Histological and molecular classification has changed our understanding of HCA
- HCA > 5 cm, male and beta-catenin mutation are risk factors for malignancy
- HCA > 5 cm should be considered for resection
Thank You

“Is life worth living? It all depends on the liver.”
William James, American philosopher (1842)

Hepatic Cyst

- Developmental origin
- Common (10-14% population)
- Female to male ratio 4:1
- Lined by cuboidal epithelium
- Asymptomatic

Imaging of hepatic cysts

- All modalities:
  - Round or ovoid unilocular lesion
  - Well circumscribed with thin/imperceptible wall
  - Non-enhancing after contrast administration

Hepatic cyst

T1  T2  T1 post-Gad
What about Eovist?

- **Hepatobiliary specific agents:** taken up by hepatocytes and excreted (in part) through the biliary tree
- FNH has delayed biliary excretion and will often appear bright on the delayed scan
- Adenomas are typically lower signal on the delayed scan

**FNH versus adenoma**

MRI with Eovist (adenoma)
Hepatocellular Adenomas (HCA)
Markers for Diagnosis

1. HNF1A Inactivation 30-40%
   - Liver Fatty acid Binding Protein (LFABP) negative

2. Inflammatory 40-50%
   - Serum Amyloid Protein (SAA) positive

3. β-catenin activation 12-19%
   - Glutamine synthetase (GS) and β-catenin positive

4. Unclassified 10%


FNH and HCA: classification

Pathological classification
- Focal nodular hyperplasia
- Hepatic pseudotumor
- Solitary hyperplastic nodule
- Benign hepatoma

- Hepatocellular Adenoma
- Liver cell adenoma
- Hepatic adenoma
- Telangiatic FNH

Molecular classification 2002-2014
- Definition of the lesions
- Markers
- Molecular subtypes