# Chapter 10

# Staging

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# Staging

## Introduction

Staging refers to the determination of overall tumor burden.

The purpose of staging is to predict the prognosis and to link the stage with the most appropriate treatment.

Many staging systems exist, none of which is proven superior. In North America, staging systems currently in use include the Radiologic T-staging system (advocated both by UNOS-OPTN and LI-RADS), the BCLC staging system (advocated by the AASLD), and the TNM system (developed and maintained by the American Joint Committee on Cancer [AJCC]).

All HCC staging systems stratify tumor stage according to the size and number of HCC nodules as well as presence of tumor in vein (TIV, synonym: macrovascular invasion). Some systems also assess extra-hepatic disease, either in lymph nodes or metastases. Some systems also incorporate information of the severity of underlying liver disease and performance status.

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## Imaging modalities for liver tumor staging

The liver containing at least one HCC must be staged with an imaging technique that provides complete anatomic coverage of the liver.

MDCT and MRI are the only acceptable imaging techniques for HCC tumor staging. Nevertheless, CT and MRI have limited accuracy for this purpose, as explained below and summarized on the Table on the next page.

- MDCT: While CT is sensitive for detection of primary tumor (sensitivity of 71-87%), the sensitivity for detecting additional observations in multifocal HCC is lower, particularly for lesions < 2 cm.

- MRI with ECA: MR with ECA is highly sensitive for detection of additional lesions > 20 mm (100% sensitivity) and 10-20 mm (84% sensitivity), but has low sensitivity for additional lesions <10 mm (32%).

- MRI with gadoxetate: Addition of MRI with gadoxetate can lead to change in staging in 14-28% of patients, affecting management in 13-19% of patients. Detection of additional HCC on MR with gadoxetate following MDCT results in 28% decrease in rate of HCC recurrence and 35% decrease in overall mortality.

CEUS has a limited role in HCC staging due to its inability to reliably visualize the entire liver. One focused application of CEUS in staging is to detect tumor in vein (sensitivity and specificity up to 100%) in cases that are equivocal on CT or MRI.

# Summary of the evidence for HCC staging

| Modality | Staging system | Staging accuracy | Understaged | Overstaged | Reference |
|---|---|---|---|---|---|
| MDCT | OPTN | 47% | 27% | 25% | Freeman et al., 2006 |
| | Milan Criteria | 92% | 8% | 0% | Valls et al., 2004 |
| | TNM staging | 39% | 35% | 26% | Zacherl et al., 2002 |
| | BCLC | 58% | 38% | 4% | Burrel et al., 2003 |
| | BCLC | 80% | - | - | Choi et al., 2009 |
| MRI with ECA | BCLC | 59% | 31% | 10% | Burrel et al., 2003 |
| | OPTN | 40% | 31% | 29% | Freeman et al., 2006 |
| MRI with gadoxetate | BCLC | 92% | - | - | Choi et al., 2009 |
| | BCLC | 92% | - | - | Wang et al., 2016 |

# Staging Systems

## Staging systems

While there are different staging systems advocated by practice guidelines, it is relatively straightforward to convert from one to another.

Below we discuss their common features and then describe the individual staging systems used in North America.

## Features common to all systems

- Currently, in North America, imaging-based diagnosis of definite HCC is applicable <u>only</u> to nodules ≥ 10 mm. Nodules < 10 mm do not contribute to imaging-based tumor staging.

  *Rationale:*
  Small lesions do not have the same specificity for imaging diagnosis of HCC as larger lesions.

- LR-4 lesions do not count toward HCC staging.

  *Rationale:*
  LR-4 observations are not recognized as HCC by OPTN for transplantation purposes.

## Exceptions:

- Innumerable LR-4 lesions that in aggregate are interpreted as unequivocal multifocal HCC (stage T4a).

- All biopsy-proven HCCs (see below) count toward intrahepatic HCC burden regardless of lesion size or LI-RADS category.

- HCC with tumor in vein (TIV) is categorized as LR-TIV in LI-RADS and also known as macrovascular invasion or portal or hepatic vein in other systems.

## Caveat:

- Lesions that are thought to represent diffuse HCC but do not meet criteria for LR-5 or LR-TIV are categorized LR-M and reported as "LR-M, probably represents HCC". Radiologists should encourage multi-disciplinary discussion for consideration of biopsy or other diagnostic workup.

## Path-proven lesions

If a nodule is biopsied, and found to be malignant, the biopsy result supersedes the LI-RADS category. See *Chapter 14, page 25*.

Path-proven HCC contributes to HCC staging. Path-proven non-HCC malignancy (iCCA, cHCC-CCA, etc.) may be staged as non-HCC, but do not contribute to HCC staging.

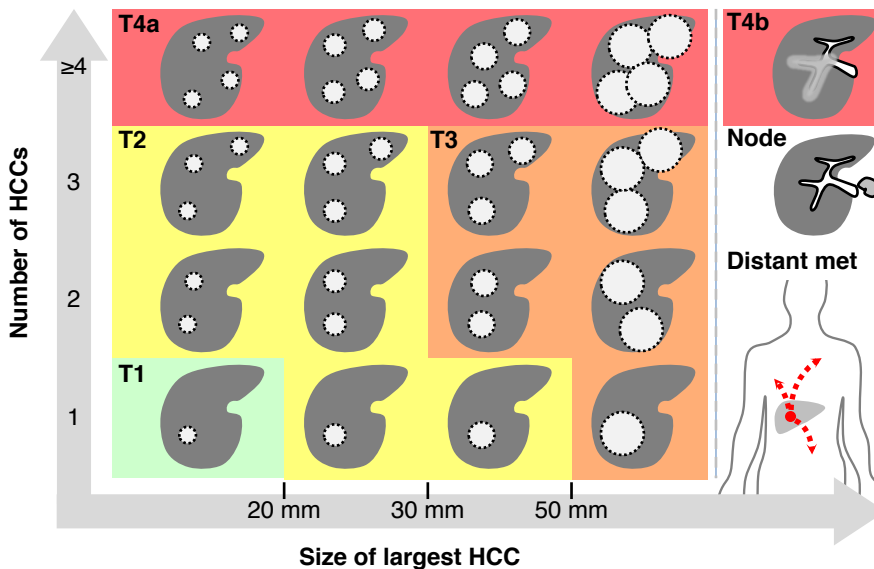# Radiologic T-staging System

## Radiologic T-staging System

The Radiologic T-staging system used by LI-RADS and UNOS-OPTN was developed by the American Liver Tumor Study Group. It identifies 4 stages. The tumor stage is based on tumor size, number, and macrovascular invasion.

Extra-hepatic disease (either lymph node or metastases) does not affect the T stage.

*Radiologic T-staging system for HCC*

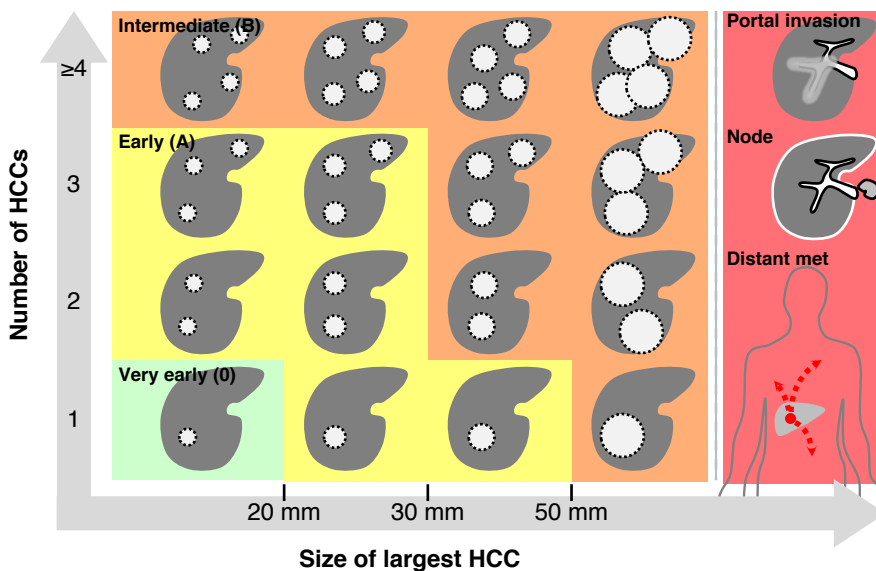| Stage | Definition |
|-------|------------|
| 0 | No HCC |
| 1 | One HCC < 20 mm |
| 2 | One HCC ≥ 20 mm and ≤ 50 mm, OR two or three HCCs, all ≤ 30 mm |
| 3 | One HCC > 50 mm, OR two or three HCCs, at least one > 30 mm |
| 4 | 4A. Four or more HCCs, regardless of size<br>4B. HCC + TIV |
| Comment specific to radiologic T-staging system: Widespread or multifocal HCC is either staged 4a in the absence of tumor in vein or 4b in presence of tumor in vein. | |

# BCLC Staging System

## BCLC Staging System

The Barcelona Clinic Liver Cancer (BCLC) staging system used by AASLD identifies 4 stages, which include imaging-based tumor size, number, macro-vascular invasion, and nodal and extra-hepatic metastases, as well as clinical criteria (according to Child-Pugh score and performance status).

*BCLC staging system combines imaging criteria and clinical criteria*

| Stage | Imaging criteria | Clinical criteria |
|---|---|---|
| Very early (0) | One HCC between 1-2 cm | -Child-Pugh A<br>-Performance status 0 |
| Early (A) | One HCC between 2 and 5 cm OR<br>Two or three HCCs between 1-3 cm | -Child-Pugh A-B<br>-Performance status 0 |
| Intermediate (B) | One HCC > 5 cm OR<br>Two or three HCCs > 3 cm OR<br>Four or or more HCCs of any size without tumor in vein | -Child-Pugh A-B<br>-Performance status 0 |
| Advanced (C) | Tumor in vein regardless of size or number of HCCs OR<br>Nodal metastases OR<br>Extra-hepatic metastases | -Child-Pugh A-B<br>-Performance status 1-2 |
| End stage (D) | Stage not dependent on imaging criteria | -Child-Pugh C<br>-Performance status 3-4 |

The BCLC staging system combines imaging criteria and clinical criteria.

# LI-RADS and OPTN Staging

**Use of LI-RADS categories for OPTN staging**

Only LR-5, LR-TIV, and path-proven HCCs (and TR-viable) contribute to OPTN staging.

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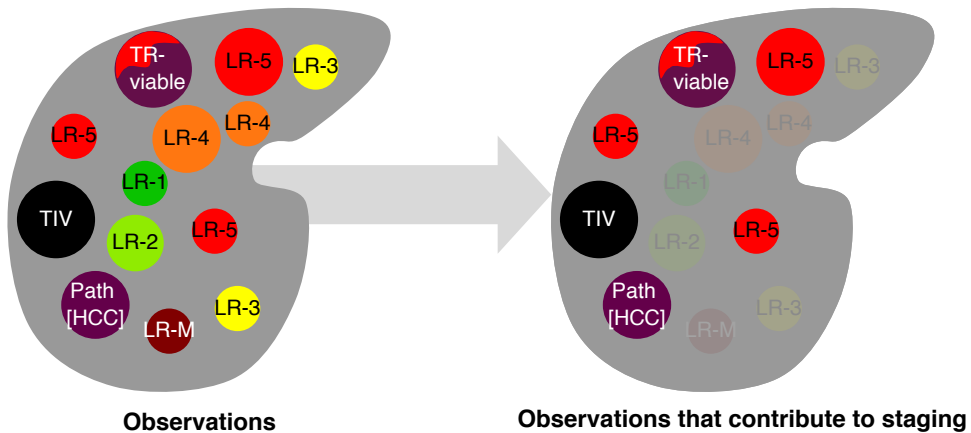All LR-5 and LR-TIV observations contribute to OPTN staging <u>except</u>:

- 10-19 mm observation with APHE, nonperipheral WO, no TG and no enhancing "capsule". These are categorized LR-5, but do not contribute to OPTN staging

- LR-TIV contiguous with a targetoid parenchymal mass. This may represent a non-HCC malignancy with macrovascular invasion. If biopsied and proven pathologically to be HCC, it then contributes to OPTN staging (Stage T4b or OPTN Class X).

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LR ≤ 4 observations (untreated or treated) do not contribute to staging.

- If they are biopsied and proven pathologically to be HCC, they then contribute to staging.

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LR-M does not contribute to staging although most LR-M observations should be biopsied.

- If they are biopsied and proven pathologically to be HCC, they then contribute to staging.

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**Observations**

**Observations that contribute to staging**

\* Note that 10-19 mm observation with APHE, nonperipheral WO, no TG and no enhancing "capsule" are categorized LR-5, but do not contribute to staging

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