Updated Clinical and Dosimetric Recommendations for Yttrium-90 Glass Microspheres in Hepatocellular Carcinoma (HCC)

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Purpose

- The TheraSphere Global Clinical and Dosimetry Steering Committee(DSC) reconvened to update the clinical and dosimetric recommendations for the treatment of unresectable HCC with Y-90 glass microspheres.
- Recommendations for treatment standardization under various clinical presentations are presented; considering treatment planning and delivery, patient selection, dosing and follow-up

Rationale

- Numerous new studies published on optimal treatment of HCC with Y-90 glass treatment since 2019 (>30 publications)
- Information from new trials on Y-90 treatment (DOSISPHERE, LEGACY & TARGET)
- Improved understanding of dosing: maximal normal liver tissue absorbed dose and threshold tumor absorbed dose
- In order to reflect updated BCLC algorithm

Key Definitions

- Single Compartment: A MIRD dosimetry model that assumes the ^{90}Y microspheres (and therefore absorbed dose) are distributed uniformly within the VOI.
- Multi Compartment: A MIRD-based dosimetry approach where absorbed dose (AD) is determined in more than one VOI, such as the tumor VOI and the normal parenchyma VOI.
- MCTB: Multidisciplinary tumor board

Materials and Methods

- The TheraSphere Global DSC is comprised of health care providers across multiple disciplines
  - Hepatology
  - Interventional Radiology
  - Medical Oncology
  - Medical Physics
  - Nuclear Medicine
  - Radiation Oncology

Literature published between January 2019 and September 2021 was reviewed, discussed and adjudicated by the Delphi method.

Recommendations included in this updated document incorporate both the results of the literature review and the expert opinion and experience of members of the committee.

The committee also considered whether new data warranted changing the Degree of Recommendation and/or the Strength of Consensus from the previous recommendations (Tables 1 and 2). Briefly, per the Delphi method, consensus was defined during virtual meetings as outlined in Table 2

Table 1. Degree of Recommendation

Degree	Meaning
A	Strongly recommended (good evidence)
B	Recommended (moderate evidence)
C	No recommendation for or against
D	Recommendation against
E	Insufficient, low quality or contradictory evidence

Table 2. Strength of Consensus

Strength of Consensus	Definition
Strong	≥ 80% consensus
Moderate	50-70% consensus
Weak	≤ 49% consensus

Results

- Committee discussion and consensus led to the expansion of recommendations from four to five common clinical scenarios in patients with HCC to support more individualized treatment with Y-90 glass microspheres.
- Existing clinical scenarios were updated to reflect recent developments in dosimetry approaches and broader treatment paradigms evolving for patients presenting with HCC.
- Scenarios were divided into
  - Curative Intent
  - Palliative Intent
- Recommended treatment days first week Wednesday to second week Tuesday
- Future directions: Several areas requiring additional investigations were highlighted

Curative Intent

Radiation Segmentectomy:

- Bridge to transplant or definitive treatment, i.e., ablative radioembolization
- Child-Pugh A and select B7
- Segmental or subsegmental (angiosome)
- CBCT defined perfused volume
- Target absorbed dose ≥400 Gy, higher absorbed dose increased CPN rate
- Strength of recommendation A; Degree of consensus strong

Radiation Lobectomy/Modified Radiation Lobectomy:

- Bridge to resection, contralateral lobe hypertrophy in cases of small FLR, biologic test of time, tumor retraction from hepatic vein and/or IVC or definitive treatment
- Child-Pugh A, unilobar treatment
- CBCT defined tumor/normal tissue
- Dosimetry: lobar 140-150 Gy, segmental tumor ≥400 Gy + lobar 100 Gy or tumor ≥205 Gy with normal tissue >88 Gy
- Strength of recommendation B; Degree of consensus strong

Palliative Intent

Multifocal unilobar without MVI/PVT:

- Child-Pugh A, MDTB for B7
- Delay progression prior to initiation of systemic Tx
- Conversion to resection
- Multicompartment dosimetry preferred: tumor dose ≥205 Gy (>250 Gy if possible), normal tissue dose ≤120 Gy with ≥30% hepatic reserve
- Strength of recommendation B; Degree of consensus strong

Multifocal bilobar without MVI/PVT:

- Child-Pugh A, ≥30% hepatic reserve is ideal
- Preservation of liver function
- Staged sequential lobar treatment preferred
- Multicompartment dosimetry preferred: tumor dose ≥205 Gy (>250 Gy if possible), normal tissue dose 40-70 Gy
- Strength of recommendation B; Degree of consensus Strong

HCC with MVI/PVT:

- Child-Pugh A, ≥30% hepatic reserve is ideal
- Unilobar: combine/bridge to systemic Tx; bilobar consider systemic upfront
- Conversion to resection
- Multicompartment dosimetry preferred: tumor dose ≥205 Gy (>250 Gy if possible), normal tissue dose ≤120 Gy
- Strength of recommendation A; Degree of consensus Strong

Conclusions

- Updated consensus recommendations are provided to guide clinical and dosimetric approaches for the use of Y-90 glass microsphere TARE in HCC, accounting for disease presentation, tumor biology, and treatment intent.

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