Targeting the Core: Yttrium-90 Radioembolization in Hepatocellular Carcinoma

Joseph McBride, MD

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SYMPOSIUM

Disclosures

- Consultant, Integer Corporation

Background

- HCC Epidemiology
  - Global incidence: 6th most common cancer
  - 4th leading cause of cancer-related death
  - Major risk factors: Hepatitis B, Hepatitis C, alcohol abuse, NAFLD
- Current HCC Treatment Landscape
  - Early stage: Resection, transplantation, ablation
  - Intermediate stage: TACE (Chemoembolization), Y90 (Radioembolization)
  - Advanced stage: Systemic therapy (e.g., sorafenib, immunotherapy)

Yttrium-90 Radioembolization: Mechanism of Action

- What is Y90?
  - Beta-emitting radioisotope
  - Half-life: 64.1 hours
  - Tissue penetration: 2.5 mm average, 11 mm maximum
- How Y90 Works
  - Delivery via hepatic arterial circulation
  - Preferential uptake by tumor vasculature
  - Local high-dose radiation with minimal systemic effects

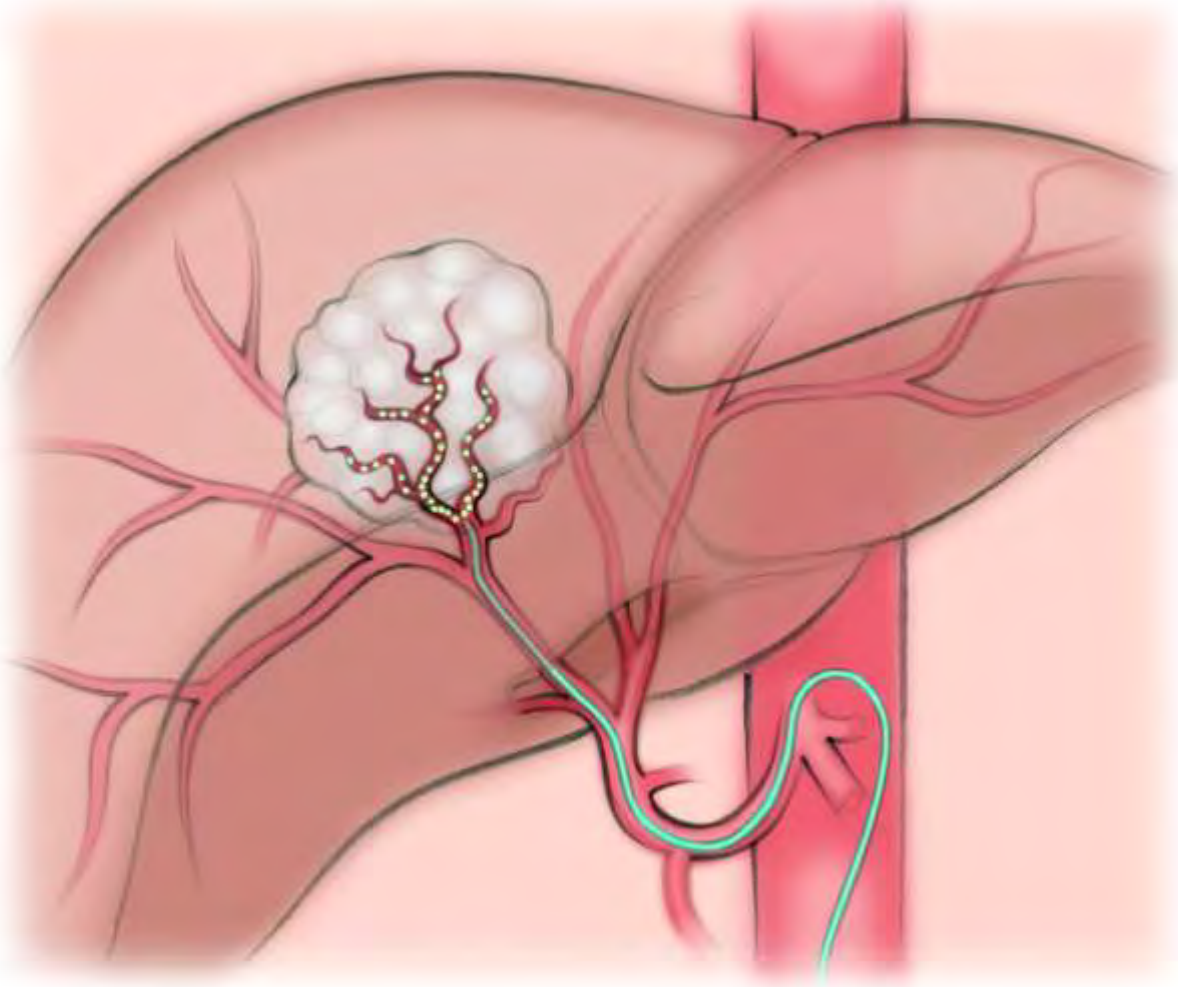
Patient Selection and Preprocedural Evaluation

- Ideal Candidates for Y90
  - Unresectable HCC
  - Good liver function (Child-Pugh A or B7)
  - ECOG performance status 0-2
  - No extrahepatic disease
- Contraindications
  - Excessive tumor burden with limited healthy liver
  - Severe liver dysfunction
  - Significant extrahepatic disease
  - Untreatable arteriovenous shunting

Procedure Overview

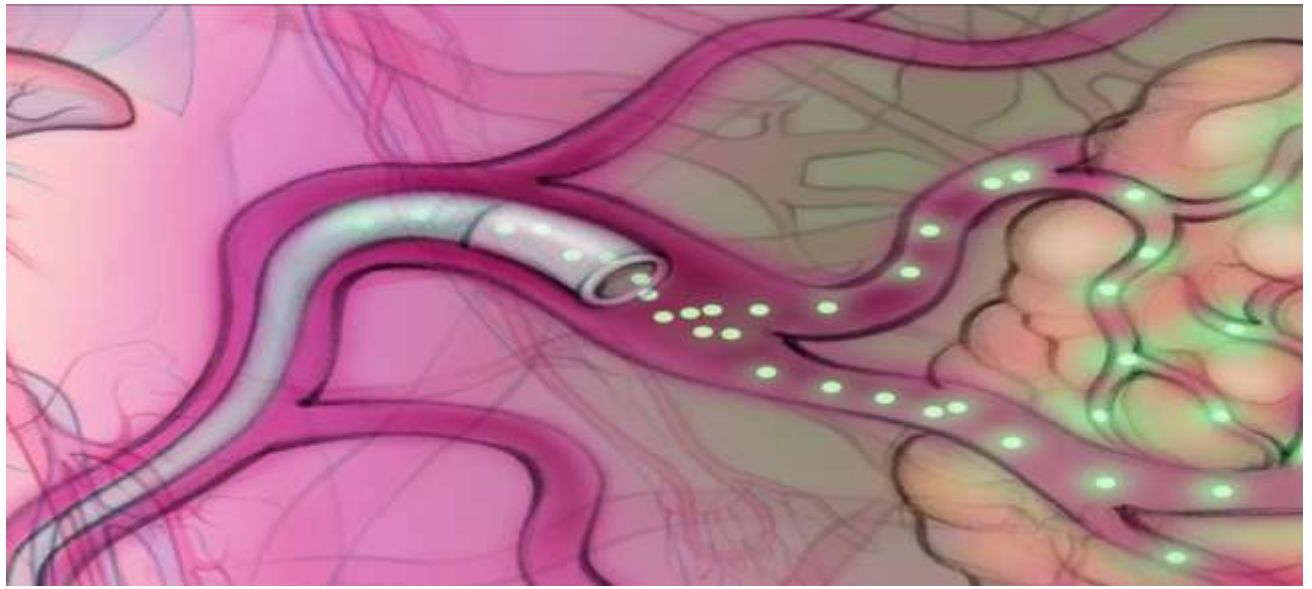
Y90 Radioembolization Procedure - Two-Step Process

- Mapping Angiogram (Rehearsal)
  - Detailed angiographic evaluation of hepatic arterial anatomy
  - Identification and coil embolization of extrahepatic vessels if needed
  - Administration of Tc-99m macroaggregated albumin (MAA) to simulate Y90 distribution
  - SPECT/CT imaging to assess lung shunt fraction and extrahepatic deposition
  - Generally, lung shunt less than 15-20% don't require dose adjusting, but each is patient specific depending on treatment area/tumor size
  - Max lung dose: 30 Gy/treatment, 50 Gy lifetime



Procedure Overview

- Treatment Angiogram
  - Usually performed 1-2 weeks after mapping
  - Selective catheterization of target hepatic arteries
  - Administration of Y90 microspheres
  - Post-procedure Bremsstrahlung SPECT/CT or PET/CT to confirm microsphere distribution (optional)



Y90 Microspheres and Special Considerations

- Types of Y90 Microspheres
  - Glass Microspheres (TheraSphere)
    - Produced by Boston Scientific
    - Higher specific activity **(2500 Bq/sphere)**
    - Smaller number of particles per treatment
  - Resin Microspheres (SIR-Spheres)
    - Produced by Sirtex Medical
    - Lower specific activity **(50 Bq/sphere)**
    - Larger number of particles per treatment

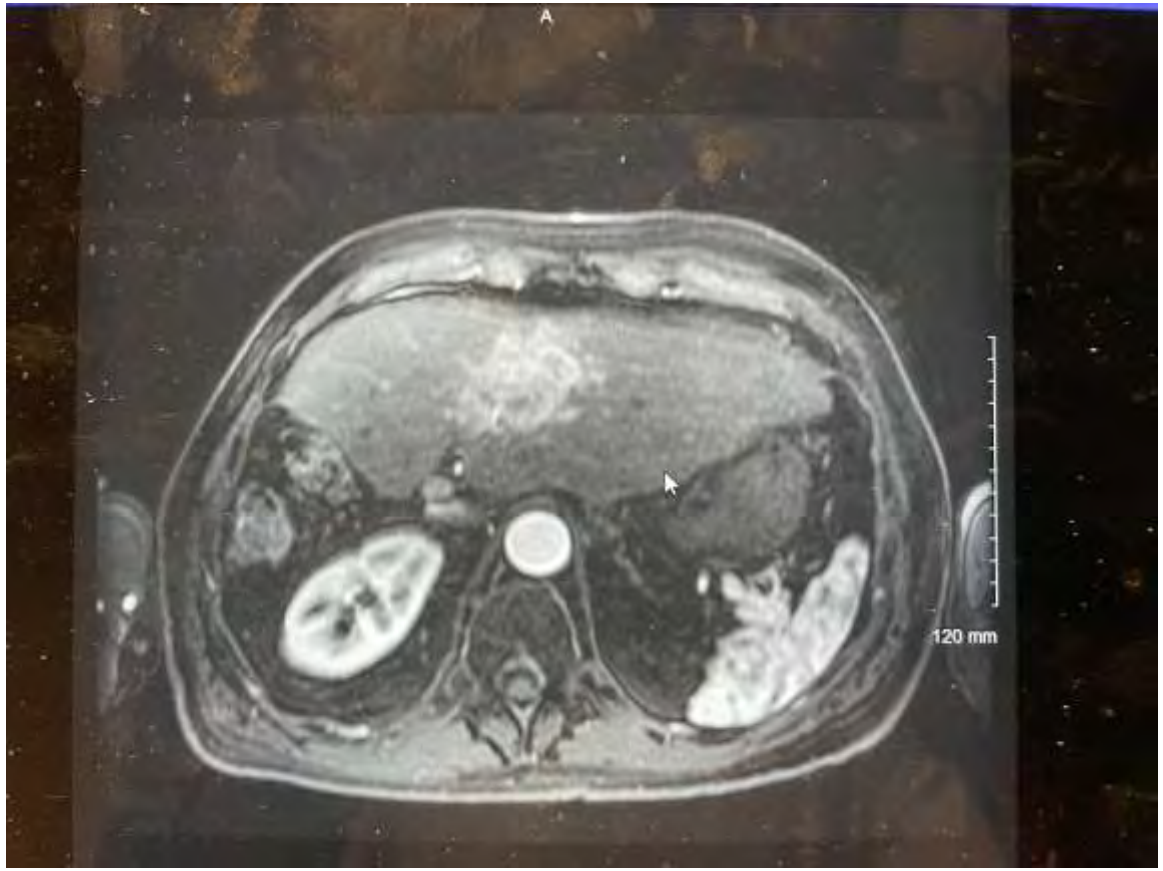
TheraSphere in Portal Vein Thrombosis (PVT)

- TheraSphere can be used in cases with portal vein thrombosis
- Reasons:
  - Lower embolic effect due to fewer particles
  - Higher specific activity allows for delivery of therapeutic dose with less volume
- SIR-Spheres generally contraindicated in PVT due to higher embolic load
- PVT patients treated with TheraSphere show:
  - Median survival of 10-13 months in various studies
  - Potential for downstaging to transplantation in select cases

Dosimetry Approaches

- Standard Dosimetry
  - Based on empirical or semi-empirical methods
  - Often uses body surface area (BSA) method or standard absorbed dose to the treated liver volume
  - Example: 120 Gy to the treated liver volume for glass microspheres
- Personalized Dosimetry
  - Tailored to individual patient and tumor characteristics
  - Uses 3D imaging and sophisticated dose calculation algorithms
  - Aims to deliver optimal dose to tumor while sparing healthy liver tissue
  - Methods may include: Partition model, Voxel-based dosimetry, Monte Carlo simulations

62 y.o. patient with metastic colorectal cancer



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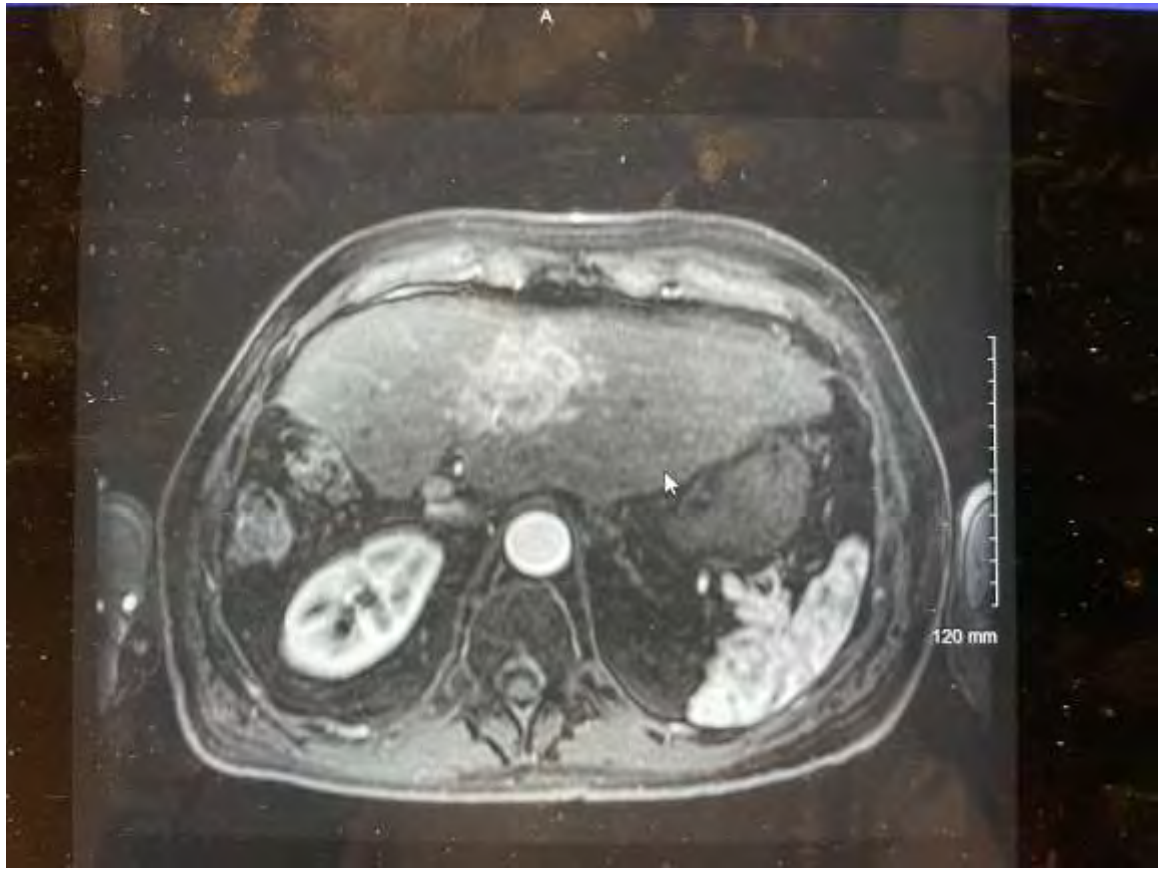
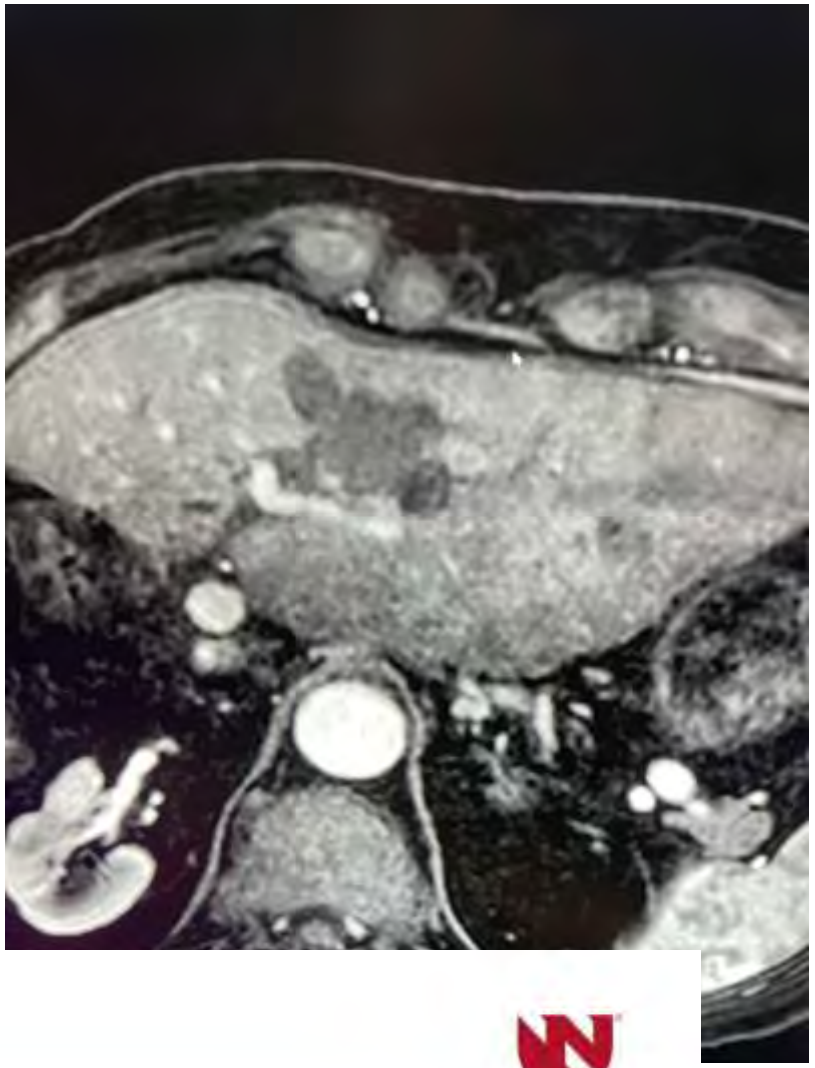
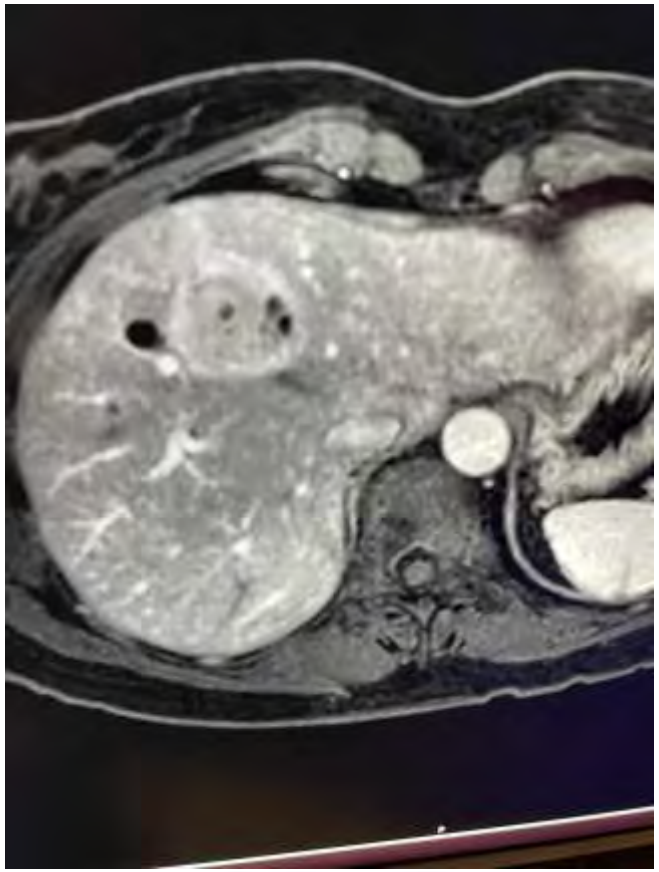
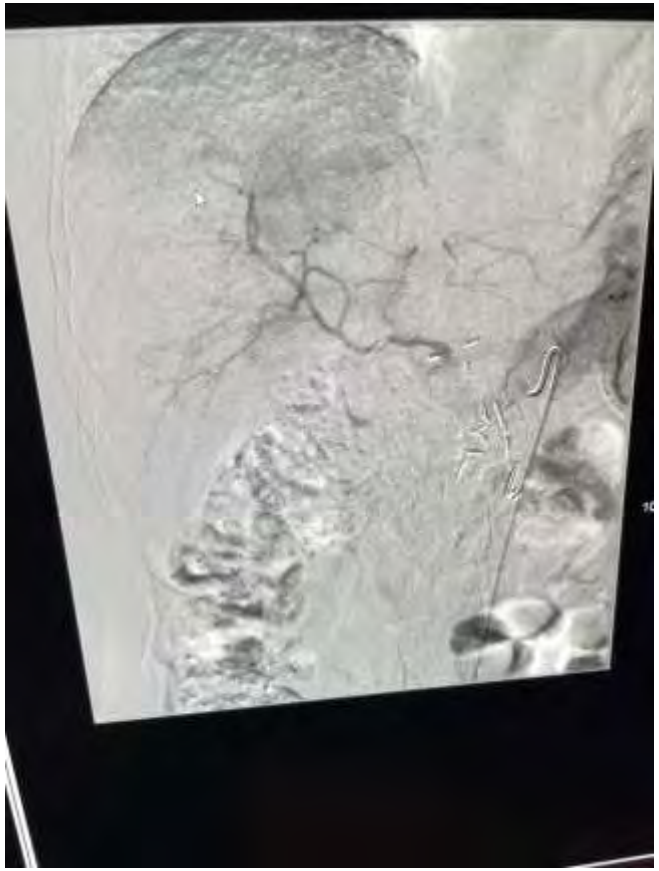




68 y.o patient with neuroendocrine tumor metastatic to liver





Clinical Evidence: DOSISPHERE-01 Trial (Garin et al., 2021)

- Design: Multicenter, open-label, randomized phase 2 trial
- Participants: 56 patients with locally advanced or inoperable HCC
- Comparison: Personalized dosimetry vs. Standard dosimetry for Y90 glass microspheres
- Dosimetry Approaches:
  - Standard arm: 120 ± 20 Gy to the treated liver volume
  - Personalized arm: At least 205 Gy to the index lesion
- Primary Outcome: Tumor response rate at 3 months
- Results:
  - Tumor response rate: Personalized 71% vs. Standard 36% (p=0.0074)
  - Median OS: Personalized 26.6 months vs. Standard 10.7 months (p=0.0096)
- Conclusion: Personalized dosimetry significantly improved outcomes compared to standard dosimetry

Y90 Evidence – Recent Studies

- LEGACY Study (Salem et al., 2021)
  - Design: Retrospective, single-arm, multicenter study
  - Participants: 162 patients with early and advanced HCC
  - Intervention: Y90 glass microspheres (TheraSphere)
  - Key Results:
    - Objective response rate: 88%
    - Median overall survival: 6.5 years
    - 3-year overall survival: 86.6%
    - Transplant/resection rate: 31%
  - Conclusion: Y90 showed high response rates and promising survival outcomes in early and advanced HCC

Recent Studies on Y90 Efficacy

- PREMIERE Study (Salem et al., 2016, with long-term follow-up)
  - Design: Randomized, prospective study
  - Participants: 45 patients with early-stage HCC
  - Comparison: Y90 vs. conventional transarterial chemoembolization (cTACE)
  - Key Results:
    - Median time to progression: Y90 >26 months vs. cTACE 6.8 months (p=0.0012)
    - Median overall survival: Y90 not reached vs. cTACE 18.5 months at the time of censoring
  - Conclusion: Y90 demonstrated superior time to progression compared to cTACE in early-stage HCC

Y90 in the HCC Treatment Algorithm

- Y90 in Multidisciplinary Management
  - Bridge to transplantation
  - Downstaging
  - Alternative to TACE in intermediate-stage HCC
  - Potential first-line therapy in selected patients
  - Combination with systemic therapies in advanced HCC

Y90 Future Directions

- Ongoing Research
  - Combination with immunotherapy
  - Further refinement of personalized dosimetry
  - Novel microsphere technologies
  - Expanding indications (e.g., early-stage HCC, metastatic liver disease)

Conclusion

- Take-Home Messages
  - Y90 is an effective locoregional therapy for HCC across various stages
  - Comparable survival outcomes to standard therapies with better quality of life and safety profile
  - Personalized dosimetry shows promise in improving outcomes
  - Potential for combination strategies with systemic therapies
  - Ongoing research may further expand indications and improve results