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Y90 Radiation Segmentectomy versus Microwave Ablation for Hepatocellular Carcinoma in Locations Suboptimal for Percutaneous Ablation

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Abstract

Purpose The purpose of our study was to evaluate outcomes following percutaneous microwave ablation (MWA) versus yttrium-90 (Y90) radiation segmentectomy (RS) for tumors in suboptimal locations for ablation.

Materials and Methods Retrospective review (January 2014–July 2019) was performed on patients who underwent Y90-RS or MWA (with or without prior transarterial chemoembolization [TACE]) with curative intent for early-stage hepatocellular carcinoma (HCC) lesions in suboptimal locations for percutaneous ablation, defined as locations in which needle placement is within 5 mm of critical structures (liver dome, liver capsule, gallbladder, and hilum). The primary endpoints were treatment response as per the modified Response Evaluation Criteria in Solid Tumors criteria and complications.

Statistical Analysis Fischer's exact test was performed for categorical variables, and Student's *t*-tests for nominal variables.

Results Twenty-three lesions in 20 patients (13 male, 67 ± 8.8 years) and 30 lesions in 30 patients (18 male, 62.5 ± 10.6 years) were treated with Y90-RS and MWA (19 with prior TACE), respectively. There were no differences in demographics ($p > 0.05$). Mean tumor diameter was 2.9 ± 1.0 in those treated with Y90-RS and 2.3 ± 0.9 for MWA ($p < 0.05$). Lesions were located adjacent to the following structures: dome ($n = 22$), capsule ($n = 16$), hilum ($n = 9$), and gallbladder ($n = 6$). All patients were Eastern Cooperative Oncology Group performance status 0 to 1. Of the MWA cohort, 19 were Child-Pugh class A, 5 were B, and 6 were C and the mean pretreatment laboratory values were as follows: Model for End-stage Liver Disease sodium (MELD-Na) 12.7 ± 4.6, alpha-fetoprotein (AFP) 848 ± 3168.0, aspartate aminotransferase (AST) 71.9 ± 49.1,

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alanine aminotransferase (ALT) 48.0 ± 32.4, and total bilirubin 2.4 ± 2.7. Of the Y90-RS cohort, 15 were Child-Pugh class A, 4 were B, and 1 was C and pretreatment laboratory values were as follows: MELD-Na 10.5 ± 3.3 (Y90-RS), AFP 762.2 ± 1793.8 (Y90), AST 50.3 ± 30.5 (Y90), ALT 30.1 ± 16.9 (Y90), and total bilirubin 1.6 ± 1.1 (Y90). Complete response rate following Y90 was 96 versus 76% for MWA, with no disease progression after Y90-RS within the follow-up period. Three (13%) lesions demonstrated progression of disease (time to progression 6.3 months) after MWA. No grade > 2 toxicities or procedure-related complications were noted following Y90-RS. There were 7 major (arterioportal fistula with hemoperitoneum, pneumothorax, liver infarction, and capsular burn) and 3 minor complications following MWA.

Conclusion Y90-RS is a valuable alternative to percutaneous MWA as a first-line therapy for early-stage HCC for tumors in suboptimal locations for ablation, offering a favorable treatment response and safety profile.

Introduction

Hepatocellular carcinoma (HCC) is the most common hepatic malignancy, accounting for approximately 75% of liver cancers globally, with poor prognosis.[1–3] Surgical resection and transplant remain the gold standard for HCC given the high curative potential; for unresectable HCC, locoregional therapies (ablation, transarterial chemoembolization [TACE], radioembolization) can be performed for curative intent, palliation, or bridge to transplant.[2,4] Specifically, for patients with Barcelona Classification of Liver Cancer (BCLC) 0 or A, surgical resection or percutaneous ablation are preferred, depending on transplant candidacy and lesion size.[2] Percutaneous ablation offers comparable overall survival to resection for lesions ≤ 3 cm while minimizing invasiveness and cost, with microwave ablation (MWA) favored over radiofrequency ablation (RFA) for lesions ≤ 4 cm given its ability to achieve better tumor necrosis.[2,5,6]

Although measures to reduce the risk of off-target ablation and injury have been described, patients with unresectable HCC may be poor candidates for ablation if lesions are in difficult locations to execute a percutaneous approach (e.g., caudate lobe or adjacent to major vessels, the hilum, hepatic dome, biliary structures, heart, or bowel).[4,7–12]

The 2022 BCLC guidelines names transarterial radioembolization with yttrium-90 (Y90) as an effective alternative to TACE and ablation in early- and intermediate-stage HCC.[2,13–15] Furthermore, recent studies indicate Y90 radiation segmentectomy (Y90-RS) may have comparable outcomes to MWA for early-stage HCC.[6,7,16] Herein, we compare the safety and efficacy of Y90-RS and MWA when performed with curative intent for HCC lesions in locations otherwise suboptimal for MWA.

Materials and Methods

Patient Selection and Inclusion Criteria

Institutional Board Review approval was obtained for this single-center retrospective study of patients who underwent Y90-RS or MWA (±prior TACE) for HCC with curative intent between January 2014 and July 2019. Treatment decisions for HCC patients at our institution were made with multidisciplinary consensus at a weekly tumor board involving interventional radiology, hepatology, oncology, and transplant surgery. Patients in both groups had lesions in suboptimal locations for percutaneous ablation, defined as lesions within 5 mm of the liver dome, capsule, hilum, or gallbladder; locations where needle placement or achieving sufficient margins may be difficult.[17,18] Those with lesions > 3 cm, vascular invasion of the tumor, extrahepatic metastases, portal venous thrombosis, prior resection, or orthotopic liver transplant were excluded. Y90 radioembolization was performed by two interventional radiologists with institutional authorized user status. All other procedures were conducted by one of five interventional radiologists with 1 to 15 years of experience. Y90-RS dosimetry and treatment protocol using glass microspheres TheraSphere (Boston Scientific Corp., Marlborough, Massachusetts, United States) have been previously detailed.[9,16,19,20] Dose was calculated using the Medical Internal Radiation Dosimetry dosing model for perused volume. Whole lobar volume was used for dose calculation with a target of 120 Gy and subsequently delivered selectively into the segment.[9] Dose to perfused volume was sufficiently higher (> 400 Gy). MWA probes (MicroThermX Varian Medical Systems, Austin, Texas, United States) were placed percutaneously under computed tomography (CT) guidance (±ultrasound [US]) to obtain a 5- to 10-mm circumferential margin. Examples for treatment and follow-up imaging are provided for Y90-RS (►**Fig. 1**) and MWA (►**Fig. 2**).

Neither temperature monitoring nor hydrodissection were performed prior to MWA. The tract was coagulated while removing the thermal probe, followed by CT to rule out complications.

Treatment Response and Toxicity Assessment

Follow-up visits and imaging were performed 6 weeks post-procedure and at 3-month intervals thereafter. Tumor response and progression was assessed by independent

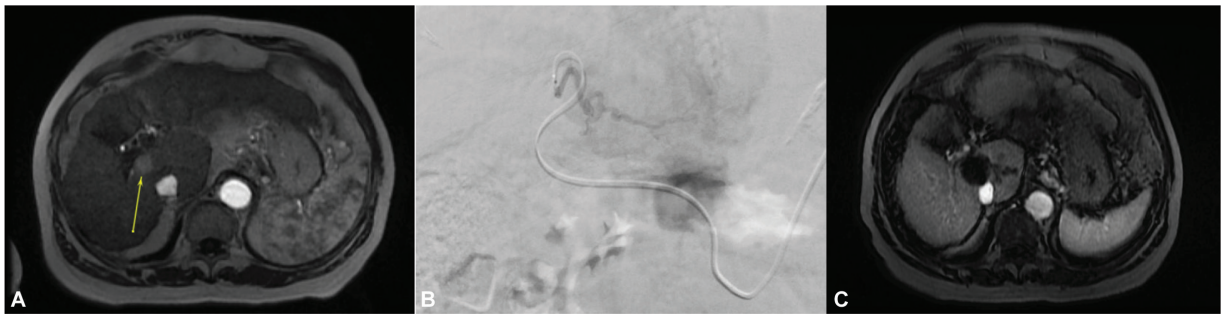

Fig. 1 Example case of yttrium-90 (Y90)-radiation segmentectomy (RS). (**A**) Axial postcontrast T1-weighted image demonstrates a rounded, 1.8-cm arterial phase enhancing lesion in segment 5/1 with washout (LR-5). (**B**) Transradial angiogram demonstrates an enhancing mass in segment 5/1. (**C**) Post-Y90-RS contrast-enhanced axial computed tomography (CT) demonstrating the treatment zone of 2.9 cm diameter with no viable tumor.

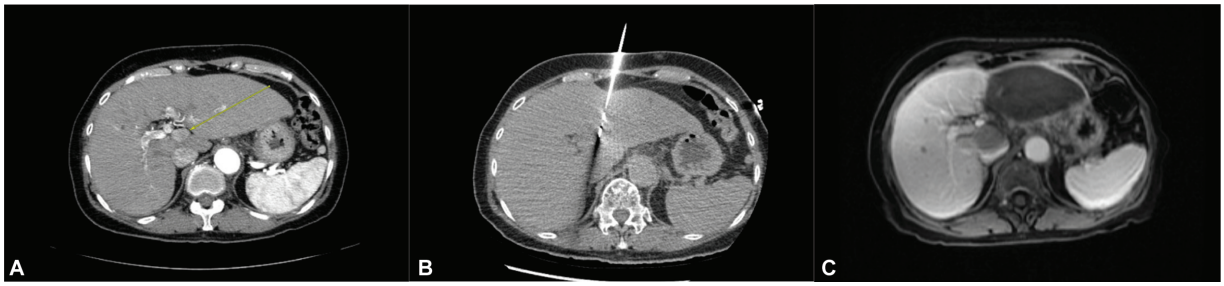

Fig. 2 Example case of microwave ablation (MWA). (**A**) Pretreatment axial contrast-enhanced computed tomography (CT) demonstrates Liver Imaging Reporting and Data System (LI-RADS) 5 lesion measuring 1.7 × 1.5 in segment 1 close to the hilum of the liver. (**B**) Intraprocedural image of MWA probe placement in segment 1 lesion. (**C**) Follow-up axial contrast-enhanced T1 magnetic resonance imaging (MRI) demonstrating necrosis of the tumor and infarction of the left lobe of the liver.

subspecialty trained abdominal radiologists with > 10 years of experience on 3-month follow-up imaging per the modified Response Evaluation Criteria in Solid Tumors algorithm.[21] Time to progression (TTP) was recorded for all patients during the study period. Liver function tests and treatment complications were assessed at 1-month postprocedure. Complications were characterized per the Common Terminology Criteria for Adverse Events (CTCAE).[22] The threshold for minor laboratory events was ≤ grade 3.

Statistical Analysis

Fischer's exact test was performed for categorical variables, and Student's *t*-tests for nominal variables. The threshold of significance was $p < 0.05$. All statistical analyses were conducted using SPSS version 25 (IBM, Armonk, New York, United States).

Results

Patient Demographics and Characteristics

Fifty patients with 53 lesions were included; 23 lesions in 20 patients received Y90-RS and 30 lesions in 30 patients received MWA. Baseline demographics and disease characteristics are displayed in ►**Table 1**. There were no significant differences in demographics between groups ($p > 0.05$). All patients were Eastern Cooperative Oncology Group performance status 0 to 1. Of the MWA cohort, 19 were Child-Pugh class A, 5 were B, and 6 were C and the mean pretreatment laboratory values were as follows: Model for End-stage Liver Disease sodium (MELD-Na) 12.7 ± 4.6, alpha-fetoprotein (AFP) 848 ± 3168.0, aspartate aminotransferase (AST) 71.9 ± 49.1, alanine aminotransferase (ALT) 48.0 ± 32.4, and total bilirubin 2.4 ± 2.7. Of the Y90-RS cohort, 15 were Child-Pugh class A, 4 were B, and 1 was C and pretreatment laboratory values were as follows: MELD-Na 10.5 ± 3.3 (Y90-RS), AFP 762.2 ± 1793.8 (Y90), AST 50.3 ± 30.5 (Y90), ALT 30.1 ± 16.9 (Y90), and total bilirubin 1.6 ± 1.1 (Y90). The MWA group had significantly higher pretreatment transaminases ($p < 0.05$) and the Y90-RS group had significantly larger tumor diameter; mean tumor diameter was 2.9 ± 1.0 in those treated with Y90-RS and 2.3 ± 0.9 for MWA ($p < 0.05$). Lesions were located adjacent to the following structures: dome ($n = 22$), capsule ($n = 16$), hilum ($n = 9$), and gallbladder ($n = 6$). There was no difference in the distribution of lesions (►**Table 1**, $p > 0.05$). Nineteen (63%) MWA patients were treated in combination with prior conventional TACE.

Posttreatment Outcomes

Posttreatment outcomes are displayed in ►**Table 2**. The mean follow-up was 17.6 months following Y90-RS, and 14.7 months following MWA ($p = 0.65$). At 3-month follow-up, 22/23 (96%) of Y90-RS treated lesions achieved complete response (CR) versus 23/30 (77%) of MWA treated lesions ($p = 0.05$). One (4%) Y90-RS patient demonstrated stable disease and 7 (23%) MWA patients demonstrated partial response. During the study period, disease progression occurred in 4 (17%) patients treated with Y90-RS versus 7 (23%)

Table 1 Patient demographics and clinical status before treatment initiation

Characteristic	All ($n = 50$)	MWA ($n = 30$), TACE/MWA ($n = 19$), MWA alone ($n = 11$)	Y90 ($n = 20$)	*p*-Value
Demographics				
Sex				
Male	31 (62)	18 (63)	13 (65)	0.13
Female	19 (38)	12 (27)	7 (35)	
Age				
Mean	64.5	62.5	67.4	0.1
Range	27–86	27–80	53–86	
Disease (at treatment)				
Child-Pugh				
A	34 (68)	19 (63)	15 (76)	0.33
B	9 (18)	5 (17)	4 (19)	
C	7 (14)	6 (20)	1 (5)	
MELD-Na score				
Mean (SD	11.8 (4.2)	12.7 (4.6)	10.5 (3.3)	0.09
Range	6.0–21.0	6.0–21.0	6.0–17.0	
Serum AFP				
Mean (SD)	807.8 (2864.0)	848.8 (3618.0)	762.2 (1793.8)	0.93
Range	1.4–16217.0	1.4–16217.0	3.0–6175.5	
AST				
Mean (SD)	64.2 (43.1)	71.9 (49.1)	50.3 (30.5)	0.03
Range	16.0–202.0	18.0–202.0	16.0–131.0	
ALT				
Mean (SD)	40.8 (28.3)	48.0 (32.4)	30.1 (16.9)	0.04
Range	7.4–157.0	16.0–157.0	7.4–62.0	
Total bilirubin				
Mean (SD)	2.0 (2.2)	2.4 (2.7)	1.6 (1.1)	0.25
Range	0.2–13.0	0.3–13.0	0.2–4.8	
Lesions, *n*	53	30	23	
Location, *n*				
Capsule	16 (30)	11 (37)	5 (22)	0.23
Dome	22 (42)	10 (33)	12 (52)	
Hilum	9 (17)	4 (13)	5 (22)	
Gallbladder	6 (11)	5 (17)	1 (4)	
Tumor diameter, cm				
Mean (SD)	2.6 (0.9)	2.3 (0.9)	2.9 (1.0)	0.01
Range	1.0–5.0	1.0–4.5	1.2–5.0	

Abbreviations: AFT, α-fetoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MELD-Na, Model for End-stage Liver Disease-sodium; MWA, microwave ablation; SD, standard deviation; TACE, transarterial chemoembolization; Y90, yttrium-90.
Note: Parenthetical values are percentages unless otherwise indicated.

treated with MWA ($p > 0.05$). TTP was 23.5 months following Y90-RS and 6.7 months following MWA ($p < 0.0001$).

No treatment-related adverse events occurred following Y90-RS during the follow-up period whereas 10 (33%) occurred following MWA, including 3 minor complications (wound infection, abdominal pain, and nausea) and 7 major complications including arterioportal fistula ($n = 1$), pneumothorax ($n = 1$), liver infarction ($n = 2$), capsular burn ($n = 1$), rectus sheath hematoma ($n = 1$), and hepatic vasculature injury ($n = 1$). Neither treatment groups experienced major posttreatment laboratory grade adverse events at 1-month follow-up (►**Table 3**).

Table 2 Tumor response and complications

Characteristic	All ($n = 53$)	MWA ($n = 30$), TACE/MWA ($n = 19$), MWA alone ($n = 11$)	Y90 ($n = 23$)	*p*-Value
Response (mRECIST)				
CR	45 (85)	23 (77)	22 (96)	0.05
PR	7 (13)	7 (23)	0 (0)	
SD	1 (2)	0 (0)	1 (4)	
PD	0 (0)	0 (0)	0 (0)	
Total, *n*	10 (19)	10 (33)	0 (0)	
Minor, *n*	3 (6)	3 (10)	0 (0)	
Wound infection	1 (2)	1 (3)	0 (0)	
Abdominal pain	1 (2)	1 (3)	0 (0)	
Nausea	1 (2)	1 (3)	0 (0)	
Major, *n*	7 (13)	7 (23)	0 (0)	
Arterioportal fistula	1 (2)	1 (3)	0 (0)	
Pneumothorax	1 (2)	1 (3)	0 (0)	
Liver infarction	2 (4)	2 (7)	0 (0)	
Capsular burn	1 (2)	1 (3)	0 (0)	
Rectus sheath hematoma	1 (2)	1 (3)	0 (0)	
Hepatic artery/portal vein injury	1 (2)	1 (3)	0 (0)	
Time to progression				
n	11 (20)	7 (23)	4 (17)	0.6
Mean TTP, mo	12.8	6.7	23.5	< 0.0001
Follow-up				
Mean, mo	15.6	14.7	17.6	0.65
Range	1.0–53.0	1.0–53.0	1.0–47.0	

Abbreviations: CR, complete response; mRECIST, modified Response Evaluation Criteria in Solid Tumors; MWA, microwave ablation; PD, progressive disease; PR, partial response; SD, stable disease; TACE, transarterial chemoembolization; TTP, time to progression; Y90, yttrium-90.
Note: Parenthetical values are percentages unless otherwise indicated. Complications were categorized by the CTCAE (Common Terminology Criteria for Adverse Events) with minor events defined as grades 1–3 and major events as grades 4–5.

Table 3 Posttreatment labs

Characteristic	All ($n = 50$)	MWA ($n = 30$), TACE/MWA ($n = 19$), MWA alone ($n = 11$)	Y90 ($n = 20$)	*p*-Value
AST				
Mean (SD)	59.4 (35.2)	65.6 (37.6)	53.2 (31.5)	0.26
Range	21.0–163.0	24.0–163.0	21.0–135.0	
ALT				
Mean (SD)	33.7 (16.6)	40.2 (16.9)	26.3 (12.9)	0.01
Range	6.6–86.0	18.0–86.0	6.6–49.0	
Total bilirubin				
Mean (SD)	2.2 (3.1)	2.6 (3.9)	1.6 (1.3)	0.3
Range	0.3–18.4	0.3–18.4	0.4–5.3	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; MWA, microwave ablation; SD, standard deviation; TACE, transarterial chemoembolization; Y90, yttrium-90.
Note: Parenthetical values are percentages unless otherwise indicated.

Discussion

RS delivers microspheres loaded with a predetermined, personalized tumor-absorbed dose of Y90 into the segmental vessel, thereby selectively targeting the lesion while minimizing radiation exposure to normal liver parenchyma.[11,23–25] Recent landmark single-arm studies have demonstrated the efficacy of Y90-RS for unresectable early-stage HCC.[4,6,23] The RASER study described the first prospective cohort of very-early to early HCC (mean 2.1 cm) treated with Y90-RS in which 90% of patients achieved CR after one treatment with a median response duration of 635 days.[7] Target lesion progression had a cumulative incidence of 4% after 1 year and 12% after 2 years and actuarial overall survival was 96% at 2 years. These findings were similar to the LEGACY study of 162 patients with tumors measuring up to 8 cm (median 2.7 cm), which demonstrated a 2- and 3-year overall survival of 94.8 and 86.6%, respectively, and a best objective response rate of 88.3%, consistent with CR rates from previous retrospective analyses.[7,26–28] Our smaller retrospective cohort shows similar CR rates of 96% with Y90-RS and 77% with MWA ± TACE. Furthermore, disease progression occurred after 23.5 months following Y90-RS and 6.7 months following MWA ± TACE, with a longer TTP following Y90-RS.

There is a paucity of literature directly comparing Y90-RS to percutaneous ablation.[6,7,26] Arndt et al evaluated the outcomes of MWA versus Y90-RS in 68 treatment-naive unresectable lesions < 4 cm. Response rates were comparable between treatment groups with 87.5% (MWA) and 88.0% (Y90-RS) achieving CR at 3 months ($p = 0.565$) as was overall survival (RS 46.1 months, MWA 46.0 months) and adverse events. All clinical and laboratory CTCAE toxicities were ≤ grade 3 with no significant difference in laboratory toxicities, although there was a higher incidence of clinical toxicities, that is, ascites ($p = 0.048$), fatigue ($p = 0.028$), and abdominal pain ($p = 0.035$) following Y90-RS. Notably, these differences were eliminated after propensity score matching and progression-free survival was longer following Y90-RS (59.0 vs. 44.3 months; $p = 0.021$). The authors attributed this to Y90-RS achieving negative margins more frequently, corroborating the results in our study.[6] Therefore, our difference in CR may be attributed to Y90-RS obtaining better negative margins compared with MWA for lesions that are adjacent to critical structures.

Biederman et al performed a propensity score-matched study in which 121 locoregional treatment-naive patients with lesions ≤ 3 cm were treated with Y90-RS or combined TACE/MWA. No statistically significant differences were observed in procedure-related complications (8.9% TACE/MWA vs. 4.9% Y90-RS; $p = 0.46$), yet major CTCAE clinical toxicities only occurred following TACE/MWA, including pneumothorax ($n = 3$), TACE access site hematoma ($n = 2$), biloma ($n = 1$), and subcapsular hematoma ($n = 1$). The Y90-RS group experienced two access site hematomas during pretreatment mapping angiography. Grade 3 to 4 elevations in bilirubin and AST occurred infrequently and with similar incidence in both treatment groups. Overall and target lesion CR was comparable regardless of propensity score matching.[16] However, in contrast to our study, lesions treated with MWA in this study were in favorable locations.

Complete necrosis following thermal ablation is as high as 97.3% for tumors < 3 cm, but local recurrence is reported to be frequent (up to 26%), particularly for those in areas suboptimal for ablation as a 0.5-cm safety margin is required to prevent local recurrence.[7,29–31] Gozzo et al investigated recurrence following percutaneous thermal ablation for 213 patients, where local recurrence occurred in 12.4% at 1 year and 19.7% over the total follow-up period.[32] Lesions in suboptimal locations may be more prone to incomplete ablation margins. In our study, 23% of the patients had disease recurrence after MWA, which was not statistically different from that of Y90-RS (17%; $p = 0.6$), however, there are considerations with respect to assessing response rates. The tumoricidal impact of MWA is mediated by hyperthermal damage resulting in coagulative necrosis, which becomes quickly visible on imaging, whereas radioembolization causes delayed hemorrhagic necrosis and edema, with persistent enhancement of the exposed area. Therefore, follow-up imaging within 3 months may result in underestimation of response, and larger tumors may even require > 6 months to fully appreciate tumor necrosis.[10,20]

With respect to safety, our study found Y90-RS to be a comparable treatment strategy compared with MWA for lesions adjacent to critical structures; there were no clinical complications following Y90-RS and a rate of 33% following MWA. A review from 2019 assessed the clinical outcomes and toxicity of 155 cases of Y90-RS, in which only two patients developed radiation-induced liver injury, the most commonly reported side effect was fatigue, and all CTCAE events were ≤ grade 3.[33] Similarly, the LEGACY and RASER trials reported grade 3 events in 19.1 and 24.1% of patients, respectively, with the most common being transient fatigue and leukopenia.[7,26] Transient laboratory toxicities were the only adverse events noted in our cohort of Y90-RS patients. In contrast, our study showed a higher minor and major complication rate for MWA, with 7 major complications including arterioportal fistula ($n = 1$), pneumothorax ($n = 1$), liver infarction ($n = 2$), capsular burn ($n = 1$), rectus sheath hematoma ($n = 1$), and hepatic vasculature injury ($n = 1$).

Reported complication rates following MWA are between 2.2 and 61.5%, with major complications ranging from 2.6 to 4.6%.[34,35] Critical structures such as the gallbladder, bowels, hilum, pericardium, diaphragm, and large vessels may complicate MWA due to their higher dielectric constants, rendering them more susceptible to necrosis than healthy liver parenchyma.[36–38] The challenges presented by lesions within 1 cm of critical structures are twofold: (1) critical structures are susceptible to mechanical damage or delayed complications if ablated, and (2) the avoidance of damaging

these structures can result in incomplete ablation of the lesion.[39,40]

Puncture-related complications include pneumothorax, pleural effusion, hemothorax, intraperitoneal bleeds, and tumor seeding.[41,42] Damage during probe placement can be mitigated by CT and US guidance or by reducing motion artifact with decreased ventilated tidal volume or the Valsalva maneuver.[12,43] Cauterization of the intraparenchymal tract reduces the risk of seeding and direct puncture of the tumor can be avoided by creating an overlapping ablation zone with multiple probes.[12,44] The endovascular approach of Y90-RS offers a theoretical advantage over percutaneous ablation by eliminating the risk of damage to surrounding structures or tract seeding.

Thermal-related complications include damage to gastrointestinal or biliary structures (e.g., gallbladder perforation, bile duct stenosis, cholecystitis, biloma), liver abscesses, or portal vein thromboses.[41,45] Additionally, large caliber vessels can alter the ablation zone away from the vessel, termed heat sink effect, leading to incomplete tumor ablation, although MWA has been shown to be less susceptible to this phenomenon than RFA.[45,46] Hydrodissection provides thermal protection by physically separating the lesion from critical structures; it can also reduce heat sink effect by displacing large vessels.[17,18] A recent study detailed 66 patients with subcapsular tumors and tumors near critical structures who underwent hydrodissection-assisted MWA; although CR occurred in 91.4%, 3.0% had a major complication (two hepatic abscesses, one biliary injury).[17] Additional disadvantages of hydrodissection include fluid overload, diffusion from the injection site, risk of peritoneal seeding, and perihepatic bleeding from forceful dissection.[47,48]

Temperature monitoring can monitor for thermal damage to surrounding structures or achievement of threshold temperature when placed adjacent to the tumor margin.[49] In a study of 89 patients with 96 lesions adjacent to the diaphragm, thermal monitoring needles placed between the lesion and diaphragm allowed for temperature control between 50 and 60°C. There was no difference in complete ablation rate (94.8%) when compared with control lesions, although the study group had statistically insignificant, yet higher, incidence of shoulder pain, pleural effusion, nausea, and vomiting.[50] Although such adjunct techniques can mitigate MWA complications, they lead to increased procedure time and complexity and are not without inherent risks.

Limitations of this study include its small size, single-center and retrospective design, limited follow-up period, and inconsistent MWA pretreatment with TACE. In addition, this study was not randomized and therefore there is a potential for bias to have been introduced during case selection. A longer follow-up period ($>$ 3 months) may be beneficial to avoid underestimation of treatment response following Y90-RS. Future studies necessitate a multi-institutional comparison of treatment-naive lesions with a longer follow-up period. Additionally, comparison using radiology-pathology correlation and an expanded characterization of toxicities will be prudent. The use of TACE prior to MWA has been postulated to increase response rates, however, we did not examine if prior TACE improved efficacy of MWA. Despite its limitations, our study directly compared Y90-RS and MWA for lesions in particular locations, demonstrating comparability in safety and efficacy between the treatment modalities.

Conclusion

Y90-RS is a suitable alternative to MWA as a first-line therapy for early-stage HCC, particularly where regional anatomy presents challenges for percutaneous ablation. Y90-RS offers both a favorable treatment response and an excellent safety profile, supporting its use as an important curative therapy for early-stage HCC.

Ethical Approval Statement

This study was conducted in accordance with ethical standards as defined in the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals guidelines, and approved by the relevant institutional review boards. The protocol (Pro2023002524) for this study was approved by the Institutional Review Board at Rutgers New Jersey Medical School.

Authors' Contribution

The authors confirm contribution to the paper as follows: study conception and design: P.S., A.K., J.C.; data collection: J.C., N.C., P.G.; analysis and interpretation of results: O.K., P.G., J.C., N.C., P.S., A.K.; manuscript preparation: O.K., J.C., P.S., A.K.; all authors reviewed the results and approved the final version of the manuscript.

Conflict of Interest

P.S. is a consultant for Varian Medical Systems. A.K. is a consultant for Boston Scientific. There are no other perceived conflicts of interest from the remaining authors.

References

1 McGlynn KA, Petrick JL, El-Serag HB. Epidemiology of hepatocellular carcinoma. Hepatology 2021;73(Suppl 1, Suppl 1):4–13
2 Reig M, Forner A, Rimola J, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. J Hepatol 2022;76(03):681–693
3 Bruix J, Reig M, Sherman M. Evidence-based diagnosis, staging, and treatment of patients with hepatocellular carcinoma. Gastroenterology 2016;150(04):835–853
4 Yu Q, Khanjyan M, Fidelman N, Pillai A. Contemporary applications of Y90 for the treatment of hepatocellular carcinoma. Hepatol Commun 2023;7(10):e0288
5 Cho YK, Kim JK, Kim WT, Chung JW. Hepatic resection versus radiofrequency ablation for very early stage hepatocellular carcinoma: a Markov model analysis. Hepatology 2010;51(04):1284–1290
6 Arndt L, Villalobos A, Wagstaff W, et al. Evaluation of medium-term efficacy of Y90 radiation segmentectomy vs percutaneous microwave ablation in patients with solitary surgically unresectable $<$ 4 cm hepatocellular carcinoma: a propensity score matched study. Cardiovasc Intervent Radiol 2021;44(03):401–413
7 Kim E, Sher A, Abboud G, et al. Radiation segmentectomy for curative intent of unresectable very early to early stage

hepatocellular carcinoma (RASER): a single-centre, single-arm study. Lancet Gastroenterol Hepatol 2022;7(09):843–850
8 Prachanronarong K, Kim E. Radiation segmentectomy. Semin Intervent Radiol 2021;38(04):425–431
9 Riaz A, Gates VL, Atassi B, et al. Radiation segmentectomy: a novel approach to increase safety and efficacy of radioembolization. Int J Radiat Oncol Biol Phys 2011;79(01):163–171
10 Johnson GE, Padia SA. Yttrium-90 radiation segmentectomy. Semin Intervent Radiol 2020;37(05):537–542
11 Saini A, Wallace A, Alzubaidi S, et al. History and evolution of yttrium-90 radioembolization for hepatocellular carcinoma. J Clin Med 2019;8(01):55
12 Smolock AR, Shaw C. Hepatic microwave ablation in challenging locations. Semin Intervent Radiol 2019;36(05):392–397
13 Miller FH, Lopes Vendrami C, Gabr A, et al. Evolution of radioembolization in treatment of hepatocellular carcinoma: a pictorial review. Radiographics 2021;41(06):1802–1818
14 Briody H, Duong D, Yeoh SW, et al. Radioembolization for treatment of hepatocellular carcinoma: current evidence and patterns of utilization. J Vasc Interv Radiol 2023;34(07):1200–1213
15 Hamad A, Aziz H, Kamel IR, Diaz DA, Pawlik TM. Yttrium-90 radioembolization: current indications and outcomes. J Gastrointest Surg 2023;27(03):604–614
16 Biederman DM, Titano JJ, Bishay VL, et al. Radiation segmentectomy versus TACE combined with microwave ablation for unresectable solitary hepatocellular carcinoma up to 3 cm: a propensity score matching study. Radiology 2017;283(03):895–905
17 Song Y, Wu M, Zhou R, Zhao P, Mao D. Application and evaluation of hydrodissection in microwave ablation of liver tumours in difficult locations. Front Oncol 2023;13:1298757
18 Garnon J, Koch G, Caudrelier J, et al. Percutaneous image-guided cryoablation of challenging mediastinal lesions using large-volume hydrodissection: technical considerations and outcomes. Cardiovasc Intervent Radiol 2016;39(11):1636–1643
19 Biederman DM, Titano JJ, Korff RA, et al. Radiation segmentectomy versus selective chemoembolization in the treatment of early-stage hepatocellular carcinoma. J Vasc Interv Radiol 2018; 29(01):30–37.e2
20 Vouche M, Habib A, Ward TJ, et al. Unresectable solitary hepatocellular carcinoma not amenable to radiofrequency ablation: multicenter radiology-pathology correlation and survival of radiation segmentectomy. Hepatology 2014;60(01):192–201
21 Lencioni R, Llovet JM. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. Semin Liver Dis 2010;30(01):52–60
22 Common Terminology Criteria for Adverse Events (CTCAE) v5.0. U.S. Department of Health and Human Services; November 27, 2017. Accessed October 31, 2023 at: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf
23 Guiu B, Garin E, Allimant C, Edeline J, Salem R. TARE in hepatocellular carcinoma: from the right to the left of BCLC. Cardiovasc Intervent Radiol 2022;45(11):1599–1607
24 Garin E, Tselikas L, Guiu B, et al; DOSISPHERE-01 Study Group. Personalised versus standard dosimetry approach of selective internal radiation therapy in patients with locally advanced hepatocellular carcinoma (DOSISPHERE-01): a randomised, multicentre, open-label phase 2 trial. Lancet Gastroenterol Hepatol 2021;6(01):17–29
25 Memon K, Lewandowski RJ, Riaz A, Salem R. Yttrium 90 microspheres for the treatment of hepatocellular carcinoma. Recent Results Cancer Res 2013;190:207–224
26 Salem R, Johnson GE, Kim E, et al. Yttrium-90 radioembolization for the treatment of solitary, unresectable HCC: the LEGACY study. Hepatology 2021;74(05):2342–2352
27 Padia SA, Johnson GE, Horton KJ, et al. Segmental yttrium-90 radioembolization versus segmental chemoembolization for localized hepatocellular carcinoma: results of a single-center, retrospective, propensity score-matched study. J Vasc Interv Radiol 2017;28(06):777–785.e1
28 Lewandowski RJ, Gabr A, Abouchaleh N, et al. Radiation segmentectomy: potential curative therapy for early hepatocellular carcinoma. Radiology 2018;287(03):1050–1058
29 Chen MS, Li JQ, Zheng Y, et al. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. Ann Surg 2006;243 (03):321–328
30 Hatzidakis A, Müller L, Krokidis M, Kloeckner R. Local and regional therapies for hepatocellular carcinoma and future combinations. Cancers (Basel) 2022;14(10):2469
31 Kloeckner R, Galle PR, Bruix J. Local and regional therapies for hepatocellular carcinoma. Hepatology 2021;73(Suppl 1):137–149
32 Gozzo C, Hermida M, Herrero A, et al. Non-transplantable recurrence after percutaneous thermal ablation of ≤3-cm HCC: predictors and implications for treatment allocation. Hepatol Commun 2022;6(10):2975–2987
33 Jia Z, Wang C, Paz-Fumagalli R, Wang W. Radiation segmentectomy for hepatic malignancies: indications, devices, dosimetry, procedure, clinical outcomes, and toxicity of yttrium-90 microspheres. J Interv Med 2019;2(01):1–4
34 Izzo F, Granata V, Grassi R, et al. Radiofrequency ablation and microwave ablation in liver tumors: an update. Oncologist 2019; 24(10):e990–e1005
35 Poggi G, Tosoratti N, Montagna B, Picchi C. Microwave ablation of hepatocellular carcinoma. World J Hepatol 2015;7(25):2578–2589
36 Lubner MG, Brace CL, Hinshaw JL, Lee FT Jr. Microwave tumor ablation: mechanism of action, clinical results, and devices. J Vasc Interv Radiol 2010;21(8, Suppl):S192–S203
37 Brace CL. Radiofrequency and microwave ablation of the liver, lung, kidney, and bone: what are the differences? Curr Probl Diagn Radiol 2009;38(03):135–143
38 Radosevic A, Quesada R, Serlavos C, et al. Microwave versus radiofrequency ablation for the treatment of liver malignancies: a randomized controlled phase 2 trial. Sci Rep 2022;12(01):316
39 Li L, Yao J, Yan X, et al. Long-term efficacy and safety of microwave ablation for hepatocellular carcinoma adjacent to the gallbladder with a diameter ≤ 5 cm: a multicenter, propensity score matching study. Int J Hyperthermia 2023;40(01):2248425
40 Han X, Ni JY, Li SL, et al. Radiofrequency versus microwave ablation for hepatocellular carcinoma within the Milan criteria in challenging locations: a retrospective controlled study. Abdom Radiol (NY) 2021;46(08):3758–3771
41 Crocetti L, de Baére T, Pereira PL, Tarantino FP. CIRSE standards of practice on thermal ablation of liver tumours. Cardiovasc Intervent Radiol 2020;43(07):951–962
42 Makovich Z, Logemann J, Chen L, et al. Liver tumor ablation in difficult locations: microwave ablation of perivascular and subdiaphragmatic hepatocellular carcinoma. Clin Imaging 2021; 71:170–177
43 An C, Cheng Z, Yu X, et al. Ultrasound-guided percutaneous microwave ablation of hepatocellular carcinoma in challenging locations: oncologic outcomes and advanced assistive technology. Int J Hyperthermia 2020;37(01):89–100
44 Patel PA, Ingram L, Wilson ID, Breen DJ. No-touch wedge ablation technique of microwave ablation for the treatment of subcapsular tumors in the liver. J Vasc Interv Radiol 2013;24(08): 1257–1262
45 De Muzio F, Cutolo C, Dell'Aversana F, et al. Complications after thermal ablation of hepatocellular carcinoma and liver metastases: imaging findings. Diagnostics (Basel) 2022;12(05):1151
46 Ahmed M, Solbiati L, Brace CL, et al; International Working Group on Image-guided Tumor Ablation Interventional Oncology Sans Frontières Expert Panel Technology Assessment Committee of the Society of Interventional Radiology Standard of Practice Committee of the Cardiovascular and Interventional Radiological Society of Europe. Image-guided tumor ablation: standardization of terminology and reporting criteria–a 10-year update. Radiology 2014;273(01):241–260

47 Shin SW, Cho SK, Hyun D, Park KB, Park HS, Do YS. Guidewire-catheter induced hydrodissection to assist radiofrequency ablation for subcapsular hepatocellular carcinoma with iodized oil retention in patients with failed artificial ascites due to perihepatic adhesion. Diagn Interv Radiol 2021;27(06):746–753
48 Tsoumakidou G, Buy X, Garnon J, Enescu J, Gangi A. Percutaneous thermal ablation: how to protect the surrounding organs. Tech Vasc Interv Radiol 2011;14(03):170–176
49 Huang H, Liang P, Yu XL, et al. Safety assessment and therapeutic efficacy of percutaneous microwave ablation therapy combined with percutaneous ethanol injection for hepatocellular carcinoma adjacent to the gallbladder. Int J Hyperthermia 2015;31(01): 40–47
50 Li M, Li Z, Yu X, et al. Percutaneous radio-frequency ablation of hepatocellular carcinoma adjacent to the gastrointestinal tract. Int J Hyperthermia 2016;32(06):600–606

