

**Resin versus Glass Microspheres for Yttrium-90 Transarterial  
Radioembolization: Comparing Survival in Unresectable  
Hepatocellular Carcinoma using Pretreatment Partition Model  
Dosimetry**

Running title: Resin vs Glass spheres for Y-90 TARE HCC

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## Abstract

The aim of this study was to compare survival of patients treated for unresectable hepatocellular carcinoma (uHCC) with Yttrium-90 ( $^{90}\text{Y}$ ) transarterial radioembolization (TARE) using pretreatment partition model dosimetry (PMD). **Methods:** We performed a retrospective analysis of prospectively collected data on 77 consecutively treated (mean age  $66.4 \pm 12.2$  y) for uHCC (36 uni-nodular, 5 multi-nodular, 36 diffuse) with  $^{90}\text{Y}$  TARE (41 resin, 36 glass) using pretreatment PMD. Study endpoints were progression-free survival (PFS) and overall survival (OS) assessed by Kaplan-Meier estimates. Several variables including Barcelona Clinic Liver Cancer (BCLC) staging system, tumor size and serum alpha-fetoprotein (AFP) level) were investigated using Cox proportional hazards regression. **Results:** Characteristics of two groups were comparable in regard to demographic data, comorbidities, Child-Pugh score, BCLC, serum AFP level and  $^{90}\text{Y}$  global administered activity. Median follow-up time was 7.7 months (range 0.4-50.1). Relapse occurred in 44 patients (57%) at a median of 6 mo (range 0.4-27.9) after  $^{90}\text{Y}$  TARE and 41 patients (53%) died from tumor progression. Comparison between resin and glass microspheres revealed a higher but not statistically significantly PFS and OS rates in  $^{90}\text{Y}$  resin group compared to  $^{90}\text{Y}$  glass group (resin PFS 6.1 mo [95% Confidence interval CI 4.7-7.4] and glass PFS 5 mo [95% CI 0.9-9.2],  $P = 0.53$ ; resin OS 7.7 mo [95% CI 7.2-8.2] and glass OS 7 mo [95% CI 1.6-12.4],  $P = 0.77$ ). No significant survival difference

between both types of  $^{90}\text{Y}$  microspheres was observed in any subgroups of patients with early/intermediate or advanced BCLC stages. Among the variables investigated Cox analyses showed that only in the glass group, the BCLC staging system and the serum AFP level were associated with PFS ( $P = 0.04$ ) and OS ( $P = 0.04$ ). Tumor size was a prognostic factor without significant influence on PFS and OS after  $^{90}\text{Y}$  TARE. **Conclusion:** Comparison between resin and glass microspheres revealed no significant survival difference in patients treated for uHCC with  $^{90}\text{Y}$  TARE using pretreatment PMD. Further larger prospective studies are warranted to confirm these findings.

**Key words:** Yttrium-90; TARE; hepatocellular carcinoma, survival, partition model dosimetry

## INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and represents the 2<sup>nd</sup> most common cause of cancer mortality worldwide (1). Despite new treatment options, HCC has a poor prognosis with an overall 5-year relative survival rate of 16% (2). Moreover, more than 70% of patients present an advanced stage, beyond potentially curative options (hepatic resection, liver transplantation, percutaneous ablation). The BCLC staging system was developed based on a retrospective analysis of various studies of HCC patients with early, intermediate, and advanced-terminal disease, which attempted to identify prognostically relevant variables for each group (3). For patients with early stage disease, survival was negatively correlated with portal hypertension and bilirubin levels > 1.5 mg/dl; for intermediate stages, the significant variable was a large multinodular tumor; and for advanced disease, deterioration of performance status and the presence of portal vein invasion (PVI) which is associated with a poor prognosis. In patients with PVI, studies have reported overall survival ranging from 2 to 4 months, compared to 10-24 months in HCC patients without PVI (3–5).

Given the hypervascularity of HCC, intra-arterially injected microspheres will be preferentially delivered to the tumor-bearing area and selectively emit high-energy, low penetration radiation to the tumor (6). Two FDA-approved <sup>90</sup>Y microsphere products are currently used: resin microspheres (SIR-Spheres™; SIRTex Medical, Sydney, Australia) and glass microspheres (TheraSphere™; BTG Biocompatibles Ltd,

Farnham, UK) which differ in several characteristics including size, the number of microspheres typically injected in a single treatment (< 5 million to 10-30 million) (7), and activity per microsphere (8).

Resin microspheres manufacturer-recommended  $^{90}\text{Y}$  activity prescription is based on a semi empiric formula including body-surface area (9,10) and tumor burden. This approach can be refined using a 3-compartment partition model (11) including the lungs, and tumoral (TV) and targeted non-tumoral liver volumes derived from a pretreatment  $^{99\text{m}}\text{Tc}$ -macroaggregated albumin single-photon emission computed tomography ( $^{99\text{m}}\text{Tc}$ -MAA SPECT/CT). Glass microspheres  $^{90}\text{Y}$  activity prescription is based on a 2-compartment model (lungs and targeted liver regions) aiming to deliver an absorbed dose of 80-150 Gy in the target liver volume.

It is now well established that  $^{90}\text{Y}$  TARE slow down disease progression and improve survival in patients with HCC (12). However, comparison of the survival of patients treated with both types of  $^{90}\text{Y}$  microspheres using partition model dosimetry (PMD) remains unclear in HCC. To the best of our knowledge, only a recent retrospective review (13) has compared the outcome of both types of  $^{90}\text{Y}$  microspheres in patients with unresectable HCC (uHCC) concluding in a survival benefit for glass microspheres. Then, aim of the current study was to compare progression-free survival (PFS) and OS between two groups of patients treated with  $^{90}\text{Y}$  resin and glass microspheres for uHCC using pretreatment PMD (14). Secondly, we have compared PFS and OS of

each type of  $^{90}\text{Y}$  microsphere according to early/intermediate (combining BCLC A and B) stages and the advanced (BCLC C) stage which is associated with a very poor prognosis.

## **MATERIALS AND METHODS**

### **Patient Selection**

We performed a retrospective analysis of prospectively collected data on 77 consecutively treated (67 men, mean age  $66.4 \pm 12.2$  y) with  $^{90}\text{Y}$  TARE (41 resin, 36 glass) for uHCC (36 uni-nodular, 5 multi-nodular, 36 diffuse) between 2010 and 2016. The American Association for the Study of Liver Diseases guidelines (15) were used to diagnose HCC. The BCLC staging system have been used to stage HCC (3). Patients were considered for  $^{90}\text{Y}$  TARE when no curative options (resection or transplantation) were possible due to a locally advanced tumor, a multifocal disease, a poor liver reserve, a PVI or an extrahepatic metastasis. Inclusion criteria consisted of patients aged 18 years or older with a liver-dominant or liver-only disease, an adequate hematologic, renal and hepatic function, a good Eastern Cooperative Oncology Group Performance Status  $< 2$  and a life expectancy  $> 3$  months. Patients with an inadequate liver reserve (bilirubin  $> 34 \mu\text{mol/L}$ , ascites), a poor Eastern Cooperative Oncology Group Performance Status  $\geq 2$ , a higher lung shunt fraction  $> 20\%$ , an estimated lung absorbed dose of  $> 30$  Gray per session

and 50 Gray in total, and an uncorrectable extrahepatic flow on the pretherapy  $^{99m}\text{Tc}$ -MAA SPECT/CT were immediately excluded.

All patients underwent  $^{90}\text{Y}$  TARE as standard care and gave their informed consent for the treatment. The local Ethics Research Committee of the State of Vaud took into account the retrospective analysis of our database, approved the protocol (Number 2016-00640) and waived the need for patient informed consent for the study analysis.

### **Data Collection**

Demographic, clinical, biological, imaging, treatments (pre- and post  $^{90}\text{Y}$  TARE procedure) and  $^{90}\text{Y}$  TARE dosimetric data were collected retrospectively from patients treated for uHCC with  $^{90}\text{Y}$  TARE using pretreatment PMD between 2010 and 2016. All patients underwent computed tomography or magnetic resonance imaging scans before the  $^{90}\text{Y}$  TARE procedure to evaluate the tumor size (calculated by the longest diameter of all measurable tumors), number and distribution of lesions and presence of ascites and PVI.

### **$^{90}\text{Y}$ Administered Activity Calculation**

Resin microsphere dosimetry is based on a 3-compartment partition model aiming at keeping the absorbed dose to the targeted non-tumoral volume below 70 and 50 Gy for lobar and total liver treatment respectively, as recommended by Lau et al. (10).  $^{90}\text{Y}$  Glass-sphere activity determination is based on a 2-compartment model (lungs +

targeted liver region) aiming at delivering an absorbed dose between 80 and 150 Gy in target liver volume. In analogy with the resin-sphere dosimetry, we refined the  $^{90}\text{Y}$  activity determination by applying as a second step a partition model accounting for TV and non-tumoral liver volume and differential particle distribution (tumoral / non-tumoral ratio) estimated from  $^{99\text{m}}\text{Tc}$ -MAA SPECT/CT to predict TV and targeted non-tumoral liver absorbed dose. In line with the suggested threshold for OS by Garin et al., in lobar TARE, we keep the average predicted absorbed dose to the targeted non-tumoral liver volume  $< 70$  Gy provided that this allows a predicted tumor-absorbed dose  $> 205$  Gy (16).

### **$^{90}\text{Y}$ TARE Planning and Procedure**

All patients underwent a pretherapy SPECT/CT with 120-180 MBq of  $^{99\text{m}}\text{Tc}$ -MAA 1-3 weeks prior to the  $^{90}\text{Y}$  TARE procedure. Whenever necessary, coiling of the gastroduodenal, right gastric artery, or gastroduodenal branches was performed and the  $^{99\text{m}}\text{Tc}$ -MAA was injected into the hepatic artery selected. The patient was immediately ( $< 20$  min) transferred to nuclear medicine for a SPECT/CT, whole-body and planar images within 1 hour. Lung shunting was evaluated on whole-body and planar images. The TV was assessed on SPECT/CT with morphologic information from any available imaging modalities (enhanced-CT, magnetic resonance or  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography-computed tomography) when needed. The TV estimated from the  $^{99\text{m}}\text{Tc}$ -MAA SPECT/CT was used to determine the

activity of  $^{90}\text{Y}$  microspheres to administer using our recently published PMD for TARE (14). Patients with small-tumor volumes were preferentially addressed to  $^{90}\text{Y}$  glass microspheres due to their higher specific  $^{90}\text{Y}$  activity and lower particle number aiming at avoiding lesion saturation and consecutive reflux to non-target volumes. A post-TARE SPECT/CT was performed to confirm the distribution of  $^{90}\text{Y}$  microspheres. All  $^{99\text{m}}\text{Tc}$ -MAA and  $^{90}\text{Y}$  TARE procedures were performed by experienced radiologists and nuclear medicine physicians.

### **Statistical Analysis**

Continuous variables are described as median (25<sup>th</sup>;75<sup>th</sup> interquartile range) and dichotomous data as percentage. Characteristics of populations were compared by using  $\chi^2$  test with Pearson's correction for discrete variables and t test or Mann-Whitney test for continuous variables. Study endpoints were PFS and OS. PFS was defined as time from the date of the  $^{90}\text{Y}$  TARE until first occurrence of disease progression which was determined by biological and contrast-enhanced magnetic resonance imaging (World Health Organization bidimensional and three-dimensional European Association for the Study of the Liver response criteria. OS was defined as time from the date of the  $^{90}\text{Y}$  TARE until death from tumor progression. Survival functions were obtained from Kaplan-Meier estimates and compared using the log-rank test. The influence of several variables including BCLC staging system, tumor size and serum

alpha-fetoprotein (AFP) level was investigated using Cox proportional hazards regression in the entire cohort and in each group. All statistical analyses were performed using SPSS software (version 23 for Windows 2010, SPSS Inc., Chicago, IL, USA). *P* values < 0.05 were considered statistically significant.

## RESULTS

### Study Population

Characteristics of two groups were statistically comparable for demographic, clinical and biological data (Table 1). In the entire cohort, using the BCLC staging system 5 patients (6%) were stage A, 30 (39%) stage B and 42 (55%) stage C. Eleven patients (14%) had normal livers, all others (86%) had cirrhotic liver disease including 51 patients Child-Pugh A and 15 patients Child-Pugh B ( $\leq$  B7). Five patients (6%) had a metastatic disease: to lymph nodes and lungs ( $n = 2$ ), to peritoneum and lungs ( $n = 1$ ), to lymph nodes and peritoneum ( $n = 1$ ) and to adrenal glands ( $n = 1$ ). Regarding  $^{90}\text{Y}$  TARE, the median  $^{90}\text{Y}$  administered activity was similar between two groups with 1.80 GBq (range 0.50-5.46 GBq) and 1.81 GBq (range 0.49-6.85 GBq) in resin and glass groups respectively ( $P = 0.52$ , Table 2) while taking into account the TV, the  $^{90}\text{Y}$  administered activity per unit of TV (expressed as MBq/cm<sup>3</sup>) was significantly higher in the glass group ( $P = 0.04$ , Table 2) explained by the higher number of segmental  $^{90}\text{Y}$  TARE in this group ( $P = 0.003$ , Table 2). There were 41 lobar, 13 whole-liver, 13 segment, 1 partial lobe, 6 lobar

and segment and 3 lobar and partial lobe treatments. Among the 77 patients, 48 (62%) were treatment naïve and 29 (38%) had already received various procedures before  $^{90}\text{Y}$  TARE including targeted therapy by Sorafenib or Everolimus ( $n = 5$ ), embolization ( $n = 6$ ), TACE ( $n = 19$ ), radiofrequency ablation ( $n = 17$ ) or ethanol ablation ( $n = 3$ ), with an association of 2 or more treatment modalities in 12 patients (16%).

### Survival Analysis

Median follow-up in living patients was 7.7 mo (range 0.4-50.1 mo). Relapse occurred in 44 patients (57%) at a median of 6 mo (range 0.4-27.9 mo) after  $^{90}\text{Y}$  TARE and 41 (53%) patients died from tumor progression. As shown in Fig. 1, comparison between resin and glass microspheres in the entire cohort revealed a higher but not statistically significantly PFS and OS rates of  $^{90}\text{Y}$  resin group compared to  $^{90}\text{Y}$  glass group (resin PFS 6.1 mo [95% CI 4.7-7.4 mo] and glass PFS 5 mo [95% CI 0.9-9.2 mo],  $P = 0.53$ ; resin OS 7.7 mo [95% CI 7.2-8.2 mo] and glass OS 7 mo [95% CI 1.6-12.4 mo],  $P = 0.77$ ). PFS and OS rates at 6 months, 1 year and 2 years from the  $^{90}\text{Y}$  TARE were 52%/63%, 7%/22%, 0%/11% in resin group and 47%/57%, 18%/29%, 6%/14% in glass group.

Regarding BCLC staging system, no significant survival difference between both types of  $^{90}\text{Y}$  microspheres was observed in subgroups of patients with early/intermediate or advanced BCLC stages (Fig. 2). However, there was a small but not significant survival benefit in PFS in

patients with early/intermediate BCLC stage compared to those with advanced BCLC stage in the glass group ( $P = 0.06$ , Fig. 3).

### **Multivariable Regression**

Results of Cox proportional hazard regression performed in the entire cohort and in each group are given in Table 3. Among the several variables investigated including BCLC, tumor size and serum AFP level, only in the glass group, the BCLC staging system and the serum AFP level were associated with PFS ( $P = 0.04$ ) and OS ( $P = 0.04$ ). Tumor size was a prognostic factor without significant influence on PFS and OS after  $^{90}\text{Y}$  TARE in the current study.

### **DISCUSSION**

We performed a retrospective analysis of prospectively collected data on two groups of patients treated with  $^{90}\text{Y}$  resin and glass microspheres for uHCC using pretreatment PMD. In brief, our study shows equal outcomes regarding PFS and OS in patients with uHCC.

There are two large phase II studies by the group of Sangro et al. (17) using resin and by Salem et al. (18) using  $^{90}\text{Y}$  glass microspheres. The study using resin microspheres revealed an overall survival of 24.4 mo in BCLC A, 16.9 mo in BCLC B and 10.0 mo in BCLC C patients. The Salem et al. study reproduced these promising results of 26.9 mo in BCLC A, 17.2 mo in BCLC B and 7.3 mo in BCLC C. However, again these studies were not comparable since the therapeutic  $^{90}\text{Y}$  administered

activities were calculated differently. In the case of the glass microspheres study,  $^{90}\text{Y}$  activities were calculated aiming a target absorbed dose of 100-120 Gy to the target liver volume (19), the resin microspheres study published by Sangro et al. (17) used a combination of the body-surface area method or modified PMD with a mean  $^{90}\text{Y}$  administered activity of 1.6 GBq and the results of these studies were not directly comparable. In glass group, our study revealed a median OS of 25.3 mo in early/intermediate BCLC stage and 20.5 mo in advanced BCLC stage (Fig. 2) which is in accordance with study published by Sangro et al. (17) and Salem et al. (18) and shows that our patient population has been chosen according to published standards. The only small but not significant survival benefit was observed in patients with early/intermediate BCLC stage compared to those with advanced BCLC stage in favor of  $^{90}\text{Y}$  glass microspheres.

A recent retrospective analysis in unresectable HCC patients with PVI claimed a superiority of glass versus resin microspheres. This report published a significant higher OS in the  $^{90}\text{Y}$  glass group ( $P < 0.001$ ) whereas PFS did not ( $P = 0.48$ ) (13). However, it is important to note that the inaccurate body-surface area method has been used in this study and may partly explained the improved OS observed in patients treated with  $^{90}\text{Y}$  glass microspheres. Here we present to our knowledge a first study comparing resin microspheres and glass microspheres using pretreatment PMD and demonstrate that both approaches seems to be comparable in regard to PFS and OS. This finding is important since there

is an ongoing discussion in how and what type of HCC to use which kind of treatment and which treatment might be superior. Others studies seem still to be warranted to investigate this question.

There are several limitations to this study. Firstly, the main limitation of the current study is that it was a retrospective and a single center study with a relatively limited number of patients. However, our study remains the second largest report after the study of Biederman et al. study (13) comparing groups of patients treated by both types of  $^{90}\text{Y}$  microspheres. Secondly, a further important potential bias was the tumor size. Indeed, patients with small tumor volumes were most often referred to glass microspheres. Although the difference in size was not statistically different between both groups, the tumor size is a well-known factor associated with outcome and may had a direct impact on our survival results. This bias is consistent with the significant higher number of segmental treatments, the significant higher administered  $^{90}\text{Y}$  activity per tumor volume (and consequently the dose delivered to tumors) in the glass group and reflects the paradigm of radiation segmentectomy which has been previously published using glass microspheres (20). Furthermore, a significant proportion of patients had undergone treatment before (38%) and after (32%)  $^{90}\text{Y}$  TARE procedure, however no statistical difference between both groups was observed and this is a classical finding in modern studies in patients with several treatment possibilities.

## **CONCLUSION**

Comparison between resin and glass microspheres revealed no significant survival difference in patients treated for uHCC with <sup>90</sup>Y TARE using pretreatment PMD. Further larger prospective studies are warranted to confirm these findings.

## **DISCLOSURE**

The authors have no potential conflicts of interest to report.

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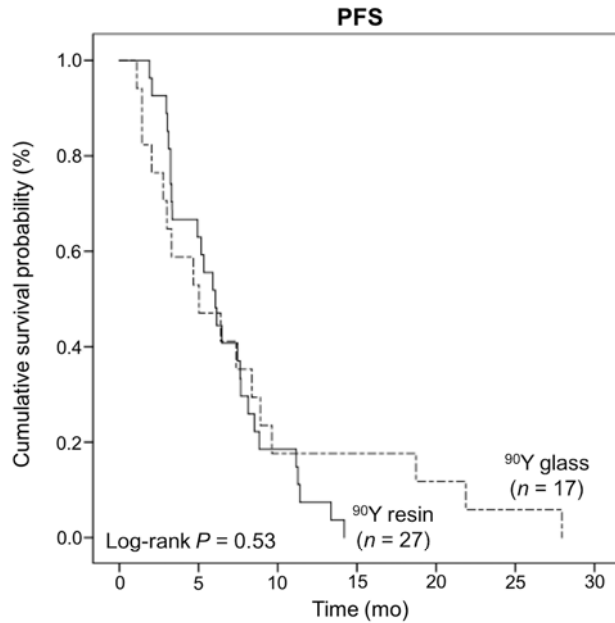
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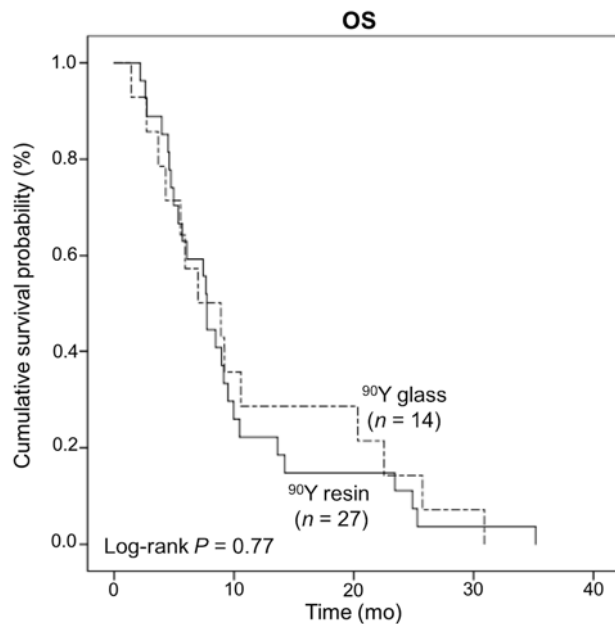
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No. at risk							
Glass	17	9	3	3	2	1	0
Resin	27	17	5	0			

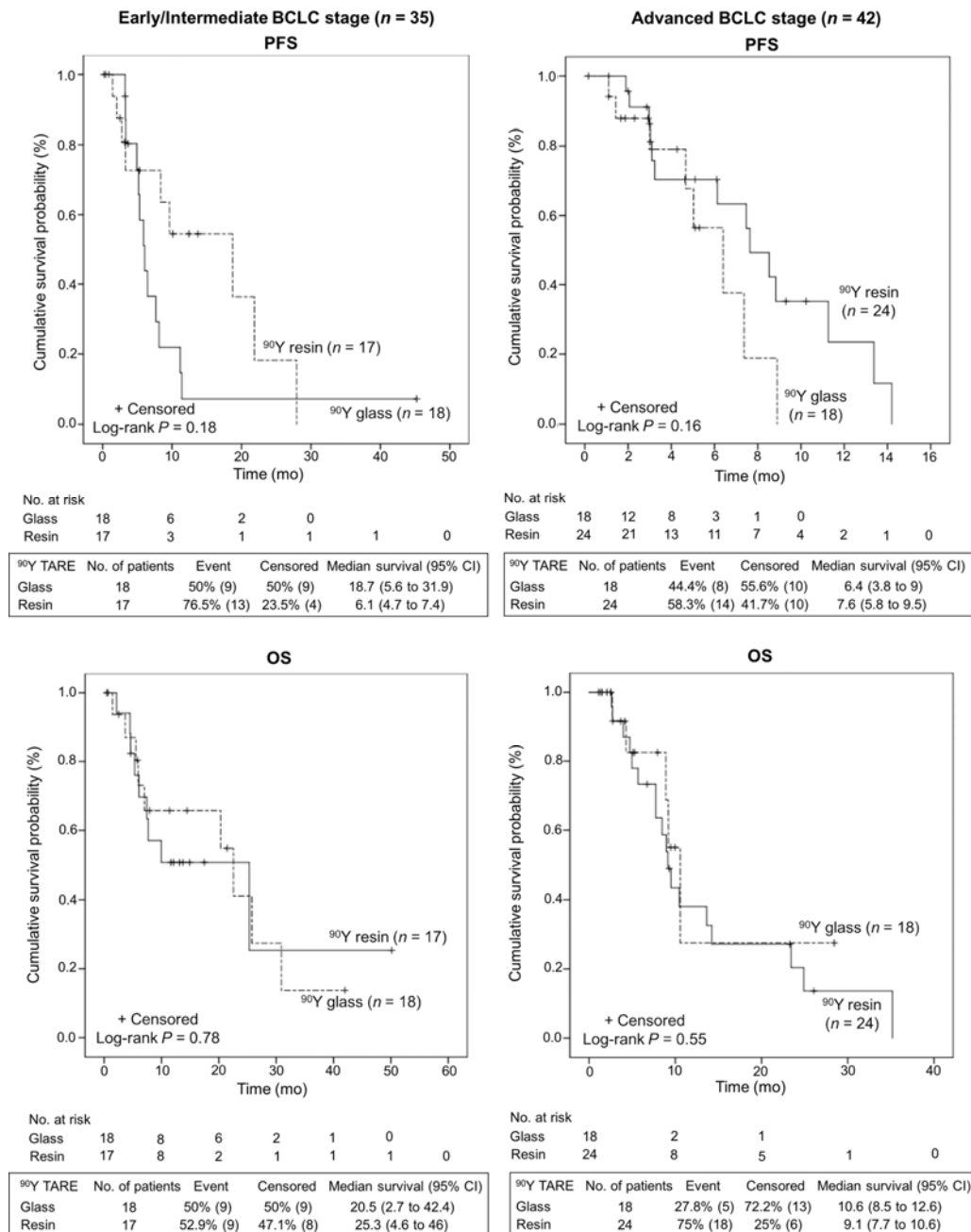
$^{90}\text{Y}$ TARE	No. of patients	Event	Censored	Median survival (95% CI)
Glass	17	100% (17)	0% (0)	5 (0.9 to 9.2)
Resin	27	100% (27)	0% (0)	6.1 (4.7 to 7.4)



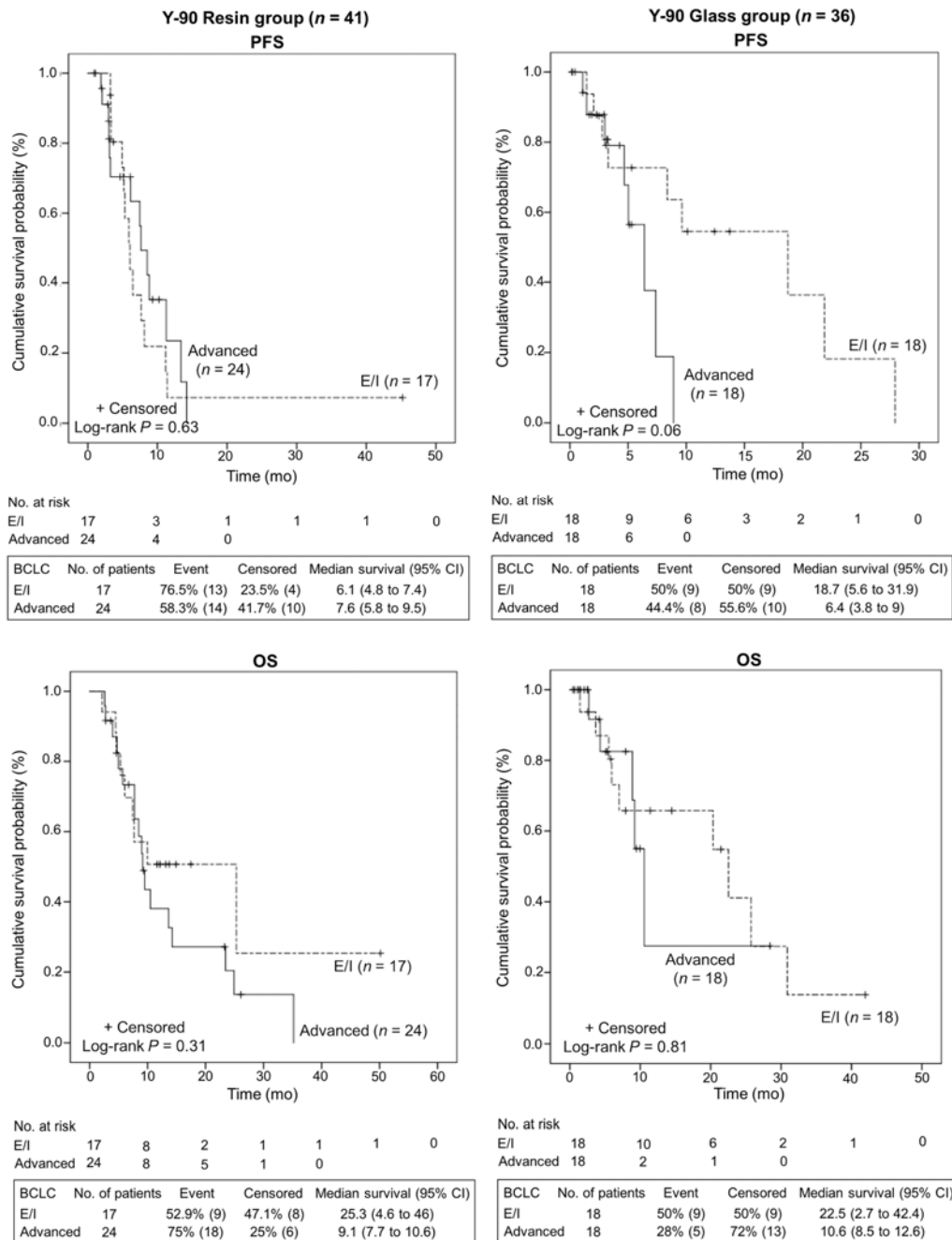
No. at risk					
Glass	14	5	4	1	0
Resin	27	7	4	1	0

$^{90}\text{Y}$ TARE	No. of patients	Event	Censored	Median survival (95% CI)
Glass	14	100% (14)	0% (0)	7 (1.6 to 12.4)
Resin	27	100% (27)	0% (0)	7.7 (7.2 to 8.2)

**FIGURE 1.** Kaplan-Meier estimates of progression-free survival (PFS) and overall survival (OS) in the entire cohort treated with resin and glass microspheres for  $^{90}\text{Y}$  transarterial radioembolization (TARE).



**FIGURE 2.** Kaplan-Meier estimates of progression-free survival (PFS) and overall survival (OS) of both types of <sup>90</sup>Y microspheres for transarterial radioembolization (TARE) in subgroups of patients with early/intermediate Barcelona Clinic Liver Cancer (BCLC) stage (combining BCLC A and B) and advanced BCLC stage (BCLC C).



**FIGURE 3.** Kaplan-Meier estimates of progression-free survival (PFS) and overall survival (OS) of subgroups of patients with early/intermediate Barcelona Clinic Liver Cancer (BCLC) stage (combining BCLC A and B) and advanced BCLC stage (BCLC C) according both types of  $^{90}\text{Y}$  microspheres for transarterial radioembolization (TARE).

**TABLE 1.** Population Characteristics.

<b>Characteristics</b>	<b>All patients (n = 77)</b>	<b><sup>90</sup>Y Resin group (n = 41)</b>	<b><sup>90</sup>Y Glass group (n = 36)</b>	<b>P</b>
Age, years	68 (60-74)	68 (58-72)	71 (62-75)	0.05
Female	10 (12.9)	4 (9.8)	6 (16.7)	0.37
Comorbidities				
Hypertension	39 (50.6)	17 (41.5)	22 (61.1)	0.09
Type 2 diabetes mellitus	29 (37.6)	14 (34.1)	15 (41.7)	0.50
Coronary artery disease	12 (15.6)	7 (17.1)	5 (13.9)	0.70
Child-Pugh score				
A	51 (66.2)	34 (82.9)	26 (72.2)	0.06
B (≤ B7)	15 (19.5)	7 (17.1)	10 (27.8)	0.06
BCLC staging system				
Stage A	5 (6.5)	3 (7.3)	2 (5.6)	0.75
Stage B	30 (39)	14 (34.1)	16 (44.4)	0.36
Stage C	42 (54.5)	24 (58.5)	18 (50)	0.45
HCC characteristics				
Tumor size, cm	5.8 (4.3-8.9)	6.7 (4.7-9)	5 (3.7-6.7)	0.13
< 5 cm	31 (40.3)	14 (34.1)	17 (47.2)	0.24
≥ 5 cm	46 (59.7)	27 (65.9)	19 (52.8)	0.24
Uni-nodular	36 (46.8)	21 (51.2)	15 (41.7)	0.40
Multi-nodular (2-5 nodules)	5 (6.5)	1 (2.4)	4 (11.1)	0.12
Diffuse (>5 nodules)	36 (46.8)	19 (46.3)	17 (47.2)	0.94
PVI	33 (42.9)	19 (46.3)	14 (38.9)	0.51
Serum AFP level, kU/l	19 (6-432)	56 (7-2442)	10 (4-62)	0.49
Ascites	8 (10.4)	4 (9.8)	4 (11.1)	0.85
Cirrhosis	66 (85.7)	36 (87.8)	30 (83.3)	0.58
Chronic alcoholism	35 (45.5)	17 (41.5)	18 (50)	0.45
Viral infection type B	8 (10.4)	5 (12.2)	3 (8.3)	0.58
Viral infection type C	19 (24.7)	12 (29.3)	7 (19.4)	0.32
Hemochromatosis	3 (3.9)	2 (4.9)	1 (2.8)	0.64
NASH	8 (10.4)	4 (9.8)	4 (11.1)	0.85
Extrahepatic metastasis	5 (6.5)	3 (7.3)	2 (5.6)	0.75

Values are median (25<sup>th</sup>;75<sup>th</sup> interquartile range) or n (%).

AFP, alpha-fetoprotein; HCC, hepatocellular carcinoma; BCLC, barcelona clinic liver cancer; PVI, portal vein invasion; NASH, non-alcoholic steatohepatitis; TARE, transarterial radioembolization

**TABLE 2.** <sup>90</sup>Y TARE and Treatment Associated Data.

Characteristics	<sup>90</sup> Y resin group (n = 41)	<sup>90</sup> Y glass group (n = 36)	P
<sup>90</sup> Y TARE			
<sup>90</sup> Y administered activity, GBq	1.80 (1.35-2.50)	1.81 (1.21-2.93)	0.52
TV based on MAA SPECT/CT, cm <sup>3</sup>	220 (125-640)	183 (100-381)	0.26
<sup>90</sup> Y administered activity per unit of TV, MBq/cm <sup>3</sup>	7.3 (5-12)	8.4 (6.5-16.3)	<b>0.04</b>
<sup>90</sup> Y tumor liver absorbed dose, Gy	160 (115-254)	242 (174-316)	0.13
<sup>90</sup> Y normal liver absorbed dose, Gy	36 (27-50)	45 (34-58)	0.09
Lobar	22 (53.7)	19 (52.8)	0.94
Bilobar	10 (24.4)	3 (8.3)	0.06
Segmental	2 (4.9)	11 (30.6)	<b>0.003</b>
Partial lobe	1 (2.4)	0 (0)	0.35
Lobar and segmental	4 (9.8)	2 (5.6)	0.49
Lobar and partial lobe	2 (4.9)	1 (2.8)	0.64
Treatments pre- <sup>90</sup> Y TARE			
Targeted therapy	3 (7.3)	2 (5.6)	0.75
Embolization	4 (9.8)	2 (5.6)	0.49
TACE	13 (31.7)	6 (16.7)	0.13
Radiofrequency ablation	8 (19.5)	9 (25)	0.56
Ethanol ablation	2 (4.9)	1 (2.8)	0.64
Treatments after <sup>90</sup> Y TARE			
Targeted therapy	6 (14.6)	4 (11.1)	0.65
Hepatectomy	1 (2.4)	0 (0)	0.35
Embolization	1 (2.4)	0 (0)	0.35
TACE	7 (17.1)	4 (11.1)	0.46
Radiofrequency ablation	3 (7.3)	4 (11.1)	0.56
Ethanol ablation	0 (0)	1 (2.8)	0.28
Chemotherapy	1 (2.4)	0 (0)	0.35
2 <sup>nd</sup> TARE	1 (2.4)	1 (2.8)	0.93

Values are median (25<sup>th</sup>;75<sup>th</sup> interquartile range) or n (%).

TV, tumor volume; TARE, transarterial radioembolization; TACE, transarterial chemoembolization; SPECT/CT, single-photon emission computed tomography

**TABLE 3.** Prognostic Factors in Multivariable Regression for PFS and OS According to The Entire Cohort and <sup>90</sup>Y Resin and Glass Groups.

Characteristics	PFS		OS	
	HR (95% CI)	P	HR (95% CI)	P
All population ( <i>n</i> = 77)				
BCLC staging system				
Stages A and B vs. Stage C	0.59 (0.30-1.15)	0.12	0.63 (0.33-1.19)	0.15
Tumor size				
< 5 vs. ≥ 5 cm	0.94 (0.70-1.25)	0.66	0.85 (0.59-1.22)	0.37
Serum AFP level	0.76 (0.38-1.52)	0.43	0.84 (0.58-1.20)	0.37
<sup>90</sup> Y resin group ( <i>n</i> = 41)				
BCLC staging system				
Stages A and B vs. Stage C	0.85 (0.35-2.03)	0.71	0.49 (0.20-1.19)	0.12
Tumor size				
< 5 vs. ≥ 5 cm	0.52 (0.19-1.42)	0.20	0.62 (0.24-1.63)	0.33
Serum AFP level	0.85 (0.60-1.20)	0.35	0.65 (0.38-1.11)	0.11
<sup>90</sup> Y glass group ( <i>n</i> = 36)				
BCLC staging system				
Stages A and B vs. Stage C	0.27 (0.08-0.96)	<b>0.04</b>	0.74 (0.23-2.44)	0.62
Tumor size				
< 5 vs. ≥ 5 cm	1.87 (0.55-6.40)	0.32	0.93 (0.30-2.93)	0.90
Serum AFP level	1.73 (0.99-3.01)	0.06	1.72 (1.02-2.90)	<b>0.04</b>

AFP, alpha-fetoprotein; CI; confidence interval; PFS, progression-free survival; OS, overall survival; BCLC, barcelona clinic liver cancer