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ORIGINAL RESEARCH

Comparison of Yttrium-90 therapy for unresectable liver metastasis: glass versus biocompatible resin microspheres

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Abstract
Objectives Yttrium-90 radioembolization is a hepatic intra-arterial-based therapy using glass- or resin-based microspheres as carriers to deliver high-dose radiation to tumors to maximize dose while minimizing collateral damage. This study aimed to compare the safety and efficacy of glass (TheraSphere) versus resin (Selective Internal Radiation Spheres, SIR-Spheres) Y-90 in the treatment of intrahepatic metastatic disease.
Methods A review of a prospectively collected, institutional review board-approved database was conducted to identify patients who underwent Y-90 therapy, excluding those with hepatocellular carcinoma (HCC).
Results Of 119 patients, 79 received SIR-Spheres and 40 received TheraSphere therapy. For intrahepatic cholangiocarcinoma, mean survival was 10.6 months in the SIR-Spheres group compared to 29.2 months in the TheraSphere group (log-rank 0.05). In colorectal cancer (CRC), mean survival was 16.3 months for SIR-Spheres therapy and 26.8 for TheraSphere therapy (log-rank 0.097). There were no documented severe (grade 3) side effects in the TheraSphere group compared to 14 % of patients who experienced side effects in the SIR-Spheres group.
Conclusions TheraSphere microsphere appears superior to SIR-Spheres in treating non-HCC intrahepatic malignancy. However, patient selection and better multi-disciplinary care may play a role in these differences. Continued studies in combination therapies for all hepatic malignancies is critical to the long-term success and sustainability of Y-90 therapy.

Keywords Cholangiocarcinoma · Colorectal · Carcinoid · Survival · Radioembolization · Radiotherapy · Yttrium-90 · SIR-Spheres · TheraSphere

Background

Yttrium-90 (Y-90) radioembolization is an intra-arterial-based therapy using microspheres as carriers to deliver internal radiation to hepatic malignancies. The delivery of Y-90 microspheres via the arterial circulation of the liver exploits the fact that hepatic tumors derive the majority of their blood supply (90 %) from the hepatic artery, while normal parenchyma derives the majority of its blood supply (70–80 %) from the portal venous system [1]. Therefore, intra-arterial delivery can maximize dose given to tumor while minimizing side effects on normal tissue. Yttrium-90 is a pure beta-emitter with a mean tissue penetration of 2.5 mm and a maximum range of 1.1 cm [2, 3]. The small depth of penetration also contributes to the ability of this modality to minimize damage to normal tissue. Because of this, very high doses of radiation can be delivered to the tumor—up to approximately 150 Gy in a single treatment—compared to traditional external beam radiation therapy in which 30–35 Gy is often the threshold for development of side effects and risk for injury to adjacent organs [3, 4].

The two commercially available forms of Yttrium-90 microspheres are Selective Internal Radiation Spheres (SIR-Spheres, SIRTeX, biocompatible resin-based microspheres) and TheraSphere (MDS Nordion, glass microsphere). While

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both forms utilize the same radioactive source and method of delivery, there are differences in preparation which are outlined in Table 1. SIR-Spheres are provided in a 5-mL vial of sterile water for injection, with each vial containing 3 GBq of Yttrium-90. The individual microspheres have a size of 20–40 μm in diameter with an activity of approximately 50 Bq, thus each vial contains approximately 40–80 million microspheres. In contrast, TheraSphere is provided in 0.05 mL of sterile water and is available in six different activity levels, 3, 5, 7, 10, 15, and 20 GBq, with a corresponding number of microspheres/vial of 1.2, 2.4, 4.8, 4, 6, and 8 million, respectively. The individual microspheres have a size of 20–30 μm in diameter with an activity of 2500 Bq. [3, 5].

Radioembolization with Yttrium-90 is primarily used for non-resectable hepatocellular carcinoma (HCC). It can be utilized neoadjuvantly as a bridge to resection or transplantation, or as definitive treatment [4, 6, 7]. However, it may also be used for intrahepatic metastatic disease [2], which is the most common form of liver malignancy [5], as well as for intrahepatic cholangiocarcinoma (ICC) [8, 9]. There is extensive data in the literature regarding the efficacy of Y-90 and radioembolization treatments as a whole; however, there is very little data directly comparing the two available forms. This is likely due in part to the lack of access to both treatments at the same institution allowing for worthwhile data collection. The data that is available directly comparing SIR-Spheres to TheraSphere has primarily investigated their relative efficacy in HCC [10, 11].

Thus, the objective of this study was to determine which formulation was the most efficacious in the treatment of intrahepatic non-HCC lesions, including primary ICC and intrahepatic metastatic disease of any histology. We hypothesized that the TheraSphere form would have increased dose delivery to neoplastic tissue due to the small diameter and decreased rate of early stasis as well as the increased activity per individual microsphere.

Methods

A review of a prospectively collected, institutional review board-approved, institutional database was conducted in order to identify patients with intrahepatic malignancies excluding HCC who underwent Y-90 microsphere therapy. This consisted of cholangiocarcinoma as well as metastatic lesions. Dates of diagnosis ranged from February 1998 to August 2013.

Radioembolization technique

Visceral angiogram was performed to evaluate arterial anatomy and determine optimal placement of the microcatheter for embolization. Tc-99m-labeled macroaggregated albumin was delivered through the hepatic artery to assess hepatopulmonary shunting and to detect hazardous extrahepatic deposition. Shunt fractions were calculated by using planar scintigraphy. If eligible, the radioembolization device used was TheraSphere (MDS Nordion) or SIR-Spheres (SIRTeX) based on disease histology, concurrent chemotherapy use, and multidisciplinary discussion. Our method for calculating the required TheraSphere activity and the mean dose delivered to the liver and lungs has been published [12]. TheraSphere dose was delivered in strict accordance with the manufacturer's recommended guidelines. Our method for calculating the required SIR-Spheres activity was by the empirical model per the manufacturer's instructions [13].

Seventy-nine patients underwent SIR-Spheres therapy and 40 patients underwent TheraSphere therapy. Tc-99m MAA imaging was used to evaluate lung shunting, and SPECT/CT was used for determination of the prescribed dose. The response to treatment was assessed by CT using modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria.

Data for all patients with a diagnosis of intrahepatic malignancy other than HCC treated with Y-90 microspheres were 2extracted from the database and separated based on treatment modality (SIR-Spheres vs. TheraSphere), including demographics (age, weight, gender, performance status), prior liver surgery, extent of liver involvement, total number of liver lesions, presence of extrahepatic metastases, prior systemic chemotherapy, and concurrent chemotherapy.

Further data was collected regarding the technical outcomes of each Yttrium-90 treatment, including number of courses, time from diagnosis to first treatment, location of

Table 1 Differences in preparation of SIR-Spheres and TheraSphere

	SIR-Spheres	TheraSphere
Material	Resin-based microsphere	Glass microsphere
Size	20–40 μm	20–30 μm
Preparation	3 GBq/5 mL	Variable (3, 5, 7, 10, 15, and 20 GBq/0.05 mL)
No. of microspheres	40–80 million	Variable (1.2, 2.4, 4.8, 6, and 8 million, respectively)
Individual activity	50 Bq	2500 Bq

treatment, dose planned/received per treatment, and side effects that were documented for each treatment. Three-, 6-, and 12-month response using mRECIST criteria were assessed as well as overall survival to determine the relative efficacy of each treatment modality. Follow-up was obtained by the treating physician and is up to date from the end of the study.

Study schedule and outcome measures

Patients were assessed for any treatment-related adverse experiences for 1 month after each treatment. Adverse events were recorded per standard and terminology set forth by the Cancer Therapy Evaluation Program's Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Pre-therapy evaluation included a three-phase CT of the abdomen and pelvis. Follow-up protocol consisted of a three-phase CT scan of the liver within 3 months post-treatment. Tumor response rates were measured according to the European Association for the Study of the Liver (EASL) or mRECIST criteria [14, 15]. Follow-up was repeated every 3 months for the first year and every 6 months for the second year. Overall response rate (ORR) refers to the combination of complete and partial responders per mRECIST. Disease control rate (DCR) refers to the combination of all responders and those with stable disease. Overall survival (OS) was defined as the time between the treatment start date and death from any cause. Progression-free-survival (PFS) was defined as the time between the start of treatment and image-based disease progression or death.

Statistical analysis

Survival was estimated with Kaplan-Meier (KM) statistics, and the differences between responders and non-responders as well as the differences between each response category were compared using the log-rank test. Overall survival was evaluated from initial treatment to death of any cause. Patients that were lost to follow-up were censored. All statistics were computed using MedCalc software version 15.2.2 (Ostend, Belgium).

Results

Demographics and patient disease characteristics

A total of 119 patients were included in the study, and the population was subdivided into patients treated with resin/SIR-Spheres (n = 79) and patients treated with glass/TheraSphere (n = 40) as seen in Table 2. The mean age of the patients was 60.8 years (range 32–80) and 63.5 years (range 38–87) for the SIR-Spheres and TheraSphere groups, respectively. Disease histology between the two treatments was similar. In the SIR-Spheres group, 7 (8.9 %) patients had ICC compared to 4 (10 %) of TheraSphere patients. Colorectal metastatic disease was the histology of 37 (46.8 %) patients in the SIR-Sphere group compared to 15 (37.5 %) of the TheraSphere group. All other metastatic diseases were found in 35 (44.3 %) of SIR-Spheres patients and 21 (52.5 %) of TheraSphere patients (Table 3).

In the SIR-Spheres and TheraSphere groups respectively, 33 patients (42 %) and 16 patients (40 %) had <25 % liver involvement, 35 (44 %) and 20 (50 %) had 26–50 % liver involvement, and 11 (14 %) and 4 (10 %) had 51–75 % liver involvement. In the SIR-Sphere and TheraSphere groups respectively, the mean size was 8.04 cm (range 0.8–20.7 cm) and 6.04 cm (range 1.2–20 cm) with a p value of 0.08. Extrahepatic metastatic disease was also noted for both groups. In the SIR-Spheres group, there were 25 patients (32 %) with documented metastatic disease outside of the liver at the time of treatment, compared to 14 patients (35 %) in the TheraSphere group.

In the SIR-Spheres group, 16 patients (20 %) had undergone hepatic resection, 12 (15 %) had undergone an ablation procedure, and 59 (75 %) had not undergone any liver surgery prior to receiving treatment, compared to the TheraSphere group in which 7 patients (18 %) had undergone hepatic resection, 8 (20 %) had undergone an ablation procedure, and 30 (75 %) had not undergone liver surgery prior to receiving treatment. Additionally, prior and current systemic chemotherapy treatment was taken into consideration with particular attention to patients on bevacizumab. In the SIR-Spheres and TheraSphere groups respectively, 23 (29 %) and 6 (15 %) patients had received bevacizumab in the past, 22 (28 %) and 15 (38 %) patients had received some other form of systemic chemotherapy, and 34 (43 %) and 19 (48 %) patients had not received any chemotherapy. Of those currently receiving chemotherapy, there were no patients in either group receiving bevacizumab. However, in the SIR-Spheres group, 27 (34 %) were receiving some form of systemic chemotherapy and 52 (66 %) were not, compared to the TheraSphere group in which 21 (52.5 %) were receiving some form of chemotherapy and 19 (47.5 %) were not. The number of patients not receiving any form of concurrent systemic chemotherapy was statistically significant with a p value of 0.05. In review of our multi-disciplinary tumor conference (MDT) a greater percentage (69 %) of patients treated with SIR-Spheres were *not* discussed in MDT when compared to TheraSphere (2 %) (p = 0.01).

Technical outcomes

There were 112 total treatments in 79 patients in the SIR-Spheres group and 60 total treatments in 40 patients in the TheraSphere group. The maximum number of treatments any individual received in either group was 2. In the SIR-

Table 2 Population of 119 patients subdivided into patients treated with resin/SIR-Spheres and patients treated with glass/TheraSphere

	SIR-Spheres (n = 79)	TheraSphere (n = 40)	p value
Age, mean (range)	60.8 (32–80)	63.5 (38–87)	ns
Weight, mean (range) kg	84.4 (43–260)	83.4 (48.7–167)	ns
Gender			
Male	47 (60 %)	24 (60 %)	Ns
Female	32 (40 %)	16 (40 %)	Ns
KPS, median (range)	100 (80–100)	100 (80–100)	Ns
Prior liver surgery			
Hepatic resection (lobectomy)	16 (20.3 %)	7 (17.5 %)	ns
Ablation	12 (15.1 %)	8 (20 %)	
None	59 (74.7 %)	30 (75 %)	
Liver involvement			
<25 %	33 (41.8 %)	16 (40 %)	ns
26–50 %	35 (44.3 %)	20 (50 %)	
51–75 %	11 (13.9 %)	4 (10 %)	
>75 %	0	0	
Number of liver lesions			
Distinct, median (range)	37 (47 %), 2 (1–25)	24 (60 %), 3.5 (1–25)	0.08
Numerous	42 (53 %)	16 (40 %)	0.06
Total sum of all target lesions size, mean (range), cm	8.04 (0.8–20.7)	6.04 (1.2–20)	0.08
Extrahepatic metastases	25 (31 %)	14 (35 %)	ns
Prior systemic chemotherapy			
Bevacizumab	23 (29.1 %)	6 (15 %)	
Other	22 (27.8 %)	15 (37.5 %)	ns
None	34 (43 %)	19 (47.5 %)	
Concurrent chemotherapy			
Yes	27 (34.2 %)	21 (52.5 %)	
No	52 (65.8 %)	19 (47.5 %)	0.05

Spheres group, 35 patients (44 %) received 2 treatments, while in the TheraSphere group 20 patients (50 %) received 2 treatments. Location of treatment in each group (final catheter position prior to delivery) was documented. In the SIR-Spheres and TheraSphere groups respectively, 30 patients (38 %) and 16 patients (40 %) received treatment only to the right lobe, 8 (10 %) and 8 (20 %) to the left lobe, 34 (43 %) and 14 (35 %) received one treatment to each lobe, 5 (6 %) and 2 (5 %) received a single treatment to the entire liver, and 2 (3 %) and 0 patients' treatment locations were unknown due to lack of documentation. The mean dose intended per treatment was higher in the TheraSphere group with a median of 2.12 GBq (range 0.36–15 GBq) compared to the SIR-Spheres group with a median of 1.12 GBq (range 0.1–2.47 GBq), which was significant with a p value of 0.04. The mean dose delivered was also higher in the TheraSphere group at 100 % compared to the SIR-Spheres group at 92.7 % (Table 4).

Table 3 Disease histologies for both Y-90 therapies

	SIR-Spheres (n = 79)	TheraSphere (n = 40)	p value
Intrahepatic cholangiocarcinoma	7 (9 %)	4 (10 %)	Ns for all of them
Metastatic (colorectal)	37(47 %)	15(38 %)	
Metastatic (other)	35	21	
Breast	2	2	
Carcinoid	21	17	
Ovarian	1	0	
Melanoma	1	0	
Sarcoma	1	0	
Lung	1	1	
Other	8	1	

Safety and efficacy of treatment

There were no side effects documented in the TheraSphere treatment group, compared to 11 patients (14 %) experiencing

Table 4 Treatment specifics for both Y-90 therapies

	SIR-Spheres (n = 79)	TheraSphere (n = 40)	p value
Total number of treatments	112	60	
Mean/median time from diagnosis to first treatment	494 days, 285.5 days	615 days, 348.5 days	ns
Number of courses			
1	42	20	
2	35	20	
Location of treatment			ns
Right	30	16	
Left	8	8	
Both	34	14	
Whole liver	5	2	
Unknown	2	0	
Dose intended per treatment (median, mean, range) GBq	1.12, 1.14, (0.1–2.47)	2.12, 2.54, (0.36–15)	
Dose delivered per treatment (median, mean, range) GBq	1.02, 1.07, (0.027–2.47)	2.12, 2.54, (0.36–15)	0.04
Mean percentage dose delivered	92.70 %	100 %	

side effects in the SIR-Spheres group (p = 0.04) as detailed in Table 5. Of the 11 patients experiencing side effects in the SIR-Spheres group, 5 were documented as high grade (grade 3 or above per CTCAE).

Table 6 demonstrates the response to treatment by mRECIST criteria at 3-, 6-, and 12 months for each treatment group. The objective response rates (complete response + partial response) in the SIR-Spheres and TheraSphere groups respectively were 27.7 and 42.5 % at 3 months (p = 0.05), 16.4 and 35 % at 6 months (p = 0.04), and 25.4 and 35 % at 12 months (p = 0.07).

Number and types of post-radioembolization retreatment can be found in Table 7. Of the 40 patients receiving TheraSphere therapy, 29 had some sort of additional treatment post-radioembolization. Patients primarily received one type of treatment, but 5 patients did receive >1 type. The breakdown of type of adjuvant therapy was as follows: 22 patients were treated with systemic chemotherapy, 7 patients were treated with octreotide, 2 patients were treated with external beam radiation therapy, 1 patient was treated with partial hepatic resection, 1 patient was treated with radiofrequency ablation, and 1 patient was treated with bland embolization. SIR-Spheres patients had a lower rate of adjuvant therapy with only 30 of the 79 patients receiving treatment post-radioembolization. We did not see that adjuvant therapy after Y-90 was a factor for short-term (3 months) or long-term (12 months) toxicity. As with the TheraSphere group, patients primarily received one type of adjuvant therapy but 5 patients received >1 type. The breakdown of treatment for the SIR-Spheres group was as follows: 22 patients were treated with systemic chemotherapy, 8 patients were treated with octreotide, 4 patients underwent partial hepatic resection, 2 patients were treated with radiofrequency ablation, and 1 patient was retreated with SIR-Spheres.

Table 5 Adverse event profile for both Y-90 therapies

	SIR-Spheres (n = 79)	TheraSphere (n = 40)	p value
Side effects all grades(n)	11	0	0.04
Nausea and vomiting	4	0	
Pain	3	0	
Other (GI, heme, pulm, cardiac, death)	4	0	
Side effects high grade (≥3)	5	0	

Overall survival was calculated for both groups and detailed in Table 8a. The median overall survival was 15 months in the SIR-Spheres group compared to 34 months in the TheraSphere group. Mean survival was 22.3 months in the SIR-Spheres group compared to 34.7 months in the TheraSphere group. This result was statistically significant between the two modalities (log-rank 0.009). Survival was also calculated for the most common disease histologies, namely, ICC, metastatic colorectal cancer (CRC), and carcinoid tumor. These results are detailed in Table 8b. Median survival could be calculated for all histologies receiving SIR-Spheres therapy, but only CRC median survival could be calculated for those receiving TheraSphere therapy. Median survival was 7 months for ICC and 62.5 months for carcinoid tumor in the SIR-Spheres group. Median survival was 8 months for CRC in the SIR-Sphere group compared to 34 months in the TheraSphere group. Mean survival could be calculated for all histologies of both treatment modalities. For ICC, mean survival was 10.6 months in the SIR-Spheres

Table 6 (A) Response at 3 months (90 days) by mRECIST, (B) response at 6 months (180 days), and (C) response at 12 months (365 days)

	SIR-Spheres (n = 79)	TheraSphere (n = 40)	p value
(A)			
CR	4 (5 %)	1 (2.5 %)	0.05
PR	18 (22.7 %)	16 (40 %)	
SD	14 (17.7 %)	5 (12.5 %)	
PD	1 (1.2 %)	2 (5 %)	
DOD	12 (15.2 %)	1 (2.5 %)	
DOC	1 (1.2 %)	0 (0 %)	
(B)			
US	29 (36.7 %)	15 (37.5 %)	
CR	5 (6.3 %)	5 (12.5 %)	0.04
PR	8 (10.1 %)	9 (22.5 %)	
SD	5 (6.3 %)	5 (12.5 %)	
PD	3 (3.8 %)	4 (10 %	
DOD	21 (26.6 %)	4 (10 %)	
DOC	1 (1.2 %)	1 (2.5 %)	
US	38 (48.1 %)	12 (30 %)	
(C)			
CR	10 (12.7 %)	7 (17.5 %)	0.07
PR	10 (12.7 %)	7 (17.5 %)	
SD	6 (7.6 %)	7 (17.5 %)	
PD	4 (5 %)	4 (10 %)	
DOD	33 (41.8 %)	6 (15 %)	
DOC	2 (2.5 %)	2 (5 %)	
US	18 (22.8 %)	7 (17.5 %)	

group compared to 29.2 months in the TheraSphere group (log-rank 0.05). In CRC, mean survival was 16.3 months for SIR-Spheres therapy and 26.8 for TheraSphere therapy (log-rank 0.097). Lastly, for carcinoid tumor, mean survival was 40 months with SIR-Spheres therapy compared to 40.5 months with TheraSphere therapy (log-rank 0.104). See also Fig. 1.

Table 7 Post-Y-90 therapy

	SIR-Spheres	TheraSphere
No. of patients	30	29
Multi-modality adjuvant therapy	5	5
Chemotherapy	22	22
Octreotide	8	7
Hepatic resection	4	1
Radiofrequency ablation	2	1
External beam radiation	0	1
Y-90 retreatment	1	0
Bland embolization	0	1

Discussion

The two most common types of Y-90 treatments are SIR-Spheres, a resin-based microsphere, and TheraSphere, a glass microsphere. Both of these are pure beta-emitters that are delivered via catheter to an intrahepatic malignancy. While they are often used for hepatic primary disease such as hepatocellular carcinoma, they have also found use in other intrahepatic lesions such as cholangiocarcinoma and metastatic lesions.

To the best of our knowledge, there is no data in the literature directly comparing the two modalities for intrahepatic non-hepatocellular carcinoma lesions as we have done in this article. It is possible that the lack of literature is at least partially a result of the small number of institutions that have access to both therapies to make a direct comparison. Our own institution is in the unique position of having both modalities available to use for a wide range of diseases, which allow a more direct comparison to be done.

The primary data points of this study were 3-, 6-, and 12-month response rates to treatment as well as overall survival. Regarding the efficacy of the two modalities, we did find similar results to the HCC data that TheraSphere is more effective in improving objective response rate (complete + partial response) as well as overall survival, results which were statistically significant. While comparing the individual histologies did not show statistical significance between the two modalities, this is likely due to the number of cases seen as all results did trend toward significance. We reason that the effectiveness is due to the increased activity per microsphere in TheraSphere compared to SIR-Spheres combined with the smaller size of the microspheres that allow an increased density of radiation to be applied to the tumor with fewer spheres injected. This is further suggested by the statistically higher dose delivered per treatment between the two groups. Additionally, side effects from TheraSphere are significantly less than those seen with SIR-Spheres therapy, which further encourages the use of TheraSphere. Lastly was the greater use of synergistic/combination therapy through an MDT with TheraSphere that probably also played a role for these improved outcomes. Given the fact that neither of these therapies is approved as a solitary/mono-therapy in Met CRC, cholangiocarcinoma, or metastatic carcinoid, it stands to reason that all Y-90 therapy for these histologies should be performed in an MDT approach with combination systemic therapy.

The most striking difference between these modalities was the use of SIR-Spheres as a monotherapy, (i.e., without any systemic therapy 6 weeks prior or after SIR-Spheres use), which is obviously in direct contradiction to SIR-Spheres current regulatory approval guidelines.

Table 8 (A) Overall survival and (B) overall survival by disease histology

	SIR-Spheres		TheraSphere		Log-rank
Survival, months (95 % CI)	Median	Mean	Median	Mean	
(A)					
	15 (7–23)	22.3 (17.3–27.3)	34 (23–45.5)	34.7 (25.8–43.6)	0.009
(B)					
Cholangiocarcinoma	7 (0–16.5)	10.6 (3.7–17.3)	N/A	29.2 (17.1–37.3)	0.05
Metastatic Colorectal	8 (3–13)	16.3 (11–21.7)	34 (17–50.5)	26.8 (20.8–32.8)	0.097
Carcinoid tumor	62.5 (22.5–103)	40 (27–52.9)	N/A	40.5 (24.3–43.6)	0.104

The utilization of SIR-Spheres outside of an MDT runs the risk of the end user not understanding the biology of the patient's disease and utilizing SIR-Spheres without combination chemotherapy. Thus, the SIR-Spheres is utilized more in a "can treat" situation when all Y-90 utilization should be performed in a "should treat" situation, similar to any other local therapy. The optimal/responsible use of Y-90 cannot be underestimated given the high incidence of radiation-induced liver disease that occurs after 9–12 months of therapy in non-HCC patients. Thus, the optimal timing of treatment and optimal combination of chemotherapy is critical to long-term success and outcomes.

Conclusion

This study does have limitations, particularly the retrospective non-randomized nature. Additionally, small sample sizes and less than ideal follow-up at the specified intervals make some of the data difficult to interpret. However, to our knowledge, this is still the only series specifically comparing the two modalities for this particular population. Continued prospective studies should be undertaken to validate these data.

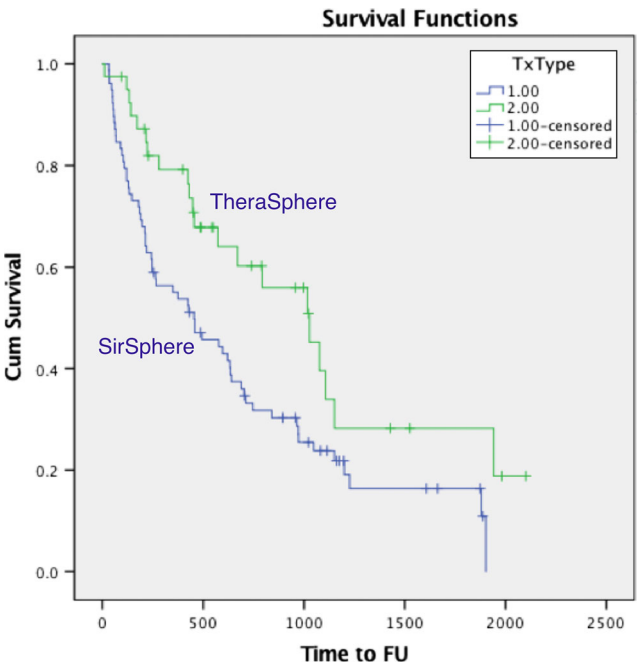

Fig. 1 Overall survival of all histologies for both Y-90 therapies

Compliance with ethical standards

Funding The work was supported by the Division of Surgical Oncology at the University of Louisville School of Medicine.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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