TOPIC HIGHLIGHT

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Role of stereotactic body radiotherapy for oligometastasis from colorectal cancer

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Abstract

Systemic chemotherapy has enabled prolongation of survival in patients with stage Ⅳ colorectal cancer. This has subsequently increased the relative significance of local therapy for patients with oligometastases because they can be cured by removal of oligometastatic lesions. One of the most frequently reported tumor histologies for oligometastases is colorectal cancer. Resection is the standard therapy in most settings of oligometastases. Recently, studies have shown that stereotactic body radiotherapy (SBRT) may become a treatment option that provides high local control with minimal morbidity. Two-year local control rates following SBRT for hepatic and pulmonary oligometastases are almost over 80% and are even higher for patients treated with high-dose regimens. The indications of SBRT for other metastatic sites or conditions include isolated lymph nodes, spinal and adrenal metastasis, and post-surgical pelvic recurrence. Many retrospective studies have indicated that SBRT for various lesions results in good outcomes with low morbidity, both in the curative and palliative setting. However, few reports with a high level of evidence have indicated the efficacy of SBRT compared to standard therapy. Hereafter, the optimal indication of SBRT needs to be prospectively investigated to obtain convincing evidence.

Key words: Oligometastasis; Colorectal cancer; Radiation therapy; Stereotactic ablation body radiation therapy; Local therapy

Core tip: Systemic chemotherapy has enabled prolongation of survival in patients with stage Ⅳ colorectal cancer. This has subsequently increased the relative significance of local therapy. Resection is the standard therapy in most settings. Recently, stereotactic body radiotherapy (SBRT) provides high local control with minimal morbidity, both in the curative and palliative setting. The indications of SBRT include liver, lung, isolated lymph nodes, spinal and adrenal metastasis, and post-surgical pelvic recurrence. However, few reports with a high level of evidence have indicated the efficacy of SBRT. Hereafter, the optimal indication of SBRT needs to be prospectively investigated to obtain convincing evidence.

INTRODUCTION

Colorectal cancer (CRC) is currently the second- or third-leading cause of death from cancer in both genders, and its frequency continues to increase[1,2]. Although there ex-

ist somewhat different characteristics between colon cancer and rectal cancer[3,4], most articles investigated them together. Among patients with CRC, 20% have metastases at initial presentation, and an additional 25%-50% develop metastases after treatment of early-stage disease. Among patients with an initial finding of metastasis, 50% will have disease limited to the liver, and at the time of death, 20% have liver metastasis only[5]. Rates of metastases are 60%-71% in the liver, 25%-40% in the lung, 5%-10% in bones, 3%-5% in the ovary, 1% in the adrenal gland, and 1% in the central nervous system[6].

Since the late 1990s, development of new agents such as irinotecan, oxaliplatin, and biologic agents targeting either epidermal growth factor receptor or vascular endothelial growth factor has greatly prolonged progression-free survival and overall survival in stage IV CRC patients[7,8]. Such prolongation of survival attributed to chemotherapy has increased the relative significance of local therapy for patients with limited metastases. An increasing amount of data suggests that curative resection of isolated metastases yields a survival benefit regardless of whether the metastatic site is the liver[9,10], lung[11,12], peritoneum[13,14], ovary[15,16], or extra-regional lymph nodes[17,18]. Although complete surgical resection of these metastases does not result in long-term survival in all patients, select patients can survive for a relatively long period without recurrence.

Stereotactic body radiotherapy (SBRT) is a high-precision conformal external-beam radiation technique that ablates the target at extracranial sites with hypofractionated high-dose radiation while sparing the surrounding normal tissue. SBRT results in minimal morbidity and provides high local control rates for medically inoperable stage I non-small-cell lung cancer (NSCLC)[19]. Currently, SBRT is considered to be a treatment option for patients with medically inoperable, early-stage NSCLC[20]. However, few adequate studies have evaluated SBRT for pulmonary oligometastases from CRC[21]. In this article, we review the clinical outcomes of SBRT for oligometastases from CRC and discuss the role of SBRT in oligometastasis treatment in general.

CONCEPT OF OLIGOMETASTASIS

Hellman *et al*[22] first proposed the idea of an oligometastatic state in 1995. These authors suggested that initially, a few metastases from various cancers exist, before the malignant cells acquire widespread metastatic potential. The term oligometastases indicates an intermediate state of cancer that lies between localized disease and widespread metastases. Metastases from solid tumors are regarded as being representative of disseminated cancer and are not considered to be curable. In contrast, evidence has emerged that patients with oligometastases can be cured by resection of these lesions. The most frequently reported tumor histologies in one surgical series of oligometastases were CRC and sarcoma[23]. Resection of liver metastases from CRC patients resulted in 5-year survival rates of 25%-50%[24-26], and a large series

of more than 1000 patients reported a 10-year overall survival rate of 22%[27]. Among resection survivors who lived for 10 years, Tomlinson *et al*[28] demonstrated high disease-specific survival, with only 1 cancer death among 102 patients, reinforcing the concept that this group was truly cured of cancer.

For patients with oligometastases from CRC, non-invasive local therapy is appropriate because they are already receiving systematic chemotherapy, are often frail, and may survive only a short time. In addition to resection, local ablation therapies such as cryoablation and radiofrequency ablation (RFA) have been reported to be feasible treatment options. SBRT may become a more suitable treatment option for these patients, because less morbidity occurs following SBRT than that following RFA[29] and resection.

CONVENTIONAL RADIOTHERAPY AND SBRT

Conventional radiotherapy (*i.e.*, 1.8-2.0 Gy per fraction) results in a tumoricidal effect by means of mitotic death of cancer cells, allowing simultaneous recovery of late sublethal damage of normal tissues. In contrast, SBRT may provide a novel mechanism of radiation-induced damage: data with higher doses per fraction (*i.e.*, 10-20 Gy per fraction) suggest that, in addition to direct cytotoxicity, a different mechanism involving microvascular damage begins to have a substantial effect on the tumor cell kill[30,31]. Endothelial apoptosis results in microvascular disruption and death of the tissue supplied by that vasculature[30].

Over 1 decade ago, conventional radiotherapy was offered to medically inoperable patients with stage I NSCLC. The prescribed doses of 60-75 Gy per 1.8-2 Gy fractions were administered to these patients. However, those doses were determined based on critical doses of serious radiation pneumonitis rather than sufficient doses to achieve high local control of primary lesions. Therefore, the 5-year local control and overall survival rates were insufficient (40% and 21%, respectively)[32]. In contrast, SBRT enables delivery of sufficiently high doses to a target volume and omission of unnecessary doses to surrounding normal lung tissue. Therefore, 5-year local control and overall survival rates associated with SBRT are relatively high (> 90% and 42%, respectively)[33]. Currently, SBRT is an established treatment option for medically inoperable patients with stage I NSCLC. Furthermore, a propensity score-matched analysis revealed superior local control and comparable overall survival of SBRT compared to video-assisted thoracoscopic surgery[34]. In addition, SBRT appears to be less costly than surgery[35]. Quality of life also appears to favor SBRT, because no statistically or clinically significant worsening of any quality of life functioning or symptom scores has been observed in patients with stage I NSCLC treated with SBRT[36]. In contrast, quality of life has been shown to be significantly impaired after surgery. Randomized,

controlled trials to compare SBRT to resection are therefore needed.

The liver is thought to be a relatively radiosensitive organ. It was difficult to irradiate with a sufficient dose to eradicate tumors without causing lethal radiation-induced liver disease. Therefore, conventional radiotherapy has played a very limited role in the treatment of hepatocellular carcinoma[37]. In contrast, reports of SBRT for hepatocellular carcinoma have been steadily increasing since 2006. Although the SBRT literature primarily consists of retrospective, small, single-institution series, SBRT has been associated with high local control rates, most in the range of 70%-90% at 1-2 years[38-40]. In a retrospective analysis of previously untreated hepatocellular carcinoma, SBRT yielded a 3-year overall survival rate of 73%, which is comparable to that of a series treated with surgery or RFA[41].

As for NSCLC and hepatocellular carcinoma, SBRT is expected to play a role in the treatment of oligometastases from CRC. However, negative factors also exist: for example, CRC metastases contain larger proportions of hypoxic cells compared to other tumor types[42], and hypoxia leads to a decrease in radiosensitivity; another is that microscopic extension of oligometastases from CRC may compromise local control[43]. In fact, the local control rates of SBRT in CRC oligometastases are significantly worse than those of oligometastases from other cancers, including NSCLC. Thus, dose escalation should be considered to achieve better local control[44].

SBRT FOR OLIGOMETASTASES BY SITE

Several studies have investigated SBRT for oligometastases. However, these have been retrospective and included small sample sizes. Furthermore, patients in these studies were affected by a variety of primary cancers in addition to CRC. Therefore, it is difficult to refer to the outcome of SBRT for oligometastases from CRC exclusively.

LIVER METASTASIS

Combination chemotherapy and resection of liver metastases has been used to manage patients with confined liver metastasis from CRC. According to the Clinical Practice Guidelines in Oncology by the National Comprehensive Cancer Network (NCCN), resection is the mainstay of treatment for CRC patients with liver metastases only[45]. This combined therapy has resulted in 5-year survival rates of 25%-50%[24-26]. The cumulative 3-year local recurrence-free survival rate following resection of solitary liver metastases was reported to be 88%-95%[46,47]. However, hepatic metastases are resectable in only about 20% of patients[48]. For the remaining 80% of patients, resection is contraindicated due to the presence of diffuse hepatic metastases, non-resectable extrahepatic disease, or impaired liver function.

Several technical improvements have been made in diagnostic assessment and treatment strategies for CRC hepatic metastases. For example, modern computed tomography (CT), magnetic resonance imaging, and positron-emission tomography-CT techniques enable accurate diagnosis and staging. Furthermore, surgical dissection techniques and potent systemic chemotherapy protocols have been optimized. As a result, even patients with > 3 metastases or with metastases > 5 cm in diameter can be cured with appropriate surgical treatment[28].

Resectability is often limited by an unfavorable anatomical metastatic site, poor function of the remaining hepatic parenchyma, and/or poor general patient condition. Postoperative hepatic function can be predicted more precisely with the aid of CT volumetry. This technique enables prediction of the remaining volume of hepatic tissue after surgery to within 10% of the actual value. Metastases are considered resectable[49] when the following criteria are met: (1) exclusion of a non-resectable extrahepatic tumor manifestation; (2) parenchymal involvement < 75%; (3) < 3 hepatic veins and < 7 hepatic segments involved; (4) no hepatic insufficiency, *i.e.*, no Child B or C cirrhosis; and (5) no severe accompanying diseases.

Retrospective studies of SBRT in patients with medically or technically unresectable liver metastases have been performed. Table 1 shows the outcomes of SBRT for liver metastasis from CRC and other origins[50-58]. Various prescribed doses of SBRT were used in these studies. The 2-year local control rates were almost over 80% and were higher for patients treated with high-dose regimens in two studies[51,57]. The 2-year overall survival rates varied from 32%-83%. It is important to note that these outcomes may depend on biased patient selection. And yet, little toxicity was observed.

As a local treatment, the use of RFA is controversial. Most centers only ablate tumors in those patients who are deemed unresectable. Patients with large, poorly placed tumors have the highest likelihood of recurrence, regardless of therapy. Retrospective analyses of RFA for liver metastases from CRC have shown broad variability in 2-year local control rates, ranging from 32%-76%[46,59-61], and in 5-year overall survival rates, ranging from 14%-55%[46,61]. A meta-analysis revealed that RFA yielded a higher rate of local intrahepatic recurrence compared to resection (OR = 4.89), although a selection bias was noted[62].

PULMONARY METASTASIS

As chemotherapeutic and biological agents have considerably improved outcomes in patients with stage IV CRC, resection of pulmonary oligometastases is increasingly performed with curative intent. In the NCCN Clinical Practice Guidelines, pulmonary resection is recommended as well as hepatic oligometastatic resection[45]. However, no prospective randomized studies have been performed to validate the efficacy of resection in this setting. Therefore, it is currently not possible to identify which CRC patients may benefit most from this surgical strategy[63].

A meta-analysis revealed that factors correlated with

Table 1 Summary of stereotactic body radiotherapy for liver metastasis

Ref.	Study	Patients (*n*) (primary sites)	Meta (*n*)	Institution	MFU (mo)	Dose (Gy)/fr	Time (d)	Prescription specification	LC (mo)	OS (mo)	Toxicity	*P* value
Herfarth *et al*[50]	P I	CRC (*n* = 18) others (*n* = 14)	60-	Heidelberg Univ	15	14-26/1	1	Isocenter, PTV surrounded by 80% isodose	0% (24)	32% (24)	N MT	*P* < 0.01
	P II					26/1	1		81% (24)	83% (24)		
Wulf *et al*[51]	Retro	39	CRC (*n* = 23) others (*n* = 28)	Wuerzburg Univ	15	28-30/3-4 36-37.5/3 or 26/1	2-3 interval	PTV periphery: 65% isodose of maximum	58% (24) 82% (24)	81% (24 for all)	N MT	*P* = 0.08
Katz *et al*[52]	Retro	CRC (*n* = 20) others (*n* = 49)	174	Rochester Univ	15	50/5f preferred	14	Maximum, PTV surrounded by the 80% isodose	57% (20)	37% (20)	N MT	
Rusthoven *et al*[53]	P I / II	CRC (*n* = 20) others (*n* = 49)	63	Multi-institution	16	36-60/3	< 14	Isocenter, PTV surrounded by 80%-90% isodose	92% (24)	30% (24)	Grade 3: 2%	
Lee *et al*[54]	P I	CRC (*n* = 40) others (*n* = 28)	-	Princess Margaret Hospital	11	27.7-60/6 (median: 41.8)	> 14	PTV periphery: 71% isodose of maximum	71% (12)	47% (18)	N MT	
van der Pool *et al*[55]	Retro	CRC (*n* = 20)	31	Erasmus Univ	26	37.5-45/3f preferred	5-6	D95 of PTV	74% (24)	83% (24)	N MT	
Rule *et al*[56]	P I	CRC (*n* = 12) others (*n* = 15)	36	Texas Southwestern Univ	20	3/30 50/5 60/5	< 14 ≤ 17 ≤ 17	PTV periphery, 70%-85% isodose of maximum	59% (24) 89% (24) 100% (24)	56% (24) 67% (24) 50% (24)	N MT	
Vautravers-Dewas *et al*[57]	Retro	CRC (*n* = 30) others (*n* = 15) CRC (*n* = 30) others (*n* = 15)	62	Centre Oscar Lambret	14	40/3 45/3	4-17 (mean: 9)	PTV periphery, 80% isodose of the maximum	86% (12) 100% (12) 86% (12) 100% (12)	48% (24 for all)	N MT	*P* = 0.07 *P* = 0.07
Scorsetti *et al*[58]	P II	CRC (*n* = 29) others (*n* = 32)	76	Humanitas Cancer Center	12	52.5-75/3	3	Mean dose to PTV	90.6% (24)	37% (24)	N MT	

MFU: Median follow up duration; LC: Local control rate; OS: Overall survival rate; P X: Phase X; retro: Retrospective; CRC: Colorectal cancer; fr: Fractions; PTV: Planning target volume; Dx: The dose delivered to x%; N MT: No major toxicity.

better survival included a prolonged disease-free interval between primary tumor and metastatic spread, normal pre-thoracotomy carcinoembryonic antigen levels, absence of thoracic node involvement, and a single pulmonary lesion[64]. Of 44 patients with ≥ 3 lesions and a < 1-year disease-free interval, 0 were cured by surgery. In contrast, recurrence-free survival was 49% at 3 years for patients with 1 lesion and a disease-free interval > 1 year. Therefore, medical management alone should be considered standard for patients who have ≥ 3 pulmonary metastases and a < 1-year disease-free interval[65].

Crude local recurrence rates following resection of oligometastasis from CRC have been reported to be 19.5%-28%[66-68]. Local recurrence may occur even in cases with pathologically negative margins[69]. A wide surgical margin around oligometastasis from CRC is required to prevent local recurrence, because satellite tumor cells are often present[68].

For medically inoperable patients with limited pulmonary metastases from CRC, SBRT may be administered. Table 2 shows the outcomes of SBRT for pulmonary metastases from CRC and other origins[44,70-80]. SBRT was given at various prescribed doses. The local control rates were almost over 80%, and the 2-year overall survival rates ranged from 33%-86%. These outcomes may have depended on patient selection. With respect to toxicities, grade ≥ 3 radiation pneumonitis was observed in only 0%-8% of patients. No other toxicities were observed.

Widder *et al*[78] compared outcomes after SBRT with those after pulmonary metastasectomy in patients with pulmonary oligometastasis. In their institution, patients were offered pulmonary metastasectomy as the first choice and SBRT in cases that they considered to be less suitable surgical candidates. Patients treated with SBRT had more unfavorable prognostic factors: they were significantly older, had a shorter metastasis-free interval, and a different distribution of primary tumor origins; thus, they were regarded as having a worse prognosis overall. Despite this selection bias, survival after SBRT was no worse than that after pulmonary metastasectomy. Prospective comparative studies are therefore required to define the role of both SBRT and pulmonary metastasectomy in oligometastatic disease.

Among minimal ablation techniques, RFA is the most

Table 2 Summary of stereotactic body radiotherapy for pulmonary metastasis

Ref.	Study	Patients (n) (primary sites)	Meta (n)	Institution	MFU (mo)	Dose (Gy)/	Time (d)	Prescription specification	LC (mo)	OS (mo)	Toxicity	P value
Wulf et al[70]	Retro	CRC (n = 4) others (n = 37)	51	Wuerzburg Univ	10	30-37.5/3 or 26/1	2-3 interval	PTV periphery: 65% isodose of maximum	80% (24)	33% (24)	N MT	
Okunieff et al[71]	Retro	CRC (n = 14) others (n = 35)	125	Rochester Univ.	19	Oct-50	1-5 times per week	Isocenter	91% (24)	38% (24)	Grade 3 pleural effusion: 2%	
Norihisa et al[72]	Retro	CRC (n = 14) others (n = 35)	43	Kyoto Univ.	27	48-60/4	4-18 (med: 12)	Isocenter	90% (24)	84.3% (24)	Grade 3 RP: 3%	
Kim et al[73]	Retro	CRC (n = 13)	18	Korea Cancer Center	28	39-51/3	3	PTV periphery: 75%-80% isodose of maximum	53% (24)	76% (24)	N MT	
Rusthoven et al[74]	P I/II	CRC (n = 9) others (n = 29)	63	multi-institution	15	48-60/3	< 14	Isocenter, PTV surrounded by 80%-90% isodose	96% (24)	39% (24)	Grade 3 RP: 8%	
Takeda et al[44]	Retro	CRC (n = 15) others (n = 19)	CRC (n = 21) others (n = 23)	Ofuna Chuo Hospital	29 15	May-50	5	PTV periphery: 75%-80% isodose of maximum	72% (24) 94% (24)	- -	N MT	P < 0.05
Oh et al[75]	Retro	57	67 CRC, HCC (n = 16) others (n = 51)	Samsung Medical Center	21	50-60/4-5	-	PTV periphery: 75%-80% isodose of maximum	92% (24) 81% (24) 100% (24)	57% (24)	Grade 5 RP: 2%	P = 0.01
Ricardi et al[76]	Retro	61	77	Giovanni Battista Univ	20	26/1 or 36-45/3	3	PTV periphery:	89% (24)	66.5% (24)	Grade 3 RP: 2%	
Inoue et al[77]	Retro	22	31	Hokkaido Univ.	25	Apr-48	4-7	80% isodose of maximum isocenter	100% (24)	80% (24)	N MT	
Widder et al[78]	Retro	CRC (n = 31) others (n = 11)	≥ 65	Groningen Univ	43	3/8/1960	-	PTV periphery: adapted risk of toxicity	94% (24)	86% (24)	-	
Inoue et al[79]	Retro	CRC (n = 37) others (n = 50)	≥ 150	Miyakojima IGRT Clinic	15	48/4, 52-60/4 or 50/5	4-5	-	80% (24)	47% (24)	Grade 3 RP: 6% Grade4 RP: 1%	

MFU: Median follow up duration; LC: Local control rate; OS: Overall survival rate; P X: Phase X; retro: Retrospective; CRC: Colorectal cancer; fr: Fractions; PTV: Planning target volume; Dx: The dose delivered to x%; N MT: No major toxicity; RP: Radiation pneumonitis.

frequently used method for pulmonary oligometastasis. In a prospective multicenter trial[81], RFA yielded a confirmed complete response rate of 88% (in both primary and metastatic lesions) and promising overall and cancer-specific survival outcomes. Retrospective analyses of RFA for pulmonary metastases from CRC have shown that the 2-year local control rates in all tumors, tumors < 3 cm, and tumors > 3 cm were 56%-80%, 69%-87%, and 19%-32%[82,83], respectively, and that the 2-year overall survival rate was 34%-68%[82-84].

ISOLATED LYMPH NODE METASTASIS

Retroperitoneal recurrence occurs in 15% of colon cancer cases and 5% of rectal cancer cases[85], and isolated retroperitoneal recurrence occurs in approximately 1% of all CRC patients following curative surgery[13,18]. Favorable results have been reported for curative surgical resection for isolated retroperitoneal lymph node recurrence of CRC[13,18]. However the indication for resection is limited. Surgery for metastatic retroperitoneal lymph nodes is not feasible when (1) a recurrent retroperitoneal tumor is encased in or involves major vascular structures such as the superior mesenteric artery, celiac axis, and aorta; (2) the tumor invades adjacent organs such as the pancreas, bile duct, and duodenum; or (3) the patient has a poor performance status or comorbid disease[13,18]. Even when lesions are localized, surgical resection is not widely accepted due to their relative rarity, high associated postoperative morbidity, and poor prognosis. In addition, the operative morbidity rate is high at 30%, which includes abscess, phlebitis, pneumonia, intestinal obstruction, and bladder

leakage[13,18].

The role of curative radiotherapy for isolated lymph node metastasis is also controversial. In a study that evaluated SBRT for isolated lymph node metastasis from CRC, preliminary results from 7 patients who received doses of 36-51 Gy in 3 fractions indicated local recurrence and Grade 4 intestinal obstruction in 1 patient each[86]. Furthermore, the 3-year overall survival rate was 71%. The indication of SBRT in this setting is also limited because the lesions are often adjacent to the gastrointestinal tract. Considering the risk of gastrointestinal toxicities, conventional fractionated radiotherapy may be a better choice. Chemoradiotherapy with prescribed doses of 55.8bed Gy in 2020 escribed doses of 55.8bed doses of 55.8 was 71% results, with a 3-year overall survival rate of 65% and no gastrointestinal toxicity ≥ Grade 3[87].

METASTASIS OF OTHER REGIONS

SBRT has played a limited palliative role in the treatment of the sites described above, and may not contribute to improved survival. The indications of SBRT remain to be determined and should be considered based on the condition of each individual patient.

Among patients treated with radical surgery for rectal cancer, 20%-50% develop loco-regional recurrence[88,89]. Most patients are not candidates for curative resection of recurrent pelvic disease, and even when radical surgery is possible, the 5-year survival rate after reoperation is < 35%. When no treatment is given, patients with locally recurrent rectal cancer have a median survival of ≤ 8 mo and suffer from severe symptoms, particularly pain, resulting in an extremely poor quality of life[89-91]. In most patients, radiotherapy and chemotherapy provide only temporary symptom relief. Kim *et al*[92] reported that 23 patients with recurrent rectal cancer were treated with SBRT at a median total dose of 39 (range, 30-51) Gy in 3 fractions. The 4-year overall survival and local control rates were 25% and 74%, respectively. Grade 4 rectal perforation was reported in 1 patient. Abusaris *et al*[93] reported that symptom relief was observed in 96% in 27 patients who were re-irradiated with SBRT after conventional radiotherapy.

In patients with spinal metastasis, conventional radiotherapy is standard palliative therapy. In contrast, SBRT enables irradiation using a higher biologically effective dose compared to conventional radiotherapy. The goal of SBRT is, therefore, aimed at maximizing both local tumor and pain control. Local control appears to be excellent, with crude rates of 81%-94%[94], although the prescribed doses vary significantly among series. A multi-institutional study revealed that caution must be used when treating with ≥ 20 Gy/fraction, particularly for patients with lytic tumors, spinal misalignment, and baseline vertebral compression fracture[95].

The incidence of adrenal metastases from CRC is approximately 1%[6]. With continuing progress in imaging techniques, an increasing number of adrenal metastases can be detected incidentally during follow-up or at the time of initial presentation. Open surgery represents the standard approach. Radiotherapy has been limited to palliation of painful adrenal metastases from lung cancer[96]. Radiotherapy contributes to prolonged survival in these patients[97]. Results of SBRT for adrenal metastasis from various origins have been reported: the 2-year local control rate was 32% with a median total dose of 32 Gy in 4 fractions[98] and 90% with a median total dose of 36 Gy in 3 fractions[99], without any ≥ Grade 3 toxicities.

FUTURE PERSPECTIVE

Many studies of SBRT for oligometastasis were retrospective and consisted of small sample sizes. In addition, patients in these studies were often affected by various types of primary cancer. We do not think the reasons for the small sample sizes and heterogeneous characteristics are uncommon indications or negative outcomes of SBRT for oligometastasis. In fact, these studies showed an improvement of survival and quality of life with low morbidity. In the future, we should evaluate whether SBRT is a valid treatment modality with a higher evidence level. For curative intent, dose escalation should be attempted for patients with pulmonary and hepatic oligometastasis to achieve better local control and subsequently to improve survival. SBRT outcomes may conceivably be comparable to those of surgery, with less morbidity in some patients. For palliative intent, optimal indications need to be defined. SBRT may have nearly equivalent efficacy compared to resection, with a shorter treatment duration and hospital stay, as well as a better quality of life. These questions should be addressed in future studies.

CONCLUSION

Many retrospective studies indicate that SBRT for various lesions achieves good outcomes with low morbidity, both in curative and palliative settings. However, few reports with a high evidence level have compared the efficacy of SBRT to that of standard therapy. Moving forward, we should prospectively investigate the indications for SBRT in robust studies.

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