Original Article

Current usage of stereotactic body radiotherapy for oligometastatic prostate cancer in Korea: patterns of care survey (KROG 19-08)

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Background: Growing evidence suggests that metastasis-directed therapy and/or prostate-directed therapy may benefit patients with oligometastatic prostate cancer (OMPC). Stereotactic body radiotherapy (SBRT) is increasingly used to treat oligometastases in various cancers. The purpose of this study was to investigate the current patterns of curative-intent SBRT for OMPC in Korea.

Methods: A 20-item questionnaire was sent to 326 radiation oncologists in 93 institutions in Korea. Only 1 physician per institution was required to complete the survey. Subsequently, the second survey consisting of 3 clinical scenarios was sent to 64 physicians with clinical experience in SBRT: case 1, cT4N0M1 (direct invasion to two pelvic bones); case 2, cT2N0M1 (three bone metastases); and case 3, solitary spine metastasis after radical prostatectomy.

Results: Seventy-six physicians from 93 institutions (82%) answered the first survey. The multidisciplinary team approach was practiced in 16 institutions (21%). Most physicians (75%) agreed on the definition of oligometastases as limited lesions and/or organs ≤5: 25% agreed with low-volume disease according to CHAARTED trial. During the last year, 49 physicians (64%) treated OMPC patients with curative intent. Sixty four physicians (84%) had a clinical experience with SBRT: 48 (75%) stated that both dose and fraction number should be considered when defining SBRT, whereas others (25%) stated that only fraction size should be considered. Fifty-five faculties (86%) answered the second survey. Physicians agreed with oligometastases in 89% for case 1, in 80% for case 2, and in 100% for case 3. The rate of SBRT application was the highest in case 3 (70%).

Conclusions: There was diversity in the patterns of SBRT for OMPC in Korea. Additional prospective studies are necessary to strengthen evidence regarding role of SBRT in OMPC.

Keywords: Korea; oligometastases; prostate cancer (PC); stereotactic body radiotherapy (SBRT); survey

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Introduction

Cancer is one of the major leading causes of death worldwide, and prostate cancer (PC) is the second most common malignancies among men worldwide. In Korea, PC is the fourth common cancer, and its incidence has been continuously increasing since 1999: approximately 10% of patients are diagnosed at distant metastatic stage (1). In patients with metastatic hormone sensitive PC, the standard treatment is androgen deprivation therapy (ADT) alone or in combination with apalutamide, abiraterone, or docetaxel with palliative intent (2,3). Unfortunately, most patients develop castration-resistant PC (CRPC) within 5 years of diagnosis, and CRPC is considered a lethal disease due to the lack of optimal treatment, although several new drugs for CRPC have shown survival benefits (4). Against this background, recent some prospective and retrospective studies reported that local treatments such as metastasis-directed therapy (MDT) and/or prostate-directed therapy (PDT) improved the survival in oligometastatic prostate cancer (OMPC), suggesting a shift in the management of metastatic PC (5-7).

The concept of oligometastases was first proposed by Hellman and Weichselbaum in 1995. For certain tumors, the anatomy and physiology may limit or concentrate theses metastases to a single or a limited number of organs, and local modalities such as radiotherapy (RT) can improve the patients' survival and have a curative potential (8). However, the definition of oligometastases remains ambiguous. Therefore, different study groups set their own arbitrary criteria, based on the total number of metastatic lesions and/or organs. Although a new technology, stereotactic body radiotherapy (SBRT), allows the delivery of high radiation doses, no consensus has been reached on the universally sufficient radiation doses to ablate oligometastases (9). The emerging interest in OMPC led to the increasing application of SBRT with a potentially curative intent; its patterns of practice vary widely in the absence of high-level evidence.

Therefore, the Korean Stereotactic Radiosurgery Group of the Korean Society for Radiation Oncology (KOSRO) conducted a national patterns-of-care survey to better understand the patterns of curative-intent SBRT practice for OMPC in Korea. We present the following article in accordance with the SURGE reporting checklist (available at https://dx.doi.org/10.21037/atm-21-1116).

Methods

A 20-item questionnaire was sent by an e-mail to 326 radiation oncologists, who are full members of KOSRO, at 93 institutions in Korea in October 2019. The questionnaire was based on their clinical experience with OMPC and SBRT. Only 1 physician per institution was required to complete the survey sent by e-mail within 1 month. We selected one survey by order of arrival when we received multiple replies from 1 institution at the same time. Subsequently, the second survey was sent to 64 radiation oncologists in 64 institutions who had clinical experience in SBRT. The second survey consisted of questions regarding three OMPC cases. The complete survey was returned by e-mail within 1 month. The full contents of the two surveys are available in Appendix 1 and 2. In the event of non-response, the respondents were contacted by telephone and sent e-mails in order to achieve a response rate of more than 80%. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the institutional review board of Soonchunhyang University College of Medicine, Bucheon (IRB No. 2019-08-023-001). The need for written informed consent from the participants was waived because this study was a survey that used retrospective data of patients who were treated and we anonymized and de-identified all records and information prior to analysis so as not to infringe any patients' rights. This study was also conducted under the authorization and cooperation of the Korea Radiation Oncology Group (KROG 19-08).

Results

Clinical experience (number of respondents =76)

Seventy-six physicians (82%) from 93 institutions responded to the first survey. Sixteen physicians have been working as radiation oncologists for <5 years after completing residency, 19 for 5–9 years, 18 for 10–19 years, and 23 for ≥20 years. Approximately 51% of these physicians are working in tertiary referral hospitals, and 46% are working in secondary care hospitals. The multidisciplinary team approach for PC patients has been adopted in 16 institutions (21%): regularly in 7 institutions and irregularly in 9 institutions. There is a radiation oncologist as a specialist for urology in 75% of respondents. The remaining institutions have either only one radiation oncologist (13%) or a non-urologic cancer specialist (12%). The annual per-physicians cases of radical RT for PC were as follows: ≤5 cases in 4 physicians (5%), 6–10 in 6 (8%), 11–30 in 27 (35%), 31–50 in 22 (29%), 51–100 in 11 (15%), and 101–300 in 6 (8%). We presented the physicians' working period and the annual per-physicians cases at *Figure 1*. The association between the physicians' working period and

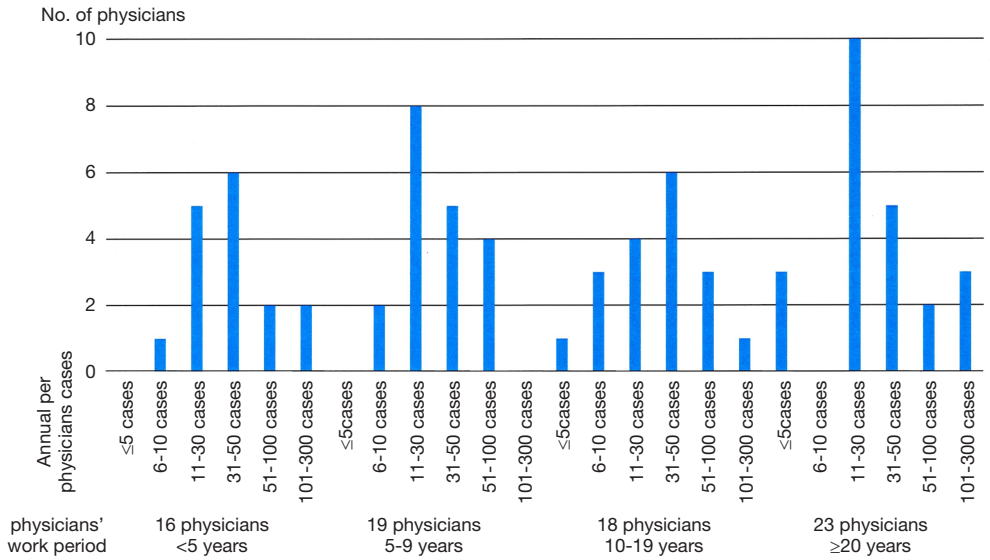


Figure 1 The annual per-physicians cases of radical radiotherapy for prostate cancer according to physicians' work period.

Table 1 The definition of oligometastatic prostate cancer (n=76)

Definition	N	%
1. Low-volume according to CHAARTED trial[a]	19	25
2. Limited lesions and/or organs	57	75
Number of lesions		
1	1	
2–3	29	
4–5	27	
Number of organs		
1	17	
2–3	32	
5	8	

[a], means all other patients except for patients with a high volume of metastases, which was defined by the presence of visceral metastases or four or more bone lesions with at least one beyond the vertebral bodies and pelvis. CHAARED, Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer.

Table 2 Required imaging studies to establish oligometastatic prostate cancer (n=76)

Image work up[a]	N	%
1. Prostate MRI	76	100
2. Whole body bone scan	69	91
3. AP CT/chest CT	49	65
4. Spine MRI	30	40
5. FDG PET-CT	28	37
6. Choline or PSMA PET-CT	5	7
7. Bone SPECT	1	1

[a], the respondents selected multiple answer. MRI, magnetic resonance imaging; CT, computed tomography; FDG, ^{18}F-fluorodeoxyglucose; PET, positron emission tomography; PSMA, prostate-specific membrane antigen, SPECT, single-photon emission computed tomography.

SBRT experience is shown in Figure S1.

View on oligometastases (number of respondents =76)

Fifty-seven respondents (75%) agreed with the definition of OMPC as 5 or less metastatic lesions and/or organs ≤5, whereas only 19 (25%) responded that oligometastases constituted a low metastatic burden based on the CHAARTED trial criteria (*Table 1*) (10). Physicians rely on diverse imaging studies to establish a diagnosis of OMPC (*Table 2*). Twenty-seven radiation oncologists (35%) had no experience treating OMPC patients with a curative intent. For the remaining 49 physicians, the annual number of OMPC patients referred for RT with curative intent are ≤5 in 49% (37 physicians), 6–10 in 11% (8), 11–20 in 4% (3), and ≥21 in 1% (1). All 49 physicians agreed on the use of

Table 3 Target volumes and timing of radiotherapy (RT) for initially diagnosed oligometastatic prostate cancer (n=76)

	N	%
Target volume		
1. No case	27	36
2. No RT	0	0
3. Prostate only	4	5
4. Up to 1–2 metastases only	5	7
5. Up to 3 metastases only	3	4
6. Up to 4–5 metastases only	0	0
7. Prostate and up to 1–2 metastases	14	18
8. Prostate and up to 3 metastases	16	21
9. Prostate and up to 4–5 metastases	6	8
10. Case by case	1	1
RT timing		
1. No case	27	36
2. Concurrent with ADT ≤1 month	10	13
3. Delay after neoadjuvant ADT 2–8 months	23	30
4. As soon as possible because patients are consulted for RT after ADT ≥6 months	11	14
5. Case by case	5	7

ADT, androgen deprivation therapy.

RT for OMPC. The target volumes and timing of RT for patients who were initially diagnosed with OMPC varied (*Table 3*).

SBRT experience (number of respondents =64)

Among the 76 respondents, 12 (16%) without SBRT experience were excluded from further survey. The remaining 64 radiation oncologists with SBRT experience continued the survey. Forty-eight physicians (75%) stated that both dose and fraction number should be considered when defining SBRT, whereas 16 (25%) stated that the only fraction size should be considered. The detailed numbers are presented in *Figure 2*. At present, the National Health Insurance Service in Korea provides reimbursements for the cost of SBRT of up to 4 fractions only, regardless of the actually delivered fractions. Six radiation oncologists (9%) are contented with the current reimbursement schemes, whereas 58 physicians (91%) opined that the insurance should cover more than 4 fractions.

SBRT for OMPC (number of respondents =64)

In the past year, the most common fractionation schemes of PDT for OMPC were as follows: hypofractionated RT in 27 (42%), SBRT in 6 (9%), conventional fractionated RT in 5 (8%), and case-by-case basis in 5 (8%) [21 physicians (33%) had no case]. The most common fractionation

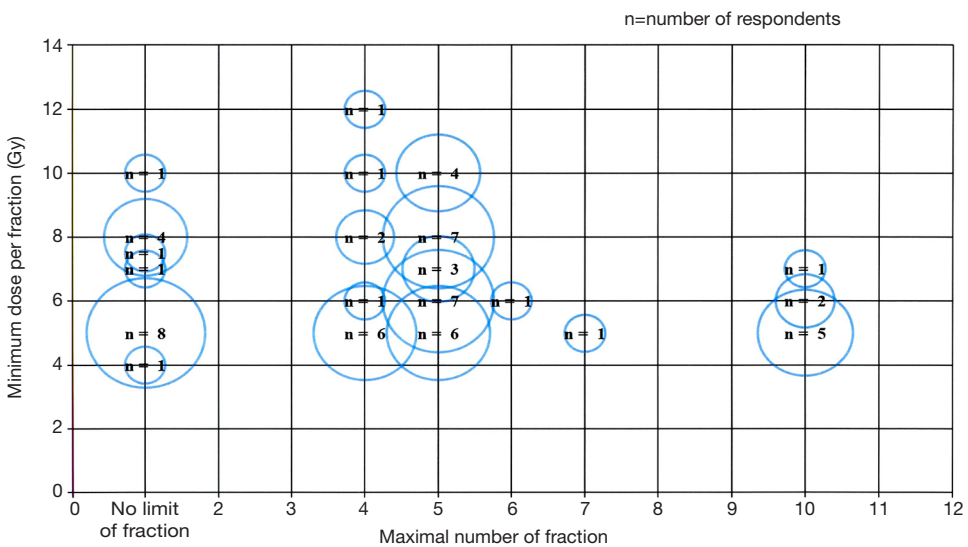


Figure 2 Definition of stereotactic body radiotherapy according to fraction and dose.

Table 4 Prostate immobilization tool, target localization, and image guided radiotherapy (IGRT) workflow during stereotactic body radiotherapy (SBRT) (n=64)

	N	%
Immobilization tool for prostate SBRT		
1. No application of SBRT for prostate	41	64
2. No use	15	23
3. Endorectal balloon	7	11
4. Fiducial	1	2
Target localization during SBRT[a]		
1. Orthogonal KV radiographs	9	14
2. Orthogonal MV radiographs	3	5
3. Fluoroscopy	0	0
4. KV or MV CBCT	52	81
5. MRI	2	3
IGRT workflow during SBRT		
1. Image → Correction → Treatment (Tx)	28	44
2. Image → Correction → Tx → Image after Tx	2	3
3. Image → Correction → Tx → Image during Tx → Tx	4	6
4. Image → Correction → Tx → Image during Tx → Tx → Image after Tx	0	0
5. Image → Correction → Image → Tx	18	28
6. Image → Correction → Image→ Tx → Image after Tx	4	6
7. Image → Correction → Image → Tx → Image during Tx → Tx	5	8
8. Image → Correction → Image → Tx → Image during Tx → Tx → Image after Tx	3	5

[a], the respondents selected multiple answer. KV, kilovoltage; MV, megavoltage; CBCT, cone beam computed tomography; MRI, magnetic resonance imaging.

schemes for MDT were as follows: SBRT in 26 (40%), hypofractionated RT in 11 (17%), case-by-case basis in 4 (6%), conventional fractionated RT in 1 (2%), and no MDT for OMPC in 1 (2%). The respondent stated that the use of SBRT for OMPC was hampered by the lack of suitable patients for SBRT (n=36, 56%), preference for other fractionation (n=21, 33%), and reimbursement issues (n=9, 14%), when allowed to select multiple answers. The pattern of PDT using SBRT is presented in *Table 4*. Most radiation oncologists did not use any immobilization device for prostate SBRT, and the preferred method for target localization was kilovoltage or megavoltage cone beam computed tomography. All physicians obtained the images before every treatment, and the image registration workflow during and after treatment varied (*Table 4*).

Clinical cases (number of respondents =55)

Of 64 physicians with SBRT experience, 55 (86%) responded to the second survey. Details of the three clinical cases are shown in *Figure 3*. They generally agreed that the three cases were categorized as OMPC to varying degrees: 49 respondents for case 1, 44 for case 2, and 55 for case 3. For case 1, 25 respondents selected to treat the whole pelvis, including regional lymph node (LN) chains and pelvic bone metastases, and 20 treated both the prostate and metastatic lesions. For case 2, 24 the respondents selected to treat the prostate and metastatic lesions, while 16 treated the whole pelvis. For case 3, all physicians treated only the metastatic lesion, but the target volume varied, as shown in *Figure 4*. The most preferred fractionation scheme for PDT was

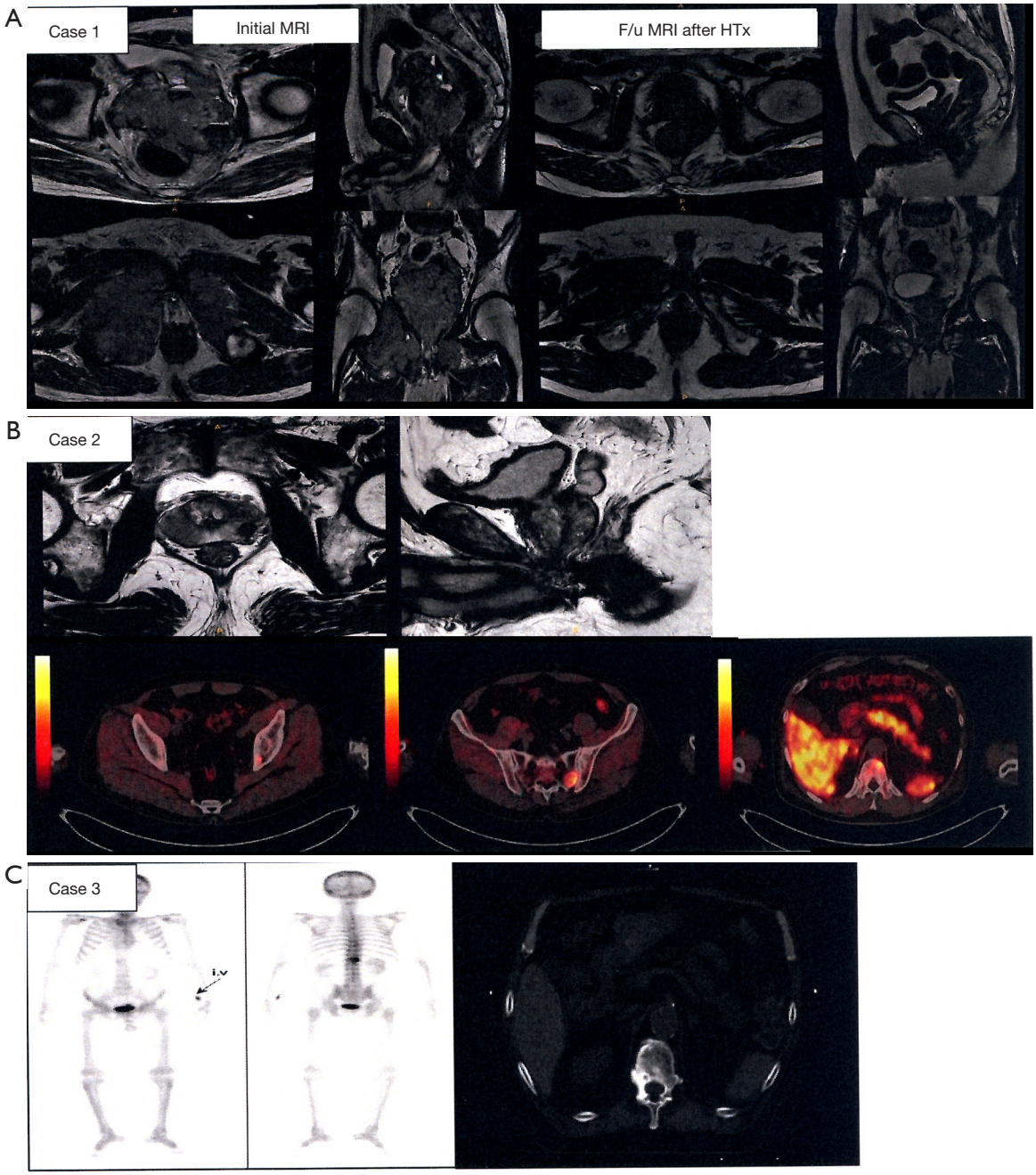
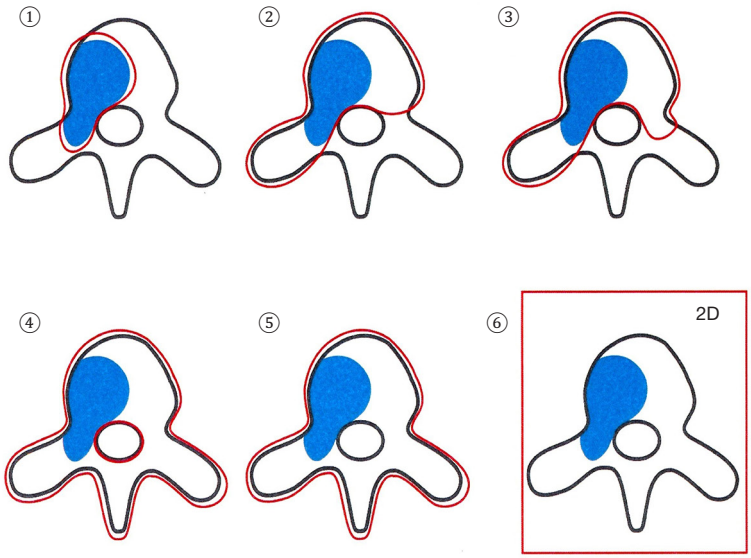


Figure 3 Three clinical cases which was presented in the second questionnaire survey (A) Case 1: a 69-year-old patient with prostate cancer with direct invasion to two pelvic bones at the right acetabulum and pubic bone [Gleason score (G/S) = 4+4, cT4N0M1, initial prostate-specific antigen (PSA) >1,000 ng/mL]. He was referred for radiotherapy (RT) when the level of PSA decreased to <0.03 ng/mL after undergoing androgen deprivation therapy (ADT) for 1 year. (B) Case 2: a 64-year-old patient with prostate cancer with three bone metastases at the left acetabulum, left sacral alar, and 11th thoracic (T11) spine (ECOG 0, G/S = 4+4, cT2N0M1, initial PSA 162.88 ng/mL). He was referred for RT when the level of PSA decreased to 41.40 ng/mL after receiving 1 cycle of ADT. (C) Case 3: a 65-year-old patient with prostate cancer with solitary metastases in the T12 spine after undergoing ADT, radical prostatectomy, salvage RT to prostate bed, and cytotoxic chemotherapy (ECOG 1, G/S = 5+4, PSA 7.89 ng/mL).



Target volume	N	%
①	1	2
②	18	34
③	21	40
④	4	7
⑤	9	17
⑥	0	0

Figure 4 Target volume for spinal metastases for case 3: A total of 53 physicians selected the target volume, except for two who did not apply radiotherapy in this case.

hypofractionated RT for PTT, whereas that for MDT varied according to the site of metastases. Hypofractionated RT is preferred for pelvic bone metastases, while SBRT is preferred for spinal metastases. Other details are summarized in *Table 5*.

Discussion

Hellman and Weichselbaum first proposed oligometastases as an intermediate state between a localized disease and a systemically metastatic disease (8). This includes comprehensively synchronous or metachronous metastases, and controlled or uncontrolled primary tumors, regardless of the number of lesions, if all viable tumors can be treated with local modalities. Afterwards Niibe *et al.* (11) proposed a new definition of oligorecurrence: one to several distant metastases/recurrences (usually one) in one to several organs (usually one) with controlled primary tumor. Recently, the EORTC and ESTRO group subclassified oligometastases into synchronous oligometastases, metachronous oligorecurrence, and metachronous oligoprogression (12). Although these subclassifications would provide a clear system and reflect the fundamental biology, the exact definition of limited metastases has not yet been determined. The first phase I and randomized phase II studies, which applied SBRT as MDT for OMPC, included patients with 1–3 metastatic lesions (13,14). On the other hand, a phase III study reported that SBRT as a PDT for synchronous metastatic PC improved the overall survival of patients with a low metastatic burden according to the CHAARTED trial (15). Recent ESTRO-ASTRO consensus recommends that oligometastases can be defined as presence of 1–5 metastatic lesions (16). Meanwhile, ongoing prospective studies on OMPC can allow 5–10 metastatic lesions or unlimited metastases (17). Our survey reported that most physicians agreed that oligometastases involved a limited number of metastases, but the allowed number varied. There is a need to reach a consensus for the standardized and harmonized practice for OMPC among radiation oncologists in Korea.

A higher RT dose improves disease control in patients with localized PC, and at least 75.6 Gy conventionally fractionated RT has been established as the modern standard treatment (18). Based on the radiobiologic sensitivity to hypofractionation of PC, patient convenience, and health care costs, non-inferiority phase 3 randomized trials have confirmed the safety and efficacy of hypofractionation compared with conventional fractionation (19). Therefore, hypofractionated RT is recommended as a standard of care across all risk groups (20). SBRT is an extreme form of hypofractionation, which utilizes either a single dose or a small number of fractions; many prospective studies reported that SBRT showed similar toxicity and non-inferior disease control compared with conventional or hypofractionated RT (21-23). Nonetheless, treatment

Table 5 Details for each case (n=55)

	Group	Case1		Case 2		Case 3	
		N	%	N	%	N	%
Oligometastases?	Agree	49	89	44	80	55	100
	Disagree	6	11	11	20	0	0
Experience treating the case	Yes	44	80	34	62	41	75
	No	11	20	21	38	14	25
RT timing	Upfront RT	48	87	16	29	53	96
	ADT followed by RT	–	–	31	56	–	–
	No RT	7	13	8	15	2	4
RT field	Prostate only	3	6	6	13	0	0
	Prostate and metastatic lesion	20	42	24	51	0	0
	WP and metastatic lesion	25	52	16	34	0	0
	Metastatic lesion only	0	0	1	2	53	100
Fx size for prostate	Conventional fx	9	19	8	17	–	–
	Hypofx	37	77	35	76	–	–
	SBRT	2	4	3	7	–	–
BED for prostate	<88.8 Gy_{10}	36	75	35	76	–	–
	≥88.8 Gy_{10}	12	25	11	24	–	–
Fx size for WP	Conventional fx	22	88	15	94	–	–
	Hypofx	3	12	1	6	–	–
BED for WP	<53.1 Gy_{10}	3	12	1	6	–	–
	≥53.1 Gy_{10}	22	88	15	94	–	–
Fx size for metastatic lesion	Conventional fx	20	45	10[a]/2[b]	24/6	1	2
	Hypofx	23	51	21[a]/11[b]	52/30	15	28
	SBRT	2	4	10[a]/23[b]	24/64	37	70
BED for metastatic lesion	<53.1 Gy_{10}	7	16	9[a]/19[b]	22[a]/53[b]	36	68
	≥53.1 Gy_{10}	38	84	32[a]/17[b]	78[a]/47[b]	17	32
Reason for not use SBRT[c]	WP including regional LNs	22	48	15	39	–	
	Preference of other fractionations	18	39	16	42	9	56
	Lack of special equipment	1	2	1	3	0	0
	Lack of experience of SBRT	8	17	9	24	4	25
	Limitation of reimbursement	5	11	15	39	3	19
	Wide margin for involved bone mets	27	59	12	32	5	31
	Others	1	2	0	0	1	6

[a], means pelvic bone metastases; [b], means T11 spine metastases; [c], the respondents selected multiple answer. RT, radiotherapy; ADT, androgen deprivation therapy; WP, whole pelvis including regional lymph nodes (LNs); Fx, fraction; Hypofx, hypofractionation; SBRT, stereotactic body radiotherapy; BED, biologically effective dose when α/β was assumed to be 10 Gy.

guidelines recommend SBRT for patients with low-risk PC and is considered as an alternative treatment option for those with intermediate-risk and high-risk PC (20). RT as a PDT for OMPC was assessed in two prospective studies (15,24). The HORRAD trial initiated study with 70 Gy in 35 fractions and additionally permitted 55.76 Gy in 19 fractions. The authors pointed out that the total dose was lower than the currently applied for PC, and it was considered as a limitation of the study. The STAMPEDE trial used 36 Gy in 6 fractions or 55 Gy in 20 fractions because the standard regimen of 74 Gy in 37 fractions would be too burdensome for patients with metastatic PC. In the current survey, most physicians (42%) selected hypofractionated RT as PDT for OMPC, and only 9% used SBRT. This partially affected by the insurance coverage. Since the inclusion of intensity-modulated RT (IMRT) in the health insurance system in 2015, IMRT use increased dramatically in Korea, and PC is the third most common cancer treated with IMRT (25,26). Whereas, the national insurance policy for SBRT remained unchanged and only covers at total ≤4 fractions, thus making it difficult to apply the standard number of SBRT fractions (5–6 fractions) in patients with PC. Although SBRT is an attractive modality for delivering higher radiation doses and reducing the overall treatment time, SBRT as a PDT for OMPC should be carefully performed in clinical trials due to the low quality of evidence and limited insurance resource in Korea.

SBRT as an MDT for oligometastases has been evaluated in various organ sites from different types of primary cancers. A recent multi-institutional randomized phase II study of 1–5 oligometastases from any type of primary cancer (OMPC, 16%) compared the standard therapy with SBRT and that without SBRT as MDT (27). SBRT is associated with a 13-months increase in the overall survival and the doubling of progression-free survival, but the risk of toxicity increased, including a 5% risk of grade 5 toxicity. Phase I and II studies on SBRT as MDT for OMPC showed that ADT-free survival was longer with MDT and the quality of life was maintained after SBRT (13,14). Other prospective and retrospective studies using SBRT as MDT for OMPC reported a promising local control rate of 80–100% at 2 years (6). Although SBRT as an MDT for OMPC is effective, there is no consensus on the target volume and RT dose for metastatic lesions. Prostate cancer mainly metastasizes to the bone and LNs: bone metastases divide into spine and nonspine bone metastases. The RTOG 0631 phase II/III study was the first study to specifically describe the target volume for spinal metastases according to the extent of tumor (28). International Spine Radiosurgery Consortium Consensus published contouring guidelines for SBRT for spine metastases in more detail (29). Although there are detailed recommendations from expert consensus exist, contouring must be completed on a case-by-case basis with each case tailored to the patient's individual clinical situation and institutional infrastructure: *Figure 4*. reflects this potential variation in the clinical setting. For nonspine bone metastases, significant heterogeneity for contouring exists worldwide due to the absence of guidelines (30). For LN metastases, the optimal target volume between regional LN chains or affected LN only is unclear. One study reporting that two out of three OMPC patients treated with SBRT for pelvic LN relapsed in the nodes again might support the inclusion of all regional LN chains (31). Our study showed that physicians selected the regional LN chains on case-by-case basis. Ongoing multicenter, randomized, phase 2 PEACE V-STORM trial might yield clues to the potential benefit about elective nodal approach with whole pelvis RT as an alternative to focal SBRT in OMPC (32). In addition, several studies on MDT for OMPC with newer imaging modalities will help in the selection of optimal patients for SBRT (17). In terms of RT dose, most studies used 16–20 Gy in 1 fraction or 27 Gy in 3 fractions for bone metastases and lower doses for LN metastases (6,9). The universally ablative dose should be clinically validated based on patients' outcomes by conducting further studies.

The current study has some limitations. First, respondents recollected SBRT experiences for OMPC from the past and recall bias may have occurred. Second, we used closed-ended questions and conducted descriptive analysis to get definite and vast information because little is unknown about practical patterns for SBRT for OMPC in Korea before this study. Further surveys composed of open-ended questions should be needed to reflect the accurate clinical practice. And last, the practical patterns of the respondents for OMPC may be different from those with no response. However, this survey may have representativeness because we have achieved response rate >80% from all radiation oncologists in Korea (82% in the first survey and 86% in the second survey).

In conclusion, this is the first survey to present the practical patterns of SBRT for OMPC in Korea. Most physicians agreed on the definition of OMPC as limited lesions and/or organs, but different institutions provided their own arbitrary cutoffs. The definition of the fractionation scheme of SBRT differed among institutions. Although the target volume were various among physicians, SBRT was

commonly used for spinal metastases. On the other hand, physicians preferred hypofractionated RT for the treatment of the prostate and nonspine bone metastases. Based on the findings of this survey, we should conduct additional prospective studies to standardize the practice and strengthen the evidence on the role of SBRT in OMPC.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/atm-21-1116). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective study was approved by the institutional review board of Soonchunhyang University College of Medicine, Bucheon (IRB No. 2019-08-023-001). Because of the retrospective nature, the requirement of written informed consent was waived.

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Supplementary

Appendix 1

Stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer (OMPC)

Hospital: Name:

1. In what kind of institution are you currently working? ( )
   ① Primary- ② Secondary- ③ Tertiary health care hospital
2. How long have you been working as a radiation oncologist after residency? ( )
   ① <5 years ② 5–9 years ③ 10–19 years ④ ≥20 years
3. Is there a multidisciplinary team (MDT) approach for patients with prostate cancer in your institution? ( )
   ① Yes: Move to question 3-1. ② No: Move to question 4.
   3-1) Is the MDT meeting regularly performed? ( )
   ① Yes ② No
   3-2) How often do you have the MDT meetings? ( )
   ① Every week ② Every month ③ About 2–3 times a month ④ Every other month
   ⑤ Every 3 months ⑥ Every 4 months ⑦ Others (Please specify) _____
4. Is there a radiation oncologist as a specialist for urology in your institution? ( )
   ① Yes ② No. We work together regardless of the disease site. ③ No. I work alone.
5. How many prostate cancer patients do you treat with RT for a cure in the past year? ( )
   ① ≤5 cases ② 6–10 cases ③ 11–30 cases ④ 31–50 cases
   ⑤ 51–100 cases ⑥ 101–300 cases
6. What is your definition of oligometastases? ( )
   ① Number of lesions/number of organs (Please specify) ____/____
   ② Low-volume of metastatic disease according to the CHAARTED trial
7. Which imaging study do you consider to evaluate disease extent and metastases? ( ) (Please select all that apply)
   ① Prostate MRI ② Bone scan ③ CT scan of abdomen and/or thorax
   ④ Spine MRI ⑤ FDG PET-CT ⑥ Choline- or PSMA PET-CT
   ⑦ Others (Please specify) _____
8. How many OMPC patients were referred for radical-intent RT in the past year? ( )
   ① No case ② ≤5 cases ③ 6–10 cases ④ 11–20 cases ⑤ ≥21 cases
9. What target volume do you treat for oligometastatic prostate cancer? ( )
   ① No case ② No RT ③ Prostate only ④ Up to 1–2 metastatic lesions only
   ⑤ Up to 3 metastatic lesions only ⑥ Up to 4–5 metastatic lesions only
   ⑦ Prostate and up to 1–2 metastatic lesions ⑧ Prostate and up to 3 metastatic lesions
   ⑨ Prostate and up to 4–5 metastatic lesions ⑩ Others (Please specify) _____
10. When do you apply RT for initially diagnosed OMPC patients? ( )
    ① No case ② Concurrent with androgen deprivation therapy (ADT): Start RT within 1 month after ADT.
    ③ Neoadjuvant ADT 2–8 months: at___months
    ④ As soon as possible, because patients are consulted for RT ≥ 6 months after ADT
    ⑤ Others (Please specify) _____
11. Do you have an experience with SBRT to treat cancer patients? ( )
    ① Yes: Move to question 12. ② No: End the survey and thank you for your time.
12. What is your definition of SBRT? ( )
    ① ( ) Gy/fx, regardless of the number of fractions
    ② Above ( ) Gy and below ( ) fractions
13. Approximately, what percentage of OMPC patients, who were referred for RT, is treated with SBRT in the past year?
    13-1-1) What is the application rate of SBRT for the primary lesion (prostate)? ( )

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① No case ② No use of SBRT: application of conventional fraction (1.8–2 Gy/fx)
③ No use of SBRT: application of hypofractionation (>2 Gy/fx)
④ No use of SBRT: application of various fractionation scheme on case-by-case
⑤ 1%–9% ⑥ 10%–40% ⑦ 41%–60% ⑧ 61%–99% ⑨ 100%

13-1-2) What fractionation scheme do you most commonly utilize? (Gy/ fx's)

13-2-1) What is the application rate of SBRT for oligometastatic lesions? ( )
① No case ② No use of SBRT: application of conventional fraction (1.8-2 Gy/fx)
③ No use of SBRT: application of hypofractionation (>2 Gy/fx)
④ No use of SBRT: application of various fractionation scheme case by case
⑤ 1%–9% ⑥ 10%–40% ⑦ 41%–60% ⑧ 61%–99% ⑨ 100%

13-2-2) What fractionation scheme do you most commonly utilize?
(Gy/ fx's) to spine metastases
(Gy/ fx's) to other bone metastases
(Gy/ fx's) to lymph node metastases
(Gy/ fx's) to other metastases (Please specify the site)

14. What are reasons why it is difficult to use SBRT for OMPC patients? ( ) Please select all that apply.
① N/A: Always use SBRT. ② The lack of special equipment
③ The lack of experience with using SBRT ④ The lack of appropriate patients for SBRT
⑤ Transfer of appropriate patients for SBRT to a larger hospital ⑥ Preference for other fractionation scheme
⑦ Insurance problems ⑧ Others (Please specify)
15. The National Health Insurance Service in Korea has approved SBRT in cases of RT regimens using ≤4 fractions applied to lesions within the body. Is it appropriate to limit the number of fractions? ( )
① Yes ② No: It is necessary to increase the number of fractions to .
16. What treatment machine do you use for SBRT to a primary lesion (prostate)? ( ) Please select all that apply.
① No RT ② CyberKnife ③ RapidArc (Varian) ④ TomoTherapy
⑤ Clinac iX (Varian) ⑥ TrueBeam (Varian) ⑦ Novalis (Varian) ⑧ VMAT (Elekta)
⑨ ViewRay™ ⑩ Proton ⑪Others (Please specify) _____
17. Do you use an immobilization tool for SBRT to the primary lesion (prostate)? ( )
① No use ② Yes: Use an endorectal balloon.
③ Yes: Use rectal spacer. ④ Others (Please specify) _____
18. What treatment machine do you use for SBRT to the oligometastatic lesions? ( ) Please select all that apply.
① No RT ② CyberKnife ③ RapidArc (Varian) ④ TomoTherapy
⑤ Clinac iX (Varian) ⑥ TrueBeam (Varian) ⑦ Novalis (Varian) ⑧ VMAT (Elekta)
⑨ ViewRay™ ⑩ Proton ⑪Others (Please specify) _____
19. What target localization methods do you prefer for SBRT? ( )
① Orthogonal MV localization images ② Orthogonal KV radiographs ③ Fluoroscopy
④ KV or MV cone beam CT ⑤ MRI ⑥ Others (Please specify) __
20. In what order do you apply the image registration during SBRT? ( )
① Image → Correction → Treat
② Image → Correction → Treat → Image after Tx
③ Image → Correction → Treat → Image during Tx → Treat
④ Image → Correction → Treat → Image during Tx → Treat → Image after Tx
⑤ Image → Correction → Image → Treat
⑥ Image → Correction → Image → Treat → Image after Tx
⑦ Image → Correction → Image → Treat → Image during Tx → Treat
⑧ Image → Correction → Image → Treat → Image during Tx → Treat → Image after Tx

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- Thank you for your time -

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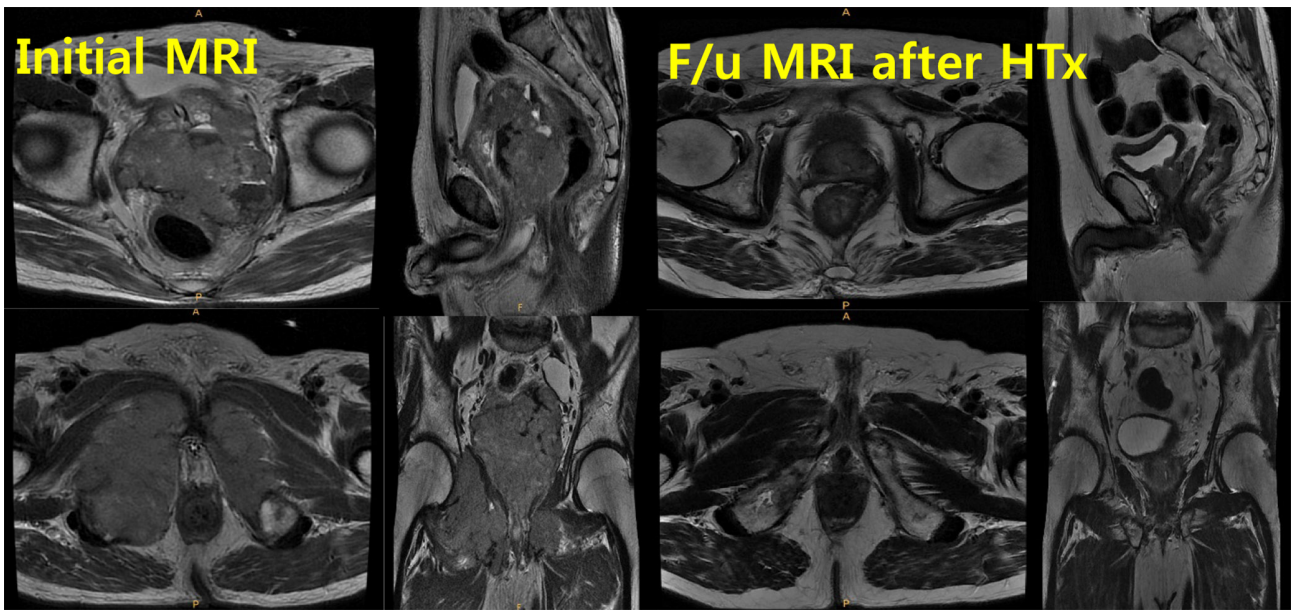
Appendix 2

This patterns-of-care survey is composed of three clinical scenarios related to the experience in the clinical setting. Please select your current practice for each case.

Hospital: Name:

Case 1.

A 69-year-old male patient was initially diagnosed with prostate cancer with two pelvic bone metastases (Eastern Cooperative Oncology Group [ECOG] 1, Gleason score [G/S] = 4+4, cT4N0M1, initial prostate-specific antigen [PSA] >1,000 ng/mL, and metastases at the right acetabulum and pubic bone). He received androgen deprivation therapy (ADT) for 1 year. The PSA level decreased to <0.03 ng/mL at 6 months after ADT and was maintained. Subsequently, he was referred for radiotherapy (RT). He had no symptoms of bone metastases.



1-1. Does this case correspond with oligometastatic prostate cancer (OMPC)? ( ) Do you agree with the delivery of a high dose in this case? ( )
① Yes ② No

1-2. Do you have experience with RT to treat prostate cancer patients with limited metastases within the pelvis similar to this? ( )
① Yes ② No

1-3. When do you initiate RT? ( )
① As soon as possible: Move to question 1-4. ② No RT: Move to Case 2.

1-4. What target volume do you treat for this case? ( )
① Prostate only ② Whole pelvis including regional lymph node (LN) chains and pelvic bone metastases
③ Prostate and pelvic bone metastases ④ Pelvic bone metastases ⑤ Others (Please specify)

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1-5. What technique and fractionation scheme do you apply? ( )

Technique type:

① 2D ② 3DCRT ③ IMRT ④ IMRT-SIB ⑤ SBRT

A. Prostate: Technique ( ), Fractionation scheme: (Gy/ fx's)

B. Bone metastases: Technique ( ), Fractionation scheme: (Gy/ fx's)

C. Whole pelvis: Technique ( ), Fractionation scheme: (Gy/ fx's)

→ Followed by prostate boost: Technique ( ), Fractionation scheme: (Gy/ fx's)

D. Comment:

1-6. What are the reasons why you are not using SBRT for this case? ( ) Can select up to two answers.

① Application of whole pelvic RT including elective LN chains ② Preference for other fractionation scheme

③ The lack of special equipment ④ The lack of experience with the use of SBRT

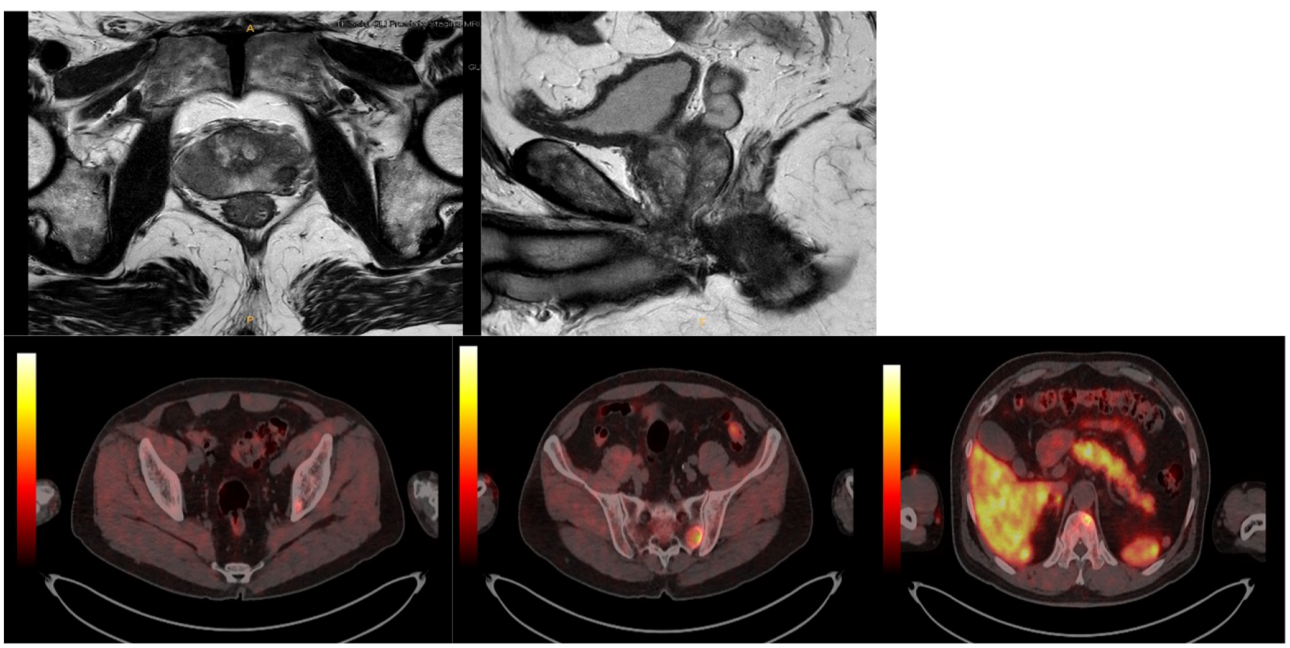
⑤ Insurance problems: limited fractions (≤4)

⑥ Application of other fractionation scheme with generous margin including involved bone metastases

⑦ Others (Please specify)

Case 2.

A 64-year-old male patient was initially diagnosed with prostate cancer with three bone metastases (ECOG 0, G/S = 4+4, cT2N0M1, initial PSA 162.88 ng/mL, metastases in the left acetabulum, left sacral alar, and 11th thoracic [T11] spine). He received 1 cycle of ADT, and the level of PSA decreased to 41.40 ng/mL at 1 month after ADT. Subsequently, he was referred for RT. He had no symptoms of bone metastases.



2-1. Does this case correspond to OMPC? ( ) Do you agree with the delivery of a high dose in this case? ( )

① Yes ② No

2-2. Do you have experience with RT to treat prostate cancer patients with limited bone metastases like this? ( )

① Yes ② No

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2-3. When do you initiate RT? ( )

① As soon as possible: Move to question 2-4.

② Beginning after ( ) months to receive additional ADT as a neoadjuvant aim: Move to question 2-4.

③ No RT: Move to Case 3.

2-4. What target volume do you treat for this case? ( )

① Prostate only ② Whole pelvis including regional LN chains and 2 pelvic bone metastases

③ Prostate and 2 pelvic bone metastases ④ Prostate and 3 bone metastases

⑤ Whole pelvis, including regional LN chains and 2 pelvic bone metastases, and T11 spine metastases

⑥ 3 bone metastases ⑦ Others (Please specify)

2-5. What technique and fractionation scheme do you apply? ( )

Technique type:

① 2D ② 3DCRT ③ IMRT ④ IMRT-SIB ⑤ SBRT

A. Prostate: Technique ( ), Fractionation scheme: (Gy/ fx's)

B. Bone metastases

- Left acetabulum: Technique ( ), Fractionation scheme: (Gy/ fx's)
- Left sacral alar: Technique ( ), Fractionation scheme: (Gy/ fx's)
- T11 spine: Technique ( ), Fractionation scheme: (Gy/ fx's)

C. Whole pelvis: Technique ( ), Fractionation scheme: (Gy/ fx's)

→ Followed by prostate boost: Technique ( ), Fractionation scheme: (Gy/ fx's)

D. Comment:

2-6. What are the reasons why you are not using SBRT for this case? ( ) Can select up to 2 answers.

① Application of whole pelvic RT including elective LN chains ② Preference for other fractionation scheme

③ The lack of special equipment ④ The lack of experience with the use of SBRT

⑤ Insurance problems: limited fractions (≤4)

⑥ Insurance problems: excess of those covered by medical insurance because the RT site is classified as cervical spine/T spine/ lumbar spine/ sacrum.

⑦ Application of other fractionation scheme with generous margin including the involved bone metastases

⑧ Others (Please specify)

2-7. In what order do you apply RT if you treat both primary lesion and metastatic lesions? ( )

① Simultaneous treatment including 3 bone metastases in a day

② Simultaneous treatment: Treat 1 site per day in case of bone metastases.

③ Sequential treatment: Treat all bone metastases in a day after the completion of RT for the primary lesion.

④ Sequential treatment: Sequentially treat 1 site per day in case of bone metastases after the completion of RT for primary lesion.

⑤ Time interval of > 1 month between RT of primary lesion and RT of bone metastases

⑥ Others (Please specify)

Case 3.

A 65-year-old male patient was initially diagnosed with prostate cancer with pelvic LN metastases (ECOG 1, G/S = 5+4, cT3N1M0, initial PSA of 161 ng/mL). He was treated with ADT for 4 years. The level of PSA decreased to 0.19 ng/mL but rebounded to 1.20 ng/mL, and laparoscopic radical prostatectomy was done. Additional ADT was undergone for 3 years. The level of PSA decreased to 0.16 ng/mL but rebounded to 1.08 ng/mL, and a salvage RT to prostate bed with 70 Gy/35 fx's was done. Duo to the continuous increase in the level of PSA, he received 4 cycles of docetaxel plus prednisone, but this treatment was discontinued due to the occurrence of neutropenia. The level of PSA at follow-up was 7.89 ng/mL, and single spine metastases at the T12 was detected on bone scan. Subsequently, he was referred for RT. He had no symptoms of bone metastases.

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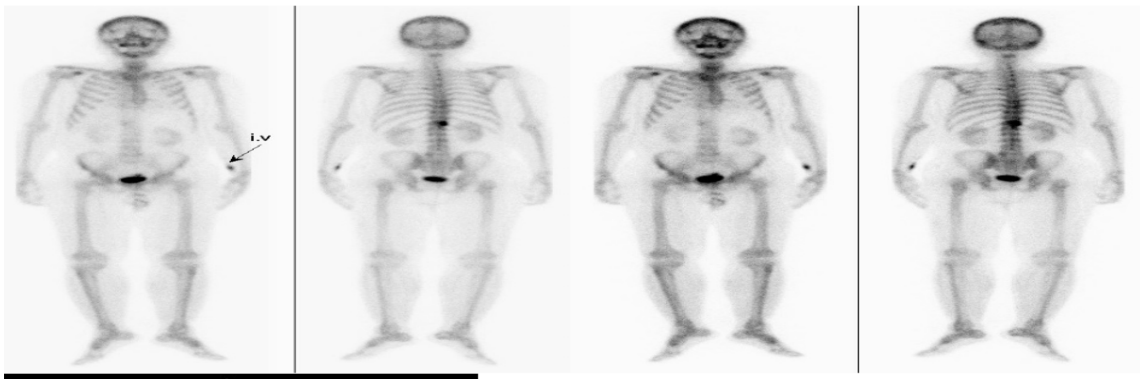
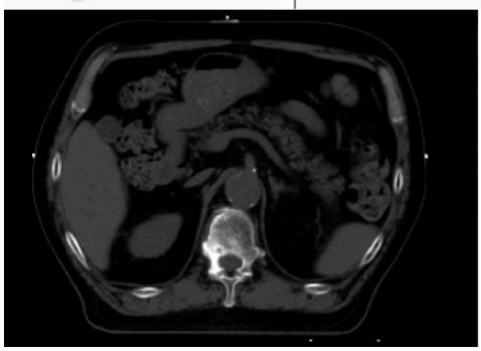


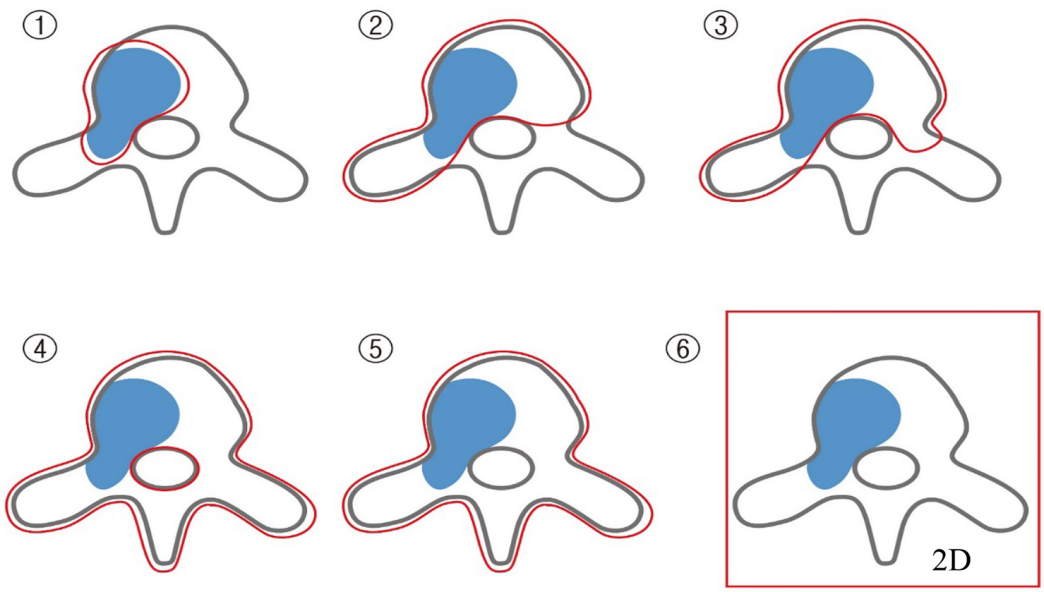


3-1. Does this case correspond to OMPC? ( ) Do you agree with the delivery of a high dose in this case? ( )
① Yes ② No

3-2. Do you have experience with RT to treat prostate cancer patients with solitary metastases similar to this? ( )
① Yes ② No

3-3. When do you initiate RT? ( )
① As soon as possible: Move to question 3-4. ② No RT: End the survey and thank you for your time.

3-4. What target volume do you treat for this case? ( )



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3-5. What technique and fractionation scheme do you apply? ( )

Technique type ( ):

① 2D ② 3DCRT ③ IMRT ④ IMRT-SIB ⑤ SBRT

Fractionation scheme: (Gy/ fx's)

3-6. What are the reasons why you do not use SBRT for this case? ( ) Can select up to 2 answers.

① Preference for other fractionation scheme ② The lack of special equipment

③ The lack of experience with the use of SBRT ④ Insurance problems: limited fractions (≤4)

⑤ Application of other fractionation scheme with generous margin including involved bone metastases

⑥ Others (Please specify)

- Thank you for your time -

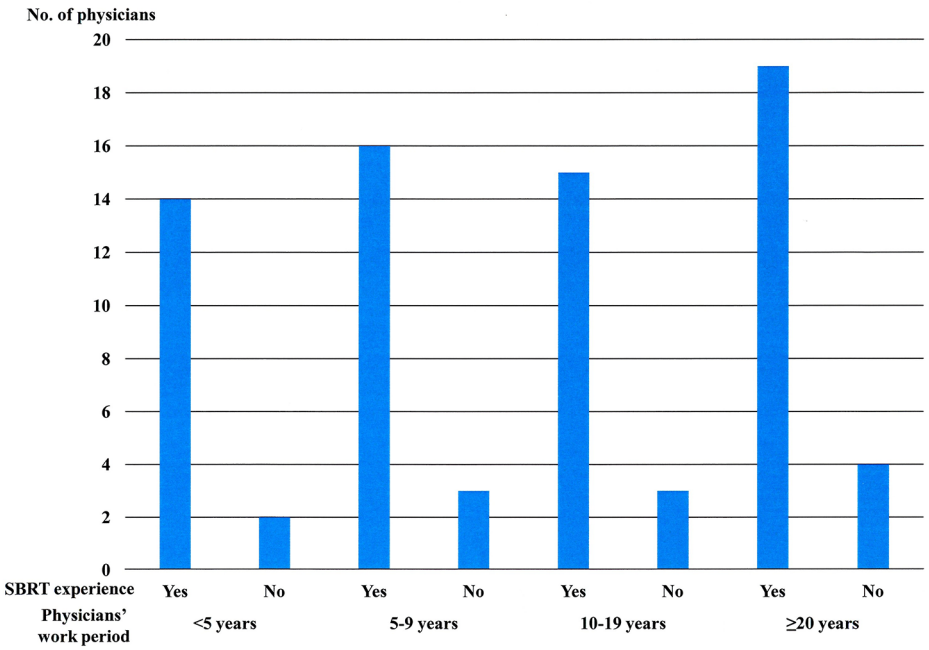

Figure S1 Stereotactic body radiotherapy (SBRT) experience according to physicians' work period.

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