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First multicentre experience of SABR for lymph node and liver oligometastatic disease on the unity MR-Linac

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ABSTRACT

Summary: The treatment of oligometastatic disease using MR guidance is an evolving field. Since August 2018 patients are treated on a 1.5 Tesla MR-Linac (MRL). We present current workflows and practice standards from seven institutions for the initial patients treated for lymph node and liver metastases.

Introduction

Stereotactic ablative body radiotherapy (SABR) [1] provides an ablative local therapy option for patients with oligometastatic disease (OMD), with a potential benefit for local control and overall survival for a variety of treatment sites [2–4]. Since SABR offers a non-invasive treatment with favorable toxicity, its role in patients with OMD is increasing. However, SABR requires appropriate image guidance in order to be delivered safely. While good results are obtained using conebeam CT (CBCT) [5], CBCT has limited soft tissue contrast [6], making the treatment of lesions in close proximity to critical organs at risk (OARs) challenging.

Due to the superior soft tissue contrast and the inbuilt functionality for daily online plan adaptation, the MRIdian [7] (ViewRay, US) and Unity [8,9] MRL (Elekta, Sweden) are appealing for SABR treatment of OMD [10,11]. The Unity MRL received regulatory approval in 2018 and best practice workflows for a variety of tumors have been in development since [12].

The aim of this paper is to present the workflows and treatment techniques employed by the first seven institutions that started treating OMD on the Unity MRL with a focus on lymph node and liver OMD.

Materials and methods

This paper concerns OMD patients treated on the Unity MRL between August 1st, 2018 and August 1st, 2020. Patients were treated at the Netherlands Cancer Institute (NKI), the Royal Marsden (RMH), IRCCS Sacro Cuore Don Calabria (Sacro Cuore), Odense University Hospital (Odense), University Hospital Tübingen (Tübingen), Medical College of Wisconsin (MCW) and the University Medical Center Utrecht (UMCU).

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While patients were treated at various anatomical sites, we only consider lymph node and liver metastases, as they represent the vast majority of treated OMD.

A questionnaire was developed to gather information regarding treatment strategies and approaches for the treatment of OMD. Questions focused on characteristics of the patient population, along with treatment details such as: fractionation, simulation and treatment planning. In addition, data regarding image guidance, online adaptation and motion management were collected.

When possible, the MOMENTUM platform (NCT04075305), a collaboration between institutions and the manufacturer of the Unity [12–14], was used to fill in the questionnaire.

This work describes implementation of a new technique according to R-IDEAL stage 2a [13].

Results

MOMENTUM data was retrieved from four institutions (UMCU, NKI, MCW, RMH), since not all institutions participated in MOMENTUM at time of data collection. The questionnaire was completed by all seven institutions.

Lymph node metastases

A total of 168 patients have been treated for lymph node metastases among seven institutes. Average age was 69 years, (range 45–86 years). A maximum of four metastases were treated in one session. Mean gross tumor volume (GTV) was 6.4 cc (range 0.1–146.1 cc) based on 155 patients, data was not provided by 2 institutions.

The majority of metastases originated from the prostate (N = 100, 60%) or colon/rectum/sigmoid (N = 20, 12%). Treated lesions were mostly located in the pelvis (N = 119, 72%) and abdomen (N = 44, 27%) (data not provided by 2 institutions). A substantial amount of patients earlier received radiotherapy in the same area (N = 34, 20%) and/or surgery (N = 96, 57%) before the MRL treatment for OMD.

Dose prescription

Fractionation differed between institutions from 2 to 25 fractions and 2 – 15 Gy per fraction. However, the majority of patients were prescribed 5 × 7 Gy (N = 112; see Table 1). In addition prescription and hot spot criteria varied, with coverage evaluated on both GTV and planning target volume (PTV) using a variety of dose volume histogram (DVH) metrics (Table 1).

Simulation and treatment planning

A planning CT for simulation, in combination with a simulation MR was used in all institutions for OAR and target contouring. Three institutions used the MR as primary scan for the reference plan, using an electron density assignment per contour, while the remaining used the planning CT. The vendor provided patient position devices were not used in three institutions, which instead used conventional, MR safe, positioning devices. A vacuum bag for additional stability was used in three institutions, where one recently stopped using them for solitary pelvic nodes [15].

For abdominal lymph nodes, breathing motion was measured on 4DCT and taken into account using an ITV at two institutions and in amplitude dependent margins at two other institutions. Three of these four institutions indicated the use of abdominal compression to limit the breathing amplitude [16]. The remaining three institutions indicated not to treat lymph node lesions in anatomical regions with relevant breathing motion.

PTV margins were 5 mm in three institutions, while in the other institutions PTV margins ranged from 3 to 6 mm. PRV margins were used by four institutions and differed from 3 mm for the spinal cord to 5 mm for the intestines or stomach. One institution indicated to only use a PRV margin if online adaptation was done without recontouring (adapt to position (ATP) workflow [17]).

For OAR constraints, all but one institution used criteria derived from Hanna et al. [18]. Maximum dose criteria were taken into account by all institutions, while the volumetric criteria (typically the D5cc, D10cc or D15cc) were applied in three institutions. One institution used a single OAR criterion for the intestines, depending on the total prescription dose (Dp): D1cc $\leq$ Dp, for Dp $\leq$ 36.25 Gy and D3cc $\leq$ 36 Gy, for 40 Gy $\leq$ Dp $\leq$ 45 Gy.

Five institutions indicated that for pre-treatment offline plans coverage was not always met due to OAR constraints. In one institution up to 8 out of 14 pre-treatment plans did not meet the coverage criteria (institution C from Table 1). Only in a total of three cases an OAR constraint violation was accepted.

Table 1
Coverage and hot spot criteria for the different institutions A-G in the treatment of lymph node oligometastases. Also show is the number of patients treated using different dose prescriptions. For clarity only those prescriptions are shown that are used more than once over all institutions.

		A	B	C	D	E	F	G
Coverage Criterium	GTV			V95%>99% Dmean ≥ 100%				V100%> 99.9%
	PTV	V100%> 95% V95% >99%	V95% > 95%	V67%>99%	V100%> 95%	V100%>95%	V80% >98%	V100%>95%
Hot spots	PTV	D1%<150%	D2%<107%		D0.1 cc < 140%	D0 < 120%	D0 < 120%	D0.1 cc < 135%
	PTV - GTV			V107% <1cc V140%<0.1 cc				
Prescription dose	3 × 10 Gy				1			9
	3 × 15 Gy			7				
	5 × 5 Gy	1	1					1
	5 × 6 Gy		6		2			
	5 × 7 Gy	8	21*		2	4	13	66**
	5 × 8 Gy	1	4			1	2	
	5 × 10 Gy	11		7				
	6 × 6 Gy		3					
	6 × 7.5 Gy		2					

* includes 2 cases prescribed as 5 × 7.25 Gy.
** includes 2 simultaneous boost cases prescribed as 5 × (5 + 2) Gy.

Online adaptation

Six institutions performed online adaptation with target and OAR recontouring (adapt to shape (ATS) workflow [17]) as default for all patients. Two of these institutions indicated that ATP was incidentally used when no relevant motion was expected and no OAR were within the vicinity of the target. One institution performed ATP by default. Four institutions indicated to routinely perform ATP after the ATS workflow to correct for motion during the adaptation. Assessment of this motion was done visually in three institutions and using a 2 mm shift criterion in one.

Intrafraction motion was monitored using 2D cine images in five institutions. Cine images were judged visually on 'GTV outside of PTV' and institutions indicated to interrupt the workflow in that case however none such interruption occurred.

ATP fractions were scheduled in 30–45 min timeslots with institutions reporting an average fraction time of 30–36 min (reported by three institutions). In all three institutions that use ATP incidentally, two radiotherapy technologists (RTTs) were present in the treatment room. In the ATP default institution the physicist and physician were not present and only available on call, in one they were always present in the treatment room for the entire procedure, while in the third, the physicist was physically present, while the physician was present either in person or virtually via webex.

ATS fractions were scheduled in 45–70 min timeslots with institutions reporting an average fraction time of 36–50 min (reported by six institutions). The number of RTTs present varied from one to three. In five institutions the physician and physicist were always present, while in one institution all tasks, including target delineation, was delegated to specifically trained RTTs. In the other institutions the target was contoured by the physician and OARs were contoured either by the physician or RTT and then checked by the physician. Three institutions indicated to only partially delineate the OAR within a margin of 2–3 cm around the target.

Institutions anecdotally indicated that ATS was especially beneficial treating two lesions in a single treatment, or when OAR are close and expected not to be stable [19]. See Fig. 1 for such an example case.

Pre-treatment and online QA

All except one institution performed pre-treatment quality assurance (QA) on all patients. Measurements were performed using array or film,

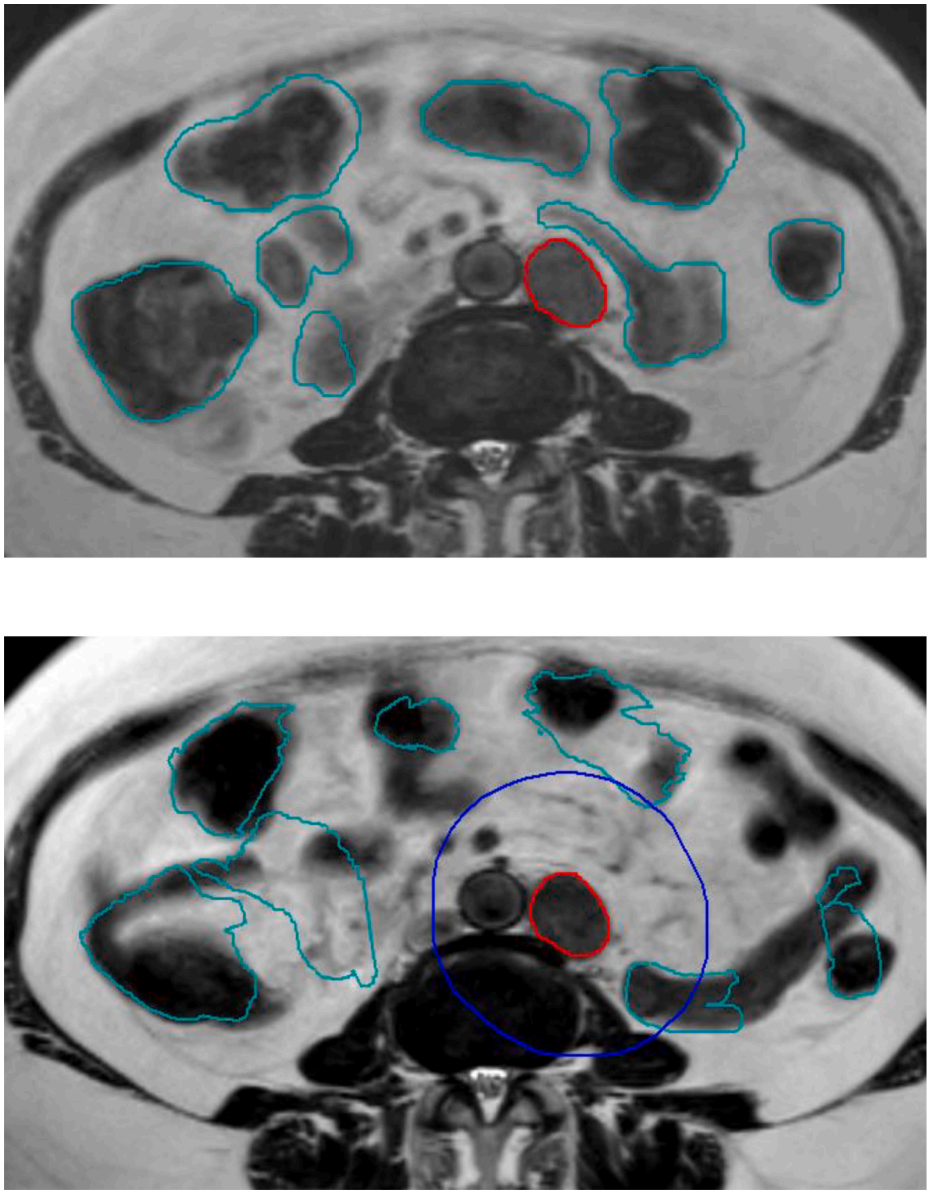

Fig. 1. An example case were ATS is beneficial. The pre-treatment image (top) shows the GTV (red) close to bowel loops (turquois) leading to underdosage of the target (PTV V95% = 92.9%, where 99% is required). The image of fraction one (bottom) shows a more favorable anatomy (the blue circle indicates a 3 cm ring within which OAR are corrected), resulting in an improved coverage of V95% = 99.1%. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

with excellent results (mean gamma pass rate > 95% reported by six institutions). Gamma criteria of 3%/3mm, 5%/2mm and 2%/2mm are used on different isodose volumes (5%, 10%, 20%, 50% of prescription dose). Only one institution indicates three cases where QA failed (evaluated on 2%/2mm in 10% volume).

After plan adaptation, QA of the online adapted plan was done in four institutions using a secondary dose algorithm, while two institutions perform a sanity check on segment shapes, monitor units, fluence and complexity by comparing these metrics with the reference plan. One institution indicated not to perform QA of online plans. No institution indicated errors were found in online QA.

Liver metastases

Four institutions treated 51 patients. The average age was 66 years (46–93 years). Ten patients treated at one institution have been previously reported [20], but are included in this present report.

Dose prescription differed over institutions from three to six fractions and fraction doses ranging from 5 to 22.5 Gy, With the most used fractionation being 3 × 15 Gy (N = 9), 3 × 20 Gy (N = 21) and 5 × 10 Gy (N = 10).

The primary difference between liver and lymph node treatment concerned the handling of breathing motion for all patients. At two institutions a 4D MRI workflow was developed [21,22], while the other two institutions used abdominal compression to limit breathing motion. One of these institutions only considers patients with a breathing amplitude < 15 mm as determined using 4DCT.

One institution has performed ATS for all patients, while two institutions have treated all patients using ATP. The fourth institution has used both, depending on tumor location and location of relevant OAR.

Online motion monitoring was done using 4D MRI in two institutions and using cine imaging in the other two. Treatment was interrupted if the GTV moves outside the PTV, which has happened in two cases.

Discussion

We report the first collaborative experience of seven institutions who treated OMD patients with 1.5 T MR-guided SABR on the Elekta Unity. The focus of this paper lies on workflows and practice standards for lymph node and liver oligometastases, representing the majority of OMD cases treated.

Considerable heterogeneity among institutions exists, reflecting the translation of CBCT-guided workflows towards MR-guided treatments for oligometastases in each institution. Differences in dose prescription and coverage criteria reflect the variety of dose prescriptions that exists for SABR worldwide. However, all prescriptions used fall within the range of prescriptions used in the SABR COMET trial [4] where “allowable doses ranged from 30 to 60 Gy in three to eight fractions”, with the exception of 5 × 5 Gy which was used thrice.

Most institutions treat with an ATS workflow, including daily recontouring of the target and OAR within 2–3 cm. Treatment slots are on average < 50 min and require the presence of a physician, although in one institution trained RTTs perform online target delineation. Especially for multiple targets and proximity of OAR, the ATS workflow appears beneficial. For spherical lesions with no adjacent OARs a simple ATP workflow might be more efficient.

SABR treatment of oligometastases has also been successfully proven feasible on the MRIdian [23,24], where the benefit of daily adaptation when OAR are close to the target has been shown, although requiring longer treatment slots (median on-table time of 79 min), mainly due to the gating procedure, substantially increasing treatment time.

In this work a large variation in treatment strategies was found. Currently there is little evidence preferring one strategy over the other and the variation reflects institutional preference and the current status of OMD treatments. However, most patients treated on the Unity have been or will be enrolled in the Momentum registry, which also captures clinical outcome measures. Therefore, we intent to study in future work the clinical relevance of the variations in institutional treatment strategies, potentially resulting in a consensus approach that makes best use of the possibilities of MR guidance.

Conflict of interest statement

A. Barry and T. Schytte report no conflicts of interest.

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A. Hosni: reports non-financial leadership of liver TSG of ELEKTA MRL consortium

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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