

Case Study

Liver Stereotactic Body Radiotherapy with Elekta Versa HD™ and Monaco® Flattening filter-free (FFF) Volumetric Modulated Arc Therapy (VMAT) for efficient SBRT delivery

Institution

Farrer Park Hospital

Location

Singapore

Contributors

Ms Hooi Yin Lim

Medical Physicist

Mr Lip Teck Chew

Chief Medical Physicist

Dr David Tan Boon Harn

Consultant Radiation Oncologist



Summary

Patient details

69-year-old male, diagnosed with hepatocellular carcinoma (HCC) in 2007, with multiple recurrences. Previous treatments include: Liver Wedge Resection of segment 7 (2007) and repeated Transcatheter Arterial Chemoembolization (TACE) and Radiofrequency Ablation (RFA) procedures.

Treatment

- Single isocenter liver SBRT: 30 Gy in 5 fractions
- Simultaneous integrated boosts: 35 Gy to ITV and 40 Gy to PTV40 in 5 fractions (1 cm internal ring)
- 2 VMAT arcs
- 6 MV FFF beams

Diagnosis

Multiple hepatocellular carcinomas in left and right hepatic lobes, including a large oligoproggressive lesion in segment 2 of the liver.

Treatment planning and delivery system:

- Monaco® treatment planning system version 5.11.02
- Versa HD™ linear accelerator
- XVI and HexaPOD™ Evo RT system
- BodyFIX®

Patient history and diagnosis

A 69-year-old male patient was diagnosed with hepatocellular carcinoma (HCC) in 2007 and has experienced multiple recurrences. A liver wedge resection of segment 7 was performed in 2007, followed by repeated transcatheter arterial chemoembolization (TACE) and radiofrequency ablation (RFA) procedures.

In May 2018, a CT scan revealed interval development of multiple hyper-enhancing nodules consistent with the presence of multicentric hepatoma. The largest lesion in the posterior aspect of segment 2 measured 6.2 x 4.5 cm (previously measured 3.3 x 3.0 cm). Other smaller lesions were seen elsewhere in the right and left hepatic lobes. A lipiodol stained nodule seen in segment 2/4A measured 3.4 x 3.2 cm and was stable. Underlying liver cirrhosis was evident but there were no CT findings of extrahepatic metastatic disease.

TACE was administered (using a mixture of 30 mg Adriamycin and 4 mg mitomycin mixed with 10 ml lipiodol) to multiple faintly enhancing tumor blushes

in both hepatic lobes. A CT scan in June 2018 revealed lipiodol uptake in the small peripheral tumors with no viable tumor tissue seen within or around them. However, the larger lesions still demonstrated areas of viable tumor tissue. The largest tumor in segment 2 measured 6.5 x 6.0 cm, with no lipiodol uptake and with portal vein tumor thrombosis evident on the left main portal vein, which was not present on the previous CT scan. TACE appeared to be stabilizing the smaller lesions, but the large lesion in S2 appeared to be growing and resistant. Blood flow was occluded in this lesion due to the portal vein thrombosis (PVT), making further TACE ineffective. If allowed to grow, this lesion would compromise liver function.

A subsequent MRI scan of the liver with IV contrast demonstrated the cirrhotic morphology of the liver and multiple hepatocellular carcinomas were seen scattered in the left and right hepatic lobes as well as the caudate lobe (Figure 1). The largest lesion measured 7.5 x 6.3 cm. The segment 2 portal vein branch was encased by the tumor with likely thrombus extending into the left main portal vein.

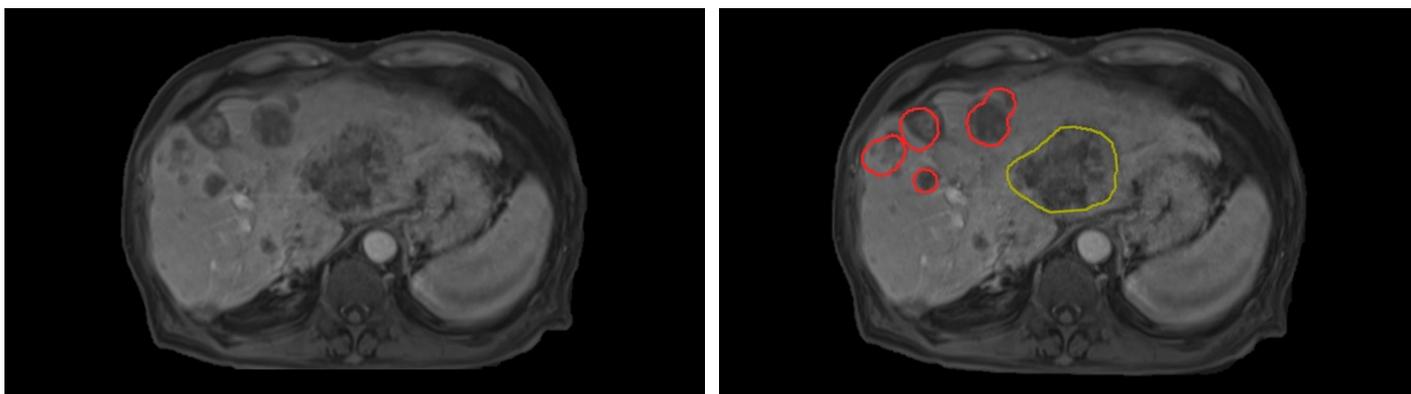


Figure 1.
MRI scan of liver showing hepatocellular carcinomas

Treatment options of stereotactic body radiotherapy (SBRT) versus systemic treatment were discussed. It was considered that Sorafenib (a kinase inhibitor approved for the treatment of advanced primary liver cancer) would have an effect on the other liver lesions, but that it would not target the oligoprogressive segment 2 lesion to the extent of incomplete/complete revascularization or

recanalization. RFA, radioembolization (Y90) and microwave ablation (MW) were deemed unsuitable for the treatment of the large segment 2 lesion due to its size and PVT. We believed SBRT of this lesion offered the potential for long term local control and recanalization. This would be followed by either Sorafenib maintenance therapy or close follow-up.

Treatment Planning

Liver SBRT treatment planning was performed using Monaco® version 5.11.02. A dose of 30 Gy was prescribed to the segment 2 lesion (PTV30) to be delivered in 5 fractions, in view of its large size, with simultaneous integrated boosts of 35 Gy to the ITVMinIP (minimum intensity projection-based ITV) and of 40 Gy to a 1 cm internal ring (PTV40).

The recent MRI of the liver was fused manually with the CT simulation dataset, with special attention to matching at the level of the segment 2 lesion and adjacent porta hepatis. The GTV was then defined on both the helical CT and MRI datasets and combined to give the final GTV tumor.

Liver tumors are usually seen as hypodensities against the normal liver parenchyma. Due to this characteristic of HCC, contouring is performed on the MinIP (minimum intensity projection) as it demonstrates the hypodense lesions most appropriately. A MinIP was generated using post-processing 4D CT data sets from the GE CT

simulator. The GTV tumor was then copied to a new "ITV" structure. The ITV was then manually expanded on the MinIP dataset, to account for the hypodense lesion in all phases of respiration. The final step was to verify the ITV by overlaying it on cine loop displaying 10 phases of the 4D CT data set and ensuring that the ITV encompassed all real-time translational movements.

A PTV was created from the ITV with a 5 mm margin to account for setup uncertainty on average intensity projection (AvgIP) images. Additionally, an internal ring structure was created from the ITV with a 1 cm reduction to create a PTV40 structure to which a higher dose could be applied safely away from liver or adjacent critical structures.

The AvgIP data set was used for treatment planning dose calculation and as the reference data set for image registration.

Treatment would be delivered every other day using two VMAT arcs and a 6 MV flattening filter-free (FFF) beam on a Versa HD linear accelerator (Table 1).

	Direction	Gantry Start (°)	Arc (°)	Increment (°)	Collimator (°)	MU / #
Arc 1	CW	180	360	20	0	1544.46
Arc 2	CW	180	360	20	30	2038.75

Table 1.
Field details for each VMAT arc on Versa HD (6MV FFF)

For the dose calculation, a grid spacing of 0.2 cm was used; statistical uncertainty was set to 0.7% per control point and calculate "dose to medium." Segment Shape Optimization (SSO) was used with a maximum number of control points set to "250," a minimum segment width of "0.5 cm" and fluence smoothing set to "low." The plan evaluation for targets is shown in Table 2; organ-at-risk (OAR) dose constraint requirements are shown in Table 3; isodose distributions and dose volume histogram (DVH) are shown in Figure 2. All plan objectives and dose constraints were met.

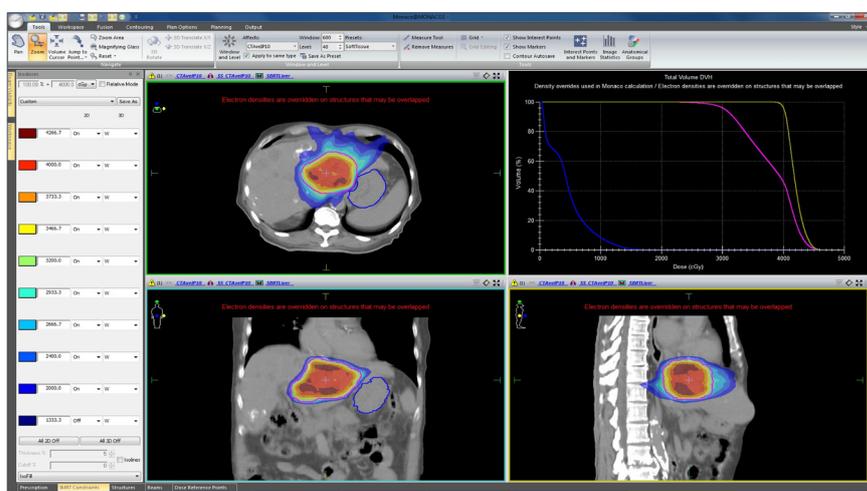


Figure 2.
Liver SBRT plan isodose distribution and dose volume histogram (DVH)

	Prescription Dose (Gy/3#)	PTV (cc)	Dmax (Gy) <125% of TPD	PTV (%)
PTV40	40	122.37	46.519	96.38% of 40 Gy
ITVMinIP	35	187.103	46.519	98.34% of 35 Gy
PTV30	30	282.882	46.519	96.03% of 30 Gy

Table 2.

Liver SBRT plan evaluation for targets

OAR	Constraints	Plan (Gy/cc/%)	
Heart (101¹, 0813²)	V32 Gy < 15 cc	0.530 cc	
	MPD 38 Gy or 105%	34.961 Gy	
Spinal Cord (0915³)	V22.5 < 0.25 cc	0	
	V13.5 < 0.5 cc	0	
	MPD 30 Gy	13.096 Gy	
Esophagus (101¹, 0813²)	V19.5 Gy < 5 cc	4.826 cc	
	MPD 35 Gy	26.658 Gy	
Liver GTV (U of C)⁸	> 700 ml < 15 Gy (minor variation < 18 Gy, acceptable < 21 Gy)	1228.613 cc	
	V12 < 50%	37.95%	
Gut (stomach/SB/colon) (101¹)	Stomach		
	V18 Gy < 5 cc (V12.5 < 10 cc) MPD 30 Gy	0.069 cc 8.841 cc 19.407 Gy	
	Duodenum		
	V18 Gy < 5 cc (V12.5 < 10 cc) MPD 30 Gy	0.0 0.0 2.999 Gy	
	Colon		
	V25 < 20 cc MPD 38 Gy	0.0 16.300 Gy	
Common bile duct	Dmax < 50 Gy	8.514 Gy	
Gall bladder	Dmax < 55 Gy	9.178 Gy	
Kidney (1112⁴/0438⁵ Montefiore/ Goodman⁹/Slo)		RT	LT
	V12 Gy < 25%	0.15%	0.0
	> 200 cc < 17.5 Gy	250.733 cc	182.307 cc
	> 75% of each kidney < 5 Gy	4.09%	0

Table 3.

Liver SBRT plan OAR constraints and planned dose values



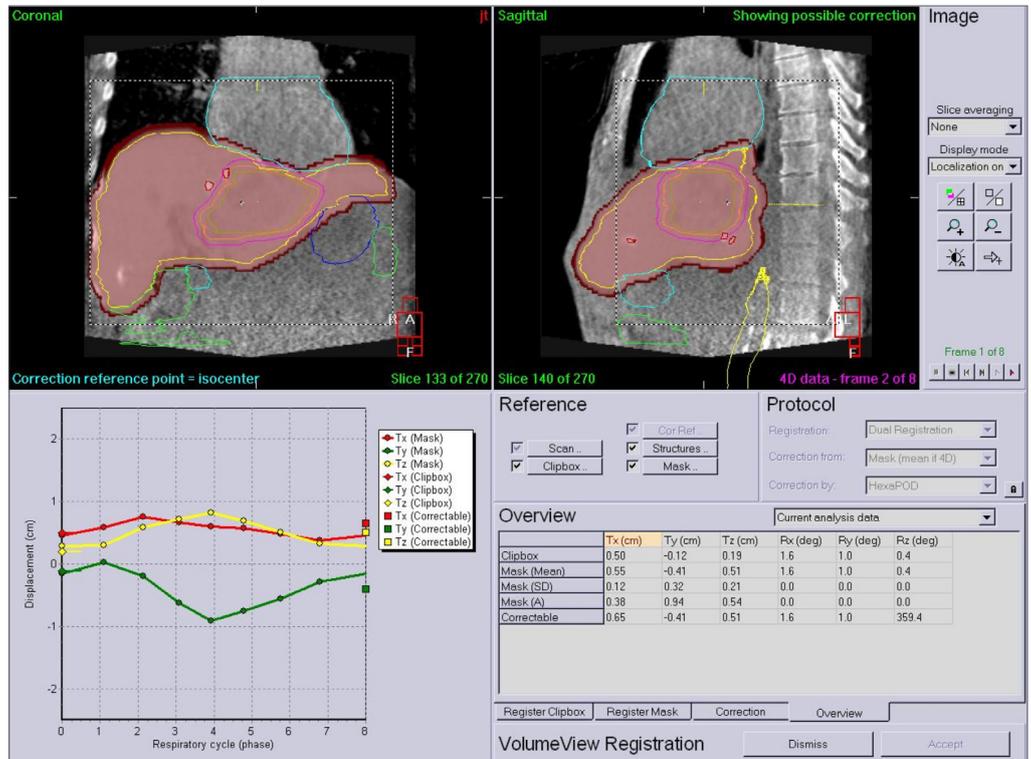


Figure 3.
Liver SBRT plan OAR
constraints and planned
dose values

Treatment quality assurance (QA)

Prior to the first treatment, the liver SBRT plan QA was performed using Mobius3DFX QA software and a measurement with a 20 cm-slabs phantom with Gafchromic EBT3 film. Mobius3DFX has an independent beam model based on a collapsed cone dose calculation algorithm to check target coverage and OAR DVH limits. A dose grid of 2 mm and 3D gamma criteria of 3%/2 mm \geq 95% were used.

Following these checks, triple channel film dosimetry analysis was performed with lateral response artifact correction. A pass rate of > 95% was achieved with 2D gamma criteria of 2%/2 mm using FilmQAPro software and with 3D gamma criteria of 3%/2 mm using the Mobius3DFX software. Quality assurance using the Mobius3DFX software was also performed for the remaining fractions using linac delivery log files.

Treatment delivery

Treatment commenced on July 18, 2018 with subsequent fractions delivered on the July 20, 23, 25 and 27. The patient was positioned supine with arms above head using BodyFIX and a Wingboard (CIVCO). The patient was positioned with two anterior and two lateral tattoos and shifted to isocenter using the couch move assist feature of MOSAIQ.

Prior to treatment, the patient was scanned on Elekta XVI CBCT using Symmetry™ (version 5.02.b72), which included a 4D CBCT image registration, correlated to find a time-weighted position of the PTV. Dual image registration, or Critical Structure Avoidance (CSA) was introduced, which involved two main steps: clipbox and mask registration. CSA is a unique Elekta tool for enhanced localization. CSA provides the user the opportunity to perform 3D dual registration of both OAR, in addition to the primary registration region.

For the first step, a clipbox was created that encompassed the whole liver and vertebrae to make a gross alignment using automation registration bone setting (T+R), which includes 6D translation. For the second registration, a mask was defined as the liver plus 5 mm margin using automation soft tissue registration grey value 4D setting for fine registration based on 10 frames of CBCT data sets. All translational and rotational errors were corrected automatically with the HexaPOD evo RT System, which enables six degrees of positioning freedom. Image matching for the first attempt was within +/- 5 mm and +/- 3 degrees. A second 4D Symmetry imaging scan was performed for shift verification. An overview of dual image registration and translation shift on the first day of treatment is shown in Figure 3.

When delivering the first arc of each beam, MotionView™ imaging was performed to monitor patient organ and target motion. MotionView is fluoroscopic-like, real-time monitoring of high contrast tumors or internal organs to accurately characterize internal motion at the time of treatment. After delivering the first arc, the software immediately reconstructs the fluoroscopic frames into a 3D dataset while treating the second arc. The resulting 3D VolumeView™ images were used for intrafractional and post-treatment evaluation. Our translational and rotational tolerances were +/- 2.0 mm and +/- 1.0 degrees.

Generally, 6 FFF plans facilitate significant treatment time reductions compared to conventional flat beam plans. Treatment delivery beam on time for this patient was seven minutes using a 6 FFF beam. The patient did not experience any discomfort during the treatment.

Outcome and follow-up

The patient tolerated SBRT well with only some fatigue that subsided a week after treatment. He was seen two weeks after SBRT for a routine post-treatment review and was asymptomatic then.

Regular alpha-fetoprotein (AFP) readings were taken before and after SBRT. The AFP level just before treatment was 67.3 ng/ml. At the two-week post-SBRT review, this had dropped to 40.9 ng/ml, and went down further to 33.3 ng/ml (more than half its initial level) by the fourth week. The patient also reported feeling better with improved energy levels and was eating better.

Unfortunately, the patient developed breathlessness two months after SBRT and investigations revealed a pulmonary embolus with superimposed bacterial pneumonia. He was admitted to the hospital and after a prolonged stay, succumbed to his comorbidities. A repeat CT or MRI of the liver could not be performed due to his poor clinical state. However, it was noted that during his regular hospital reviews there were no side effects from the liver SBRT treatment; liver function remained normal and no gastrointestinal symptoms were reported.

Discussion and conclusions

Two large challenges in radiation therapy are the setup error related to target motion and the overall uncertainty of the systems used to deliver the treatment. Setup error due to random target motion is very significant. This challenge has been managed by using a higher number of fractions and large target margins. However, in SBRT this is not an option.

Elekta's 4D Symmetry imaging enables us to acquire and compare time-weighted average images with the average 4D CT simulated image set used for treatment planning. This allows a 4D setup to 4D simulated CT image comparison instead of a standard CBCT setup image. This technology helps us to image appropriately in the presence of target and organ motion, and set up more accurately to overcome the error of random target motion. Additionally, the unique features of MotionView and VolumeView allow us to treat with confidence without additional imaging time.

The dual image registration feature found in XVI enables us to use both bone and soft tissue algorithms for the best overall image matching. We first perform the rotational correction using the bone algorithm. This results in a match based on the bony structures' relationship to the target followed by a translational correction based on a soft tissue algorithm match. After image registration, an overview of the 6D translational shift correction is informed by HexaPOD evo RT. HexaPOD evo RT is then able to correct residual misalignments with submillimeter 6D accuracy after the precise couch shift. This workflow further increases image guidance accuracy by reducing the uncertainty of tumour location.

Versa HD High Dose Rate Mode (FFF) enables faster treatments and reduces the risk of intrafractional motion. We observe significant treatment time reduction in high dose per fraction treatments such as SBRT. The average treatment time is about five and seven minutes respectively using 10 FFF at 2200 MU/min and 6 FFF at 1400 MU/min.

An alternative approach to manage motion for liver SBRT patients is the expiration breath-hold technique using the Elekta Active Breathing Coordinator device with standard CBCT imaging. This technique is suitable for patients with relatively good respiratory function. In addition, suitability is assessed by whether the patient can cooperate well after undergoing a few coaching sessions on Active Breathing Coordinator guided by a radiation therapist.

From our experience, the end expiration breath-hold technique can allow a PTV reduction of 2 mm

compared to the 4D CT approach. Once target motion is suppressed, the resulting CBCT becomes clearer. Together with a consistent volume expiration throughout the treatment, we have much higher confidence in matching the PTV and OAR compared to a 4D CT that can still present motion artifacts due to breathing. Nevertheless, the overall treatment delivery time for 4D CT and the breath-hold technique depends on the beam arrangement, complexity and modulation of the treatment plan, tumor motion with respect to the OAR, and patient breath-hold capability.

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Elekta Offices

Elekta AB

Box 7593
SE-103 93
Stockholm, Sweden

T +46 8 587 254 00
F +46 8 587 255 00

Europe

T +46 8 587 254 00
F +46 8 587 255 00

Turkey, India, Middle East & Africa

T +90 216 474 3500
F +90 216 474 3406

North & Central America including the Caribbean

T +1 770 300 9725
F +1 770 448 6338

South America & Cuba

T +55 11 5054 4550
F +55 11 5054 4568

Asia Pacific

T +852 2891 2208
F +852 2575 7133

Japan

T +81 3 6722 3800
F +81 3 6436 4231

China

T +86 10 5669 2800
F +86 10 5669 2900