Keerthaanaa Y[1,2], Gokula Kumar A[1,2*], Muhamad Zabidi A[1,2], Jasmin J[1,2], Syahir M[1,3], Mohd Zahri AA[1,2]

[1]Advanced Management of Liver Malignancies Program, Advanced Medical and Dental Institute, Universiti Sains Malaysia, Penang, Malaysia

[2]Radiotherapy Unit, Pusat Perubatan Universiti Sains Malaysia Bertam, Penang, Malaysia

[3]Nuclear Medicine Unit, Pusat Perubatan Universiti Sains Malaysia Bertam, Penang, Malaysia

*Corresponding author
Gokula Kumar Appalanaido
gokula@usm.my

Marginal Recurrence in Pre-Chemotherapy Tumor Volume after HDR-IBT for Colorectal Liver Metastasis: A Case Report

Abstract – High dose rate interstitial brachytherapy (HDR-IBT) is a potent local therapy for hepatic tumors, with local control (LC) rates in the range of 80 – 95% (1). However, poor tumor margin identification and delineation due to tumor shrinkage after systemic chemotherapy or targeted therapy, challenging anatomy for applicator placement, and conservative planning in patients with compromised liver function can all result in marginal misses (MM). MM occur when radiation does not sufficiently cover the microscopic disease beyond the visible tumor edge, hence lead to local recurrence (LR). A 66-year-old male with a solitary colorectal liver metastasis (CRLM) detected by positron emission tomography-computed tomography (PET-CT) scan underwent CT-guided HDR-IBT. LR of the treated lesion was noted within two months, outside 20Gy of HDR-IBT isodose line. This patient had systemic chemotherapy with XELOX and Avastin regimen before the procedure. The CT-guided HDR-IBT plan were fused with pre-chemotherapy and post HDR-IBT radiological images (CT and PET-CT) and analysed. It was noted that the tumor recurrence was within the pre-chemotherapy disease volume, which was not covered in the HDR-IBT prescription isodose. This suboptimal coverage is due to uncertainties in the target's peripheral margin after systemic therapy and difficult anatomic location of the target in order to achieve good dose coverage. Despite the optimal dose to the target, this case illustrates how marginal recurrences can still occur due to suboptimal dose coverage of the pre-chemotherapy disease volume which may still contain subclinical microscopic disease and anatomic limitations for optimal applicator placement. To enhance LC in HDR-IBT for CRLM, it is essential to adopt proactive approaches, such as integrating pre-treatment tumor volumes into the planning process, identifying the optimal applicator placement via pre-planning, and using a more lenient or larger isodose coverage of the target in post chemotherapy setting if liver reserve allows (2–4).

Keywords – Acute coronary syndrome, biomarker, cardiovascular disease, chronic stable angina, PIGF, sRAGE

1 INTRODUCTION

Liver metastases are increasingly managed using minimally invasive, image-guided local therapies that offer curative or palliative potential when surgical resection is not feasible [1]. Among these, high dose rate interstitial brachytherapy (HDR-IBT) has emerged as an effective option, capable of delivering highly conformal radiation doses directly to the tumor while maintaining a steep dose gradient to spare surrounding healthy liver parenchyma and organs at risk (OARs) [2, 3]. HDR-IBT has demonstrated favorable local control (LC) rates and safety profiles across various primary tumor origins, including colorectal, breast, and neuroendocrine metastases [2, 3].

Despite its precision and steep dose fall-off, local recurrence (LR) can still occur, often due to marginal misses (MM) or microscopic tumor spread beyond the prescribed isodose volume [4, 5]. Anatomical constraints, prior treatments, or dose reductions necessitated by compromised liver function may further limit the achievable coverage margin, thereby increasing the risk of underdosage at the periphery of the target volume.

This case report highlights a recurrence outside the 20 Gy isodose line following HDR-IBT for a colorectal liver metastasis (CRLM). It underscores the interplay between anatomic proximity to critical structures, recent systemic therapy, and conservative dose margins in patients with pre-existing hepatic impairment. Furthermore, it emphasizes the need for optimized pre-treatment imaging, individualized pre-planning, and evidence-based isodose margin recommendations to mitigate the risk of marginal failure.

2 METHODOLOGY

2.1 Patient History

A 66-year-old male with a history of stage IIIc colorectal adenocarcinoma was referred for liver-directed therapy following disease recurrence. The patient had previously undergone a right hemicolectomy in 2023, followed by adjuvant systemic chemotherapy with capecitabine and oxaliplatin (XELOX) in combination with bevacizumab (Avastin). Restaging computed tomography (CT) in late 2023 revealed five hepatic lesions, three of which were located in the right hepatic lobe. Subsequent positron emission tomography–computed tomography (PET-CT) in early 2024 confirmed three fluorodeoxyglucose (FDG)-avid lesions in hepatic segments V, VII, and VIII, consistent with metastatic disease.

The radiation oncology team elected to treat one lesion at a time using HDR-IBT, with close post-treatment surveillance. The first selected liver lesion, in segment VIII, was deemed unresectable due to its proximity to the diaphragm. During HDR-IBT planning, fusion of PET-CT and contrast-enhanced CT images was not achievable due to technical limitations, preventing accurate alignment of metabolic and anatomical data. Additionally, recent chemotherapy-related hepatic parenchymal changes further obscured lesion margins, complicating target delineation.

2.2 Treatment Procedure

In April 2025, HDR-IBT was performed using two applicators inserted via the right anterior approach, centrally placed within gross tumor volume (GTV), located in the subdiaphragmatic region (Figure 1A). A total dose of 25 Gy was prescribed to the GTV using Iridium-192 (^{192}Ir) radioactive source via HDR remote afterloader. Considering the patient's prior hepatic treatments and compromised liver function, the dose coverage margins were deliberately constrained to minimize the risk of radiation-induced liver injury. Following HDR-IBT, the patient received adjuvant oral chemotherapy with cetuximab.

HDR-IBT planning was performed by the medical physicist using Oncentra Brachy treatment planning system (TPS) with graphical optimization mode. The planning objective were defined as follows: the dose delivered to 100% of the GTV ($D_{100\%}$) was required to be ≥ 25 Gy, while the volume of healthy liver (excluding the GTV) receiving 5 Gy and 8 Gy was constrained to V_{5Gy} < 30% and V_{8Gy} < 60%, respectively.

3 RESULTS

3.1 Post-treatment Course

The HDR-IBT procedure was well tolerated by the patient without any acute complications. At the two-month follow-up, PET-CT demonstrated a focal area of increased standardised uptake value (SUV) adjacent to, but outside, the previously treated liver lesion (Figure 1). Image fusion with the HDR-IBT planning CT revealed that the recurrence was located just beyond the 20 Gy isodose line, indicating a MM. To preserve the uninvolved liver parenchyma, a salvage HDR-IBT procedure was performed instead of surgery resection. A brief timeline of events is illustrated in Figure 2.

3.2 HDR-IBT Plan Review

A detailed retrospective review of the HDR-IBT treatment plan is presented in Table 1. All institutional dosimetric objectives were successfully achieved, with the following parameters: $D_{100\%}$ = 27.56 Gy (≥ 25 Gy), V_{5Gy} = 18.69% (< 30%) and V_{8Gy} = 9.84% (< 60% of the healthy liver volume). Despite meeting all dose constraints, post-treatment imaging revealed a MM occurring just beyond the 20 Gy isodose boundary (Figure 1).

4 DISCUSSIONS

This case exemplifies that the efficacy of HDR-IBT depends not only on achieving dosimetric objectives but also on precise target delineation and applicator geometry, particularly in anatomically constrained regions such as the subdiaphragmatic liver. MM may occur despite meeting prescribed dose metrics when systemic therapy induces parenchymal changes that obscure lesion boundaries, thereby reducing the accuracy of tumor contouring [6, 7]. Integrating pre-systemic therapy PET-CT or MRI with the HDR-IBT planning CT images has been shown to improve target definition by better differentiating viable tumor tissue from therapy-induced changes [8, 9].

Another key determinant of treatment success is applicator placement geometry. In this case, both applicators were positioned centrally within the oval-shaped lesion in segment VIII, resulting in a predominantly spherical dose distribution (Figure 1). However, due to anatomical constraints beneath the diaphragm, achieving a combined central and spaced-out catheter configuration, which ensures adequate dose coverage of the

tumor margins was not feasible. When anatomy permits, peripheral catheter arrangements should be employed to fully encompass the GTV and a small safety margin [2, 10].

Additionally, tight dose margins were intentionally applied in this patient due to prior systemic therapy and compromised liver function, limiting dose expansion beyond the visible tumor boundary. Given that LR often originate at underdosed peripheries, the absence of a high-dose margin encompassing the pre-chemotherapy GTV likely contributed to the marginal recurrence observed just beyond the 20 Gy isodose line [10]. Although the prescribed dose coverage goals ($D_{100\%}$ = 27.56 Gy; $D_{90\%}$ = 46.27 Gy) were met, the recurrence highlights the importance of ensuring that the ≥ 20 Gy isodose adequately covers the visible lesion and an appropriate safety margin [11].

Based on our experience and prior articles, defining a planning target volume (PTV) that accounts for catheter motion and respiratory-induced target displacement can further mitigate the risk of MM. In HDR-IBT, the GTV is often equated with the clinical target volume (CTV) and PTV, however, this may not be sufficient in mobile organs such as the liver [12]. Accounting for possible applicator movement by expanding the contour along the catheter insertion pathway has been suggested as a practical strategy to ensure consistent coverage during both planning and delivery [13].

5 CONCLUSION

This case report highlights that even with full dosimetric compliance, MM can occur when margin coverage is restricted by anatomical constraints, applicator geometry or poor tumor visualization after systemic therapy. Proactive strategies should include integration of pre-treatment multimodality imaging for accurate target definition, optimization of applicator trajectories, and robust isodose margin planning that accommodates anatomical variability and treatment-related changes. Clinically, ensuring that the ≥ 20 Gy isodose line encompasses the entire pre-treatment tumor volume with an adequate safety margin, may reduce the risk of marginal recurrence and enhance LC.

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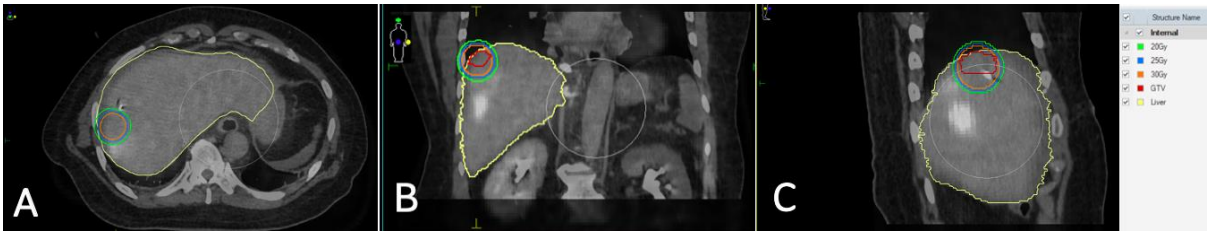

Figure 1. Image fusion of post-treatment PET CT and CT based HDR-IBT planning in (A) axial, (B) coronal and (C) sagittal views.

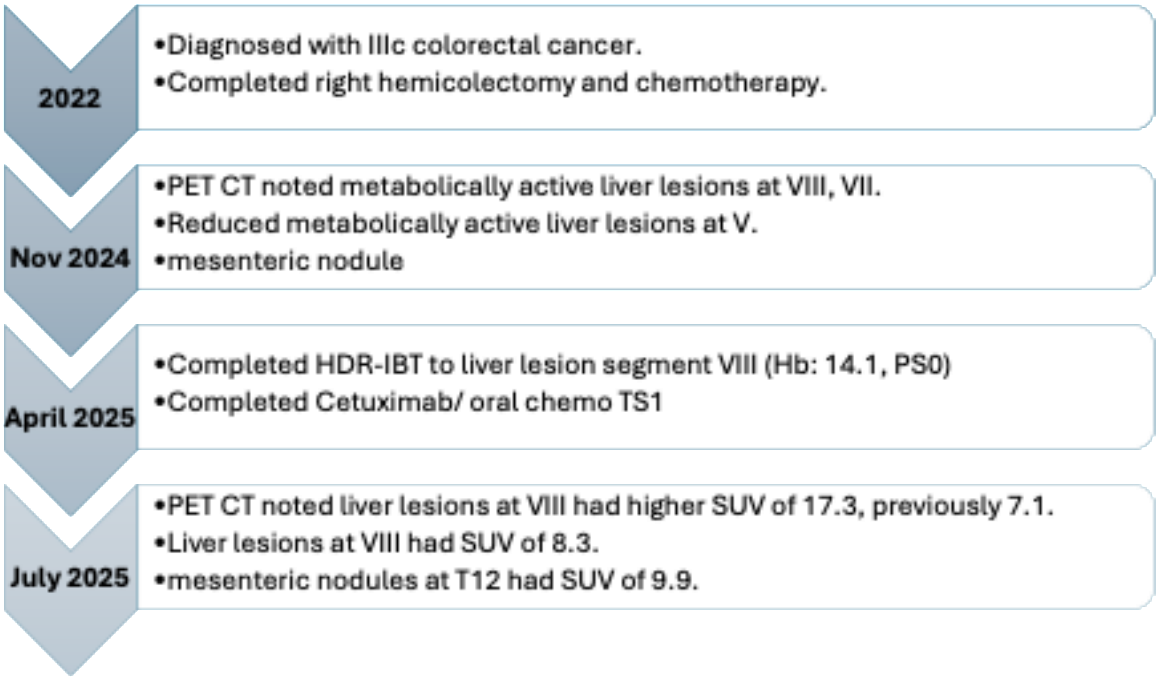

Figure 2. Timeline of events.

Table 1. HDR-IBT dosimetric output.

Structure	Largest dimension (cm)	Total volume (cm^3)	$D_{100\%}$ (Gy)	$D_{99\%}$ (Gy)	$D_{95\%}$ (Gy)	$D_{90\%}$ (Gy)	V_{5Gy} (%)	V_{8Gy} (%)
Gross tumor volume (GTV)	3.76	10.55	27.56 ≥ 25	34.19	41.33	46.27	-	-
Liver	-	1434.17	-	-	-	-	18.69 < 30	9.84 < 60

$D_{100\%}$, $D_{99\%}$, $D_{95\%}$ and $D_{90\%}$: dose received by 100, 99, 95 and 90% of GTV volume; V_{5Gy} and V_{8Gy}: healthy liver volume (exclude GTV) receiving 5 and 8 Gy; cm: centimeter; cm^3: cubic centimeter; Gy: Gray.