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Association Between a Novel MTV-Based Effective Absorbed Dose Index and ALBI Score Changes in Metastatic Colorectal Cancer Patients Treated with Yttrium-90 Glass Microspheres

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Abstract

Objective(s):

TARE aims to selectively deliver high-dose radiation to tumour tissue while preserving non-tumoural liver parenchyma. Although metabolic imaging parameters such as metabolic tumour volume (MTV) and total lesion glycolysis (TLG) are widely used for response assessment, their integration with dosimetric data and liver function parameters remains limited. This study aimed to evaluate the relationship between a novel MTV-based Effective Absorbed Dose Index and changes in ALBI score in metastatic colorectal cancer (mCRC) patients treated with ^{90}Y glass microspheres.

Methods

Seventy-seven mCRC patients undergoing 93 TARE procedures were included. Post-treatment absorbed doses to perfused tumour and non-tumoural liver parenchyma were calculated from ^{90}Y SPECT/CT using Simplicit90Y™ software. Pre- and post-treatment FDG PET/CT provided MTV and normal liver volumes. Indices were defined as: A=(tumour absorbed dose/MTV)x100, B=(non-tumoural absorbed dose/normal liver volume)×100. The “Effective Absorbed Dose Index for MTV” was defined as A/B. ALBI scores were calculated at baseline and at 8–9 weeks post-TARE. Changes in ALBI score were recorded for each case, and their relationship with the Effective Absorbed Dose Index for MTV was analysed.

Results

ALBI score deterioration occurred in 20.4% of sessions. Higher MTV-based Effective Absorbed Dose Index values were significantly associated with stable liver function (p = 0.038; negative predictive value = 88%). ROC analysis demonstrated moderate predictive performance (AUC = 0.66).

Conclusions

The MTV-based Effective Absorbed Dose Index may provide a clinically useful metric for balancing therapeutic efficacy and hepatic toxicity in TARE and has potential to support individualized treatment planning and risk stratification in patients with liver-dominant mCRC.

Introduction

Colorectal cancer remains one of the leading causes of cancer-related morbidity and mortality worldwide. The liver is the most common site of metastatic spread and a key determinant of patient prognosis [1]. In patients with metastatic colorectal cancer (mCRC), effective management of liver-

dominant disease is critical for improving survival outcomes, especially in heavily pretreated populations with limited systemic treatment options [2].

Hybrid imaging, particularly ^{18}F-FDG PET/CT, plays an indispensable role in characterizing tumour biology and evaluating treatment response. While the standardized uptake value (SUV) reflects glucose metabolism at a voxel level, volumetric parameters such as metabolic tumour volume (MTV) and total lesion glycolysis (TLG) provide a more comprehensive assessment of the global metabolic tumour burden. These parameters, have demonstrated significant prognostic value in colorectal cancer and other malignancies [3–8].

Transarterial radioembolization (TARE) with Yttrium-90 (^{90}Y) microspheres is an established locoregional therapy that delivers high-dose internal radiation selectively to hepatic tumours. Glass microspheres are characterised by high activity per particle, while extended shelf-life formulations allow broader distribution with lower activity per sphere. Although previous studies have shown a clear association between tumour-absorbed dose and therapeutic response, most have focused on absolute tumour dose metrics. The combined impact of dose distribution across tumour burden and non-tumoural liver parenchyma -particularly its effect on post-treatment liver function- remains insufficiently characterised, especially in mCRC patients undergoing repeated TARE sessions [9–11].

Accurate assessment of liver function is essential in this setting. The albumin–bilirubin (ALBI) score is an objective, reproducible biomarker of hepatic functional reserve that relies solely on serum albumin and bilirubin levels and has gained increasing acceptance for monitoring treatment-related hepatotoxicity [12].

Building upon our previous analysis of the same cohort of 77 mCRC patients who underwent 93 TARE procedures with ^{90}Y glass microspheres [13], the present study introduces a novel MTV-based Effective Absorbed Dose Index, derived from post-TARE ^{90}Y SPECT/CT dosimetry and FDG PET/CT metabolic parameters, and evaluates its relationship with subsequent changes in ALBI score. By integrating personalised dosimetry with metabolic tumour burden and functional liver assessment, this study aimed to provide a more comprehensive framework for balancing therapeutic efficacy and hepatic toxicity following TARE.

Materials And Methods

Study Design and Patient Population

This retrospective and prospective cohort study included 77 patients with mCRC who underwent a total of 93 TARE procedures with ^{90}Y glass microspheres between September 2017 and June 2023. Prospective data collection began in 2020; while data from earlier periods were collected retrospectively from institutional records. All patients had an Eastern Cooperative Oncology Group (ECOG) score of ≤ 2 and adequate liver function to tolerate the procedure. Patients were excluded if they had poor image

registration quality, tumours with low ^{18}F-FDG uptake, baseline MTV < 5 cm³ on ^{18}F-FDG PET/CT, or an expected survival of less than three months. All cases were evaluated and approved by the institutional multidisciplinary oncology team.

The study protocol was approved by the Marmara University Ethics Committee (approval number: 1141; date: 02 September 2022). Written informed consent was obtained from prospectively enrolled patients; the requirement for informed consent was waived for retrospective cases.

TARE Procedures

All TARE procedures were performed by experienced two interventional radiologists using ^{90}Y glass microspheres via lobar or selective/super-selective approaches. Prior to treatment, planning angiography with ^{99m}Technetium-labeled macro-aggregated albumin (^{99m}Tc-MAA) was performed to evaluate intra- and extrahepatic particle distribution and to calculate the lung shunt fraction (LSF). Procedures were conducted under local anesthesia via a transfemoral approach. A 5F diagnostic catheter was used to access the celiac trunk, and a 2.4-2.7F microcatheter was advanced into the target hepatic arterial branch. Cone-beam CT was utilised intra-procedurally to confirm catheter position and perfusion territory. Quantitative SPECT/CT imaging was performed to verify preferential ^{99m}Tc-MAA uptake in tumour tissue compared with non-tumoural liver and to obtain target and non-target volumes for dosimetry. Treatment proceeded only when lung dose and LSF were within accepted safety limits.

For prospectively enrolled patients, contrast-enhanced CT, MRI, or ^{18}F-FDG PET/CT images were coregistered with pre-treatment ^{99m}Tc-MAA single-photon emission computed tomography combined with computed tomography (SPECT/CT) using Simplicit90Y™ software (Mirada Medical Ltd, Oxford, UK). Volumes of interest (VOIs) were segmented to include the whole liver, perfused tissue, normal liver tissue, perfused normal tissue, perfused tumour, and viable perfused tumour. In retrospective cases, treatment planning was performed using a one-compartment MIRD model, aiming for a mean absorbed dose of 50–200 Gy (or > 200 Gy for radiation segmentectomy cases) in the treated volume with a personalized approach.

Dosimetric Calculations

Post-treatment dosimetry was performed using Simplicit90Y™ software. Diagnostic CT, MRI, or ^{18}F-FDG PET/CT images were coregistered with post-therapy ^{90}Y Bremsstrahlung SPECT/CT images (Siemens Symbia TruePoint). VOIs were segmented to include the whole liver, perfused tissue, normal liver tissue, perfused normal tissue, perfused tumour, and viable tumour regions. Tumours and necrotic areas were manually delineated on pre-treatment imaging. Perfused volumes were defined using adaptive thresholding. Absorbed doses to the perfused tumour and non-tumoural liver parenchyma were calculated in Gray (Gy).

MTV-Based Effective Absorbed Dose Index and Its Association with ALBI Score Changes

Baseline and follow-up ^{18}F-FDG PET/CT scans (Discovery ST PET/CT scanner, GE Healthcare, Milwaukee, WI, USA) were performed to quantify MTV. MTV was defined on baseline ^{18}F-FDG PET/CT using PERCIST 1.0 criteria (as previously described in our cohort [13]). The volume of non-tumoural liver parenchyma was also measured. To normalise absorbed dose to tissue volume, two indices were defined:

Tumour dose index A = (perfused tumour absorbed dose / MTV) x 100

Normal liver dose index B = (non-tumoural liver absorbed dose / normal liver volume) x 100

The MTV-based Effective Absorbed Dose Index was calculated as the ratio A/B.

Liver function was assessed using the ALBI score, calculated before treatment and at 8–9 weeks after each TARE session using the formula:

ALBI = [$\log_{10}$ bilirubin (µmol/L) × 0.66] + [albumin (g/L) × (− 0.085)].

Follow-up and Outcome Assessment

Patients underwent clinical and laboratory evaluation at baseline, 2, 4, and 8 weeks after TARE. Laboratory parameters included serum albumin, total bilirubin, alkaline phosphatase, gamma-glutamyltransferase, aspartate aminotransferase, alanine transaminase, complete blood count with platelets, and international normalized ratio. Adverse events were graded according to CTCAE version 5.0 [14]. Radioembolization-induced liver disease (REILD) was defined as deterioration of liver function within 2 weeks to 2 months after TARE, according to the criteria proposed by Gil-Alzugaray [15] and Sangro [16] (total bilirubin ≥ 3 mg/dL and new-onset ascites in the absence of tumour progression or biliary obstruction).

Patients were followed for a minimum of 6 months to assess radioembolization-induced chronic hepatotoxicity (RECHT), defined as new, persistent grade ≥ 3 hepatotoxicity unrelated to disease progression or other treatments. Survival data (diagnosis-to-death and post-TARE overall survival) were collected from institutional records and national death registries.

Statistical Analysis

Statistical analyses were performed using SPSS software (version 26.0, IBM Corp., Armonk, NY, USA). Continuous variables were compared between groups using the Mann-Whitney U test. Receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive performance of the MTV-based Effective Absorbed Dose Index for ALBI score preservation or deterioration. Survival data were

summarised as median (range) and compared across subgroups. A *p*-value < 0.05 was considered statistically significant.

Results

A total of 77 patients who underwent 93 TARE procedures with ^{90}Y glass microspheres were included. The median age was 65 years (range, 32–85), with 53 males (69%) and 24 females (31%). Multiple hepatic lesions were present in 49 patients (64%), whereas 28 (36%) had a solitary lesion. Bilobar liver involvement was identified in 45 patients (58%).

The median absorbed dose to perfused tumour tissue was 137.6 Gy, while the median dose to perfused normal liver tissue was 110.8 Gy. The healthy liver parenchyma received a substantially lower median dose of 19.6 Gy. The median percent change in MTV demonstrated a reduction of 29.4% (range, -100% to + 2528%).

Baseline patient and treatment characteristics are summarised in Table 1.

Table 1
Baseline patient and treatment characteristics (77 patients, 93 TARE procedures)

Parameter	**Value**
Patients, *n*	77
TARE procedures, *n*	93
Age (years), *median (range)*	65 (32–85)
Male / Female, *n (%)*	53 (69%) / 24 (31%)
ECOG Performance status 0 / 1 / 2, *n (%)*	50 (65) / 22 (29) / 5 (6)
Primary Tumour Location	
- Right-sided	55 (71%)
- Left-sided	22 (29%)
Tumour number	
- Single	28 (36%)
- Multiple	49 (64%)
Index tumour size	
- <5cm	29 (38%)
- ≥5 cm	48 (62%)
Bilobar Disease, *n (%)*	45 (58%)
Liver volume, *(cm^3)*	1659 (961–4387)
Metabolic tumour volume, *(cm^3)*	52 (1.46–1498)
Extrahepatic disease at baseline	16 (21%)
Previous systemic chemotherapy, *n (%)*	77 (100%)
Number of TARE sessions per patient, *median (range)*	1 (1–6)
- Single session, *n (%)*	40 (52%)
- Two or more sessions of TARE, *n (%)*	37 (48%)
- Two sessions of TARE, *n (%)*	23 (30%)
- Three sessions of TARE, *n (%)*	11 (14%)
- Four / five / six sessions of TARE, *n (%)*	1/1/1 (%1)
Radioembolization approach	

Parameter	Value
- Unilobar treatment (for whole lobe)	43 (46%)
- Selective unilobar infusion	46 (50%)
- Selective bilobar infusion	4 (4%)
Activity ordered, *GBq*	10.5 (3.0-34.5)
Time after calibration, *days*	10 (8–12)
Lung shunt fraction, *%*	5 (5–20)
Administered activity, *GBq*	0.99 (0.22–3.23)
Perfused tissue absorbed dose, *Gy*	114.9 (18.4-661.3)
Perfused tumour tissue absorbed dose, *Gy*	137.6 (20.6-711.7)
Perfused normal tissue absorbed dose, *Gy*	110.8 (16.9-638.8)
Healthy liver absorbed dose, *Gy*	19.6 (1.5–63)
Absorbed lung dose, *Gy*	2.9 (0.6–16.2)
Percent change of MTV, *%*	-29.4% (-100% to 2528%)
Absorbed tumour dose for pre-treatment unit MTV	305 (6.09-7917.81)
Continuous variables are presented as median with minimum and maximum values while categorical variables are reported as frequencies and percentages.	

The MTV-based Effective Absorbed Dose Index ranged from 4.3 to 17,079. Higher MTV-based Effective Absorbed Dose Index values were significantly associated with preservation of liver function (Mann–Whitney U test, $p = 0.038$), with a negative predictive value of 88%. The distribution of the MTV-based Effective Absorbed Dose Index according to ALBI score changes is presented in Table 2.

Table 2
MTV-based Effective Absorbed Dose Index according to ALBI score changes following TARE (93 TARE procedures)

Parameter	***n (%)***	**MTV-based Effective Absorbed Dose Index *median (range)***
All patients - Baseline	93 (100%)	142.1 (4.3-17079)
- Grade 1	71 (76%)	159.4 (4.3–8039)
- Grade 2	22 (24%)	101.9 (8.1-17079)
- Grade 3	-	-
All patients - Post-TARE	93 (100%)	142.1 (4.3-17079)
- Grade 1	60 (65%)	177.2 (4.3–8039)
- Grade 2	32 (34%)	85.2 (8.1-17079)
- Grade 3	1 (1%)	139.8
Worsened	19 (20.4%)	55.3 (18.6-4529.8)
- Grade 1 ◊ Grade 2	18 (19%)	55.3 (18.6-4529.8)
- Grade 2 ◊ Grade 3	1 (1%)	139.8
- Grade 1 ◊ Grade 3	-	-
Continuous variables are presented as median with minimum and maximum values while categorical variables are reported as frequencies and percentages.		

ROC analysis was performed to evaluate the discriminative performance of the MTV-based Effective Absorbed Dose Index for ALBI score deterioration (Fig. 1). The analysis demonstrated moderate predictive ability, with an area under the curve (AUC) of 0.66 (standard error, 0.069; 95% confidence interval, 0.519–0.791; $p = 0.038$). Two potential cut-off values were identified using the Youden index method. A cut-off value of 65 provided a sensitivity of 57.9% and a specificity of 79.7%, while a cut-off value of 156 yielded a sensitivity of 73.7% and a specificity of 50%. The cut-off value of 65 was considered more clinically useful due to its higher specificity, allowing better identification of patients at risk of ALBI score deterioration. The higher cut-off (156) correctly identified both the REILD and RECHT patients. The lower cut-off of 65 identified the REILD patient after the first two treatments. Diagnostic performance of these cut-off values is summarized in Table 3.

Table 3
Diagnostic performance of pre-treatment MTV-based index cut-off values determined by the Youden index method

Cut-off value (Youden index)	***Sensitivity (%)***	***Specificity (%)***	***Clinical Interpretation***
65	57.9	79.7	Higher specificity
156	73.7	50.0	Balanced

ALBI score deterioration was observed in 19 of 93 TARE sessions (20.4%). These 19 events occurred in 17 unique patients; one patient experienced no ALBI change after the first TARE, developed Grade 1◊2 deterioration after the second TARE (with a reduced dose compared to the first treatment), and received another reduced dose for the third treatment. This third treatment resulted in a dosimetric value that was below the higher cut-off (156) but above the lower cut-off (65); REILD developed after this session. Another patient maintained stable ALBI Grade 1 after both TARE sessions but later developed RECHT (Fig. 2).

The toxicity profile of TARE with ^{90}Y glass microspheres was favourable. No unexpected or clinically significant additional toxicities were observed beyond those anticipated with the procedure (Table 4). Among the 12 patients who died within the first 6 months, disease progression was the primary cause of death in 11 cases. Biliary complications occurred in two patients (one bile leak and one case requiring cholecystectomy after the second TARE session). Six patients required percutaneous transhepatic biliary drainage within the first six months due to tumour progression or mass effect.

Table 4
CTCAE grading of new clinical and laboratory toxicity per patient for at least 6 months after treatment

Parameter	CTCAE Grade	
	III	IV
Laboratory toxicity		
Albumin	-	1
Total bilirubin	1	1
Alkaline phosphatase	1	-
Aspartate aminotransferase	1	-
Alanine transaminase	-	-
INR	-	-
Thrombocytopenia	-	-
Clinical toxicity		
Abdominal pain	1	-
Nausea	1	-
Fever	-	-
Ascites	-	-
Encephalopathy	-	-
REILD	1 (after 3rd TARE)	
RECHT	1 (after 3rd TARE)	

Survival Outcomes

Survival data were available for all 77 patients (Table 5). At the time of analysis, 74 patients (96%) had died. The median survival from initial diagnosis to death was 40.9 months (38.3 months among deceased patients). The median overall survival after the first TARE procedure was 13.6 months (13 months among deceased patients).

Table 5

Survival outcomes in patients with mCRC treated with ^{90}Y glass microsphere TARE

Subgroup	***n (deceased)***	***Median diagnosis-to-death (months)***	***Median OS after TARE (months)***
All patients	**77 (74)**	**40.9 (38.3)**	**13.6 (13)**
Without extrahepatic metastases	61 (58)	41.9 (40.9)	15.2 (14.8)
With bilobar disease	45 (43)	38.1 (37.9)	13.1 (13)
With synchronous metastases	35 (33)	38.7 (37.9)	13.6 (13.1)
Single TARE session	**40 (40)**	**34.6 (34.6)**	**10.4 (10.4)**
Without extrahepatic metastases	29 (29)	34.6 (34.6)	12.4 (12.4)
With bilobar disease	23 (23)	34.3 (34.3)	11.6 (11.6)
Without extrahepatic metastases	17 (17)	35.0 (35.0)	12.3 (12.3)
Two or more TARE sessions	**37 (34)**	**45.7 (41.9)**	**18.5 (16.4)**
With extrahepatic metastases	32 (29)	48.5 (45.7)	19.6 (16.4)
With bilobar disease	22 (20)	41.9 (38.7)	15.4 (15.2)
With synchronous metastases	18 (16)	41.7 (38.7)	18.5 (17.1)
Two sessions	23 (22)	45.7 (41.9)	15.4 (15.2)
Three sessions	11 (9)	50.0 (42.6)	**31.7 (31.3)**
Four sessions	1 (1)	38.1 (38.1)	26.7 (26.7)
Five sessions	1 (1)	27.6 (27.6)	20.2 (20.2)
Six sessions	1 (1)	48.6 (48.6)	30.2 (30.2)

Numbers in parentheses refer to deceased patients only. OS= overall survival from first TARE procedure.

Patients without extrahepatic metastases at baseline had numerically longer median post-TARE survival (15.2 months) compared with the overall cohort. Patients who received two or more TARE sessions (n = 37) had substantially longer median survival after treatment (18.5 months) than those who received a single session (10.4 months). Among patients who received multiple sessions, those treated with three sessions showed the longest median post-TARE survival (31.7 months).

Survival outcomes according to treatment subgroups are detailed in Table 5.

Discussion

This study demonstrates that a novel MTV-based Effective Absorbed Dose Index is significantly associated with preservation of liver function, as measured by the ALBI score, in patients with mCRC undergoing TARE with ^{90}Y glass microspheres. Higher index values were associated with stable ALBI scores (p = 0.038, negative predictive value = 88%), while ROC analysis showed moderate predictive performance (AUC = 0.66).

Building upon our previous analysis of the same cohort of 77 mCRC patients who underwent 93 TARE procedures [13], the present study shifts the focus from metabolic tumour response to hepatic functional reserve by integrating personalised dosimetry with metabolic tumour volume. To our knowledge, this is the first to correlate an MTV-normalised absorbed dose index with post-TARE changes in ALBI score in mCRC patients. The index provides a simple, clinically relevant metric that accounts for the relative distribution of radiation between tumour burden and non-tumoural liver parenchyma.

Radioembolization-induced liver disease (REILD), the clinical manifestation of veno-occlusive disease or sinusoidal obstruction syndrome, is a rare but potentially serious complication following TARE [17]. Its chronic form, radioembolization-induced chronic hepatotoxicity (RECHT), which develops at least 6 months after treatment, is associated with persistent liver function deterioration and has been reported in up to 13% of patients, with fatal outcomes in selected cases [18]. In this context, we specifically chose the ALBI score because it is an objective and reproducible biomarker based solely on serum albumin and bilirubin levels, thereby eliminating the subjective parameters and categorical limitations of the Child-Pugh classification. The ALBI score is widely accepted as an early and objective indicator of REILD and has been shown to be more sensitive than the Child-Pugh score in predicting RECHT risk. Baseline ALBI grade 2 or 3 is associated with significantly higher risk of both REILD and RECHT after TARE [12, 18–21].

Although the prognostic value of the ALBI score has been extensively investigated in hepatocellular carcinoma, its utility in mCRC patients undergoing TARE is less well established. In the large CIRT registry, which included 237 mCRC patients treated with resin microspheres, the ALBI score emerged as an independent predictor of hepatic progression-free survival [22]. Studies on neoadjuvant chemotherapy and surgery have shown that baseline ALBI grade and changes in ALBI after treatment predict overall survival and liver decompensation risk in metastatic colorectal cancer (mCRC). These results support increased use of ALBI as a practical and objective tool for assessing liver function in non-cirrhotic patients [23, 24].

The dose–response relationship in TARE is well established for tumour control. Several studies have demonstrated that higher absolute tumour-absorbed doses are associated with improved tumour response and survival in patients with mCRC [9, 11, 25, 26]. However, none of these studies normalised tumour-absorbed dose to metabolic tumour volume. More recently, Alsultan et al. [27] and our previous analysis of the same cohort [13] showed that tumour absorbed dose normalised to MTV (or TLG) is a stronger predictor of metabolic response. Despite these advances in dosimetric evaluation, data on liver function preservation in mCRC remain limited, particularly when integrating dosimetric parameters with

metabolic tumour burden. The present study addresses this gap by demonstrating that a higher MTV-based Effective Absorbed Dose Index is associated with stable ALBI scores.

Detailed analysis of the two patients who developed severe hepatotoxicity provides important insights (Fig. 2). In the patient who developed REILD after the third TARE, there was no ALBI change after the first treatment, but ALBI deteriorated from Grade 1 to Grade 2 after the second treatment. Both the first and second treatments were flagged by the lower cut-off of 65. For the third treatment, the dose was reduced; however, the resulting MTV-based Effective Absorbed Dose Index value remained above the lower cut-off (65) but below the higher cut-off (156). REILD developed after this third treatment.

In contrast, the patient who developed RECHT maintained stable ALBI Grade 1 after three TARE sessions (with dose reduction applied in the third treatment), yet the higher cut-off of 156 successfully identified this patient as being at elevated risk. These observations suggest that the two cut-offs may have complementary roles: the lower cut-off (65) appears sensitive for detecting patients at risk of progressive ALBI deterioration and subsequent REILD, while the higher cut-off (156) may be particularly useful for identifying patients at risk of RECHT even when ALBI scores remain stable. The fact that REILD still occurred in the “grey zone” between the two cut-offs after dose reduction in the third treatment of the first patient highlights the need for more refined risk stratification.

Importantly, these findings were based on post-treatment ^{90}Y Bremsstrahlung SPECT/CT dosimetry. Ideally, similar risk assessment should be possible using pre-treatment ^{99m}Tc-MAA SPECT/CT planning images, allowing dose adjustment or even deferral of treatment before the therapeutic activity is administered. This approach may be particularly valuable in patients undergoing repeat TARE sessions, where dosimetric data from prior treatments, including the MTV-based Effective Absorbed Dose Index, could guide safer and more effective dose planning while better preserving liver function. Prospective studies comparing pre- and post-treatment dosimetry in relation to ALBI trajectory and severe hepatotoxicity are warranted.

This study is limited by its single-center design and the partly retrospective nature of data collection. However, the cohort reflects real-world clinical practice, consisting of heavily pretreated mCRC patients, many of whom underwent repeated TARE sessions. Among the 93 TARE procedures, ALBI score progression occurred in 19 cases, and 37 patients received multiple treatments, including up to six sessions in some instances; some also underwent separate resin microsphere treatments. Despite this heterogeneity, we were able to demonstrate a statistically significant association between the MTV-based Effective Absorbed Dose Index and post-TARE ALBI score progression, supporting the clinical relevance of our findings.

In conclusion, the MTV-based Effective Absorbed Dose Index appears to be a promising tool for balancing therapeutic efficacy and hepatic toxicity in TARE. Its incorporation into dosimetric planning may support more individualised treatment strategies in patients with liver-dominant mCRC, including

consideration of repeat procedures in those with preserved liver function and favourable dosimetry. Prospective multicentre validation is warranted.

Declarations

Competing Interests:

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval:

The study protocol was approved by the Marmara University Ethics Committee (approval number: 1141; date: 02 September 2022).

Consent to participate:

Written informed consent was obtained from prospectively enrolled patients; the requirement for informed consent was waived for retrospective cases.

Consent to publish:

The authors affirm that human research participants provided informed consent for publication of the images in Fig. 2a and 2b.

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Author Contributions:

ES, SK and TÖ contributed to the conceptualization, methodology, formal analysis, investigation, data curation, writing of the original draft, and review and editing of the manuscript. ŞÇ, EA and ZCBG contributed to the conceptualization, methodology, investigation, data curation, formal analysis, and review and editing of the manuscript. ÖE, EC, NZ and AE contributed to the investigation and data curation. TYE and ÇÇ contributed to the conceptualization, methodology, and critical revision of the manuscript. TÖ also contributed to the supervision and project administration. All authors read and approved the final version of the manuscript.

Data Availability:

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

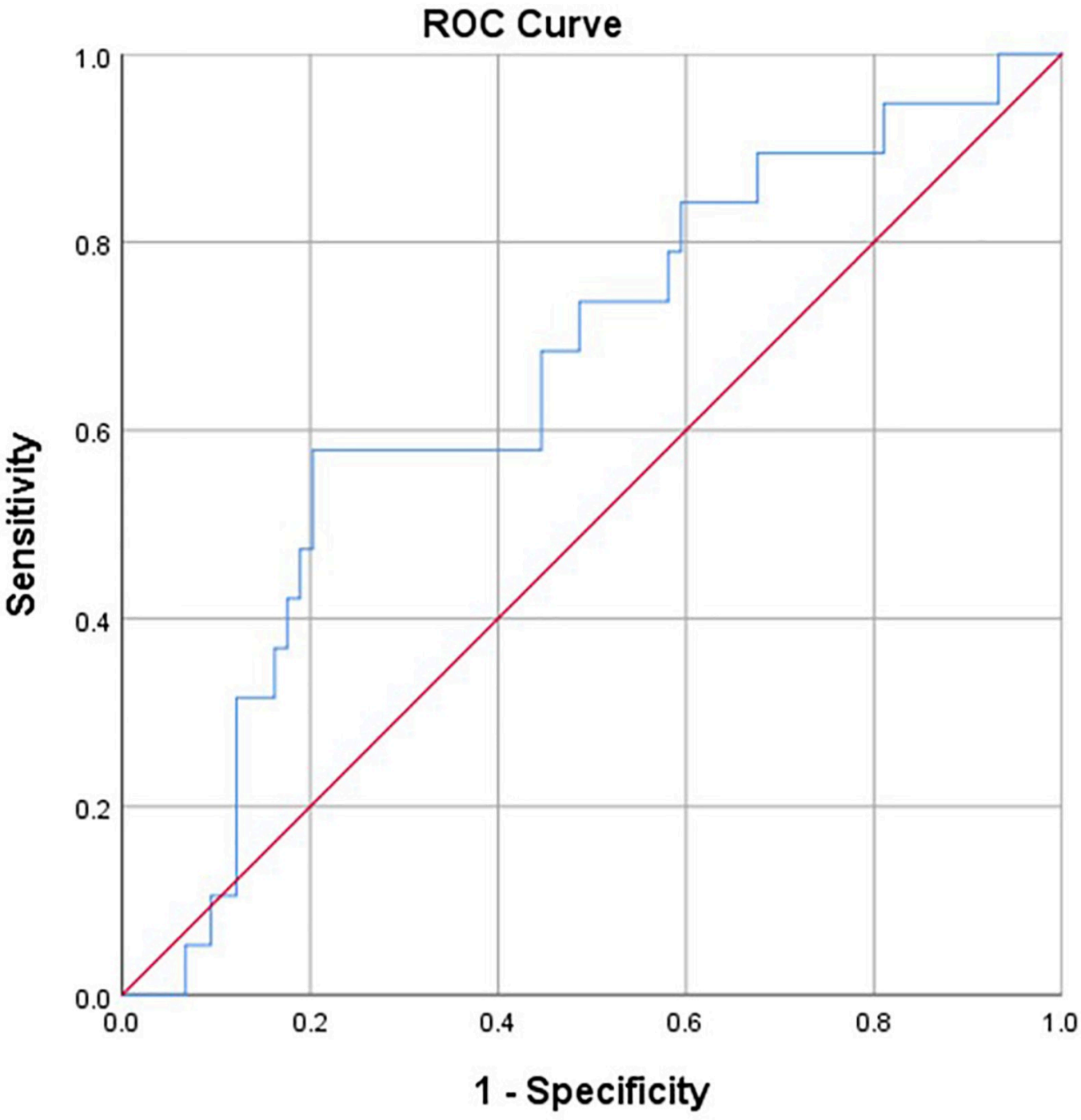


Figure 1

Receiver operating characteristic (ROC) curve for the MTV-based Effective Absorbed Dose Index in predicting ALBI score deterioration

Figure Legend 1:

Receiver operating characteristic (ROC) curve showing the performance of the MTV-based Effective Absorbed Dose Index in predicting ALBI score deterioration following TARE. The area under curve (AUC) was 0.66 (p=0.038). Cut-off values of 65 and 156 were identified using the Youden index method.

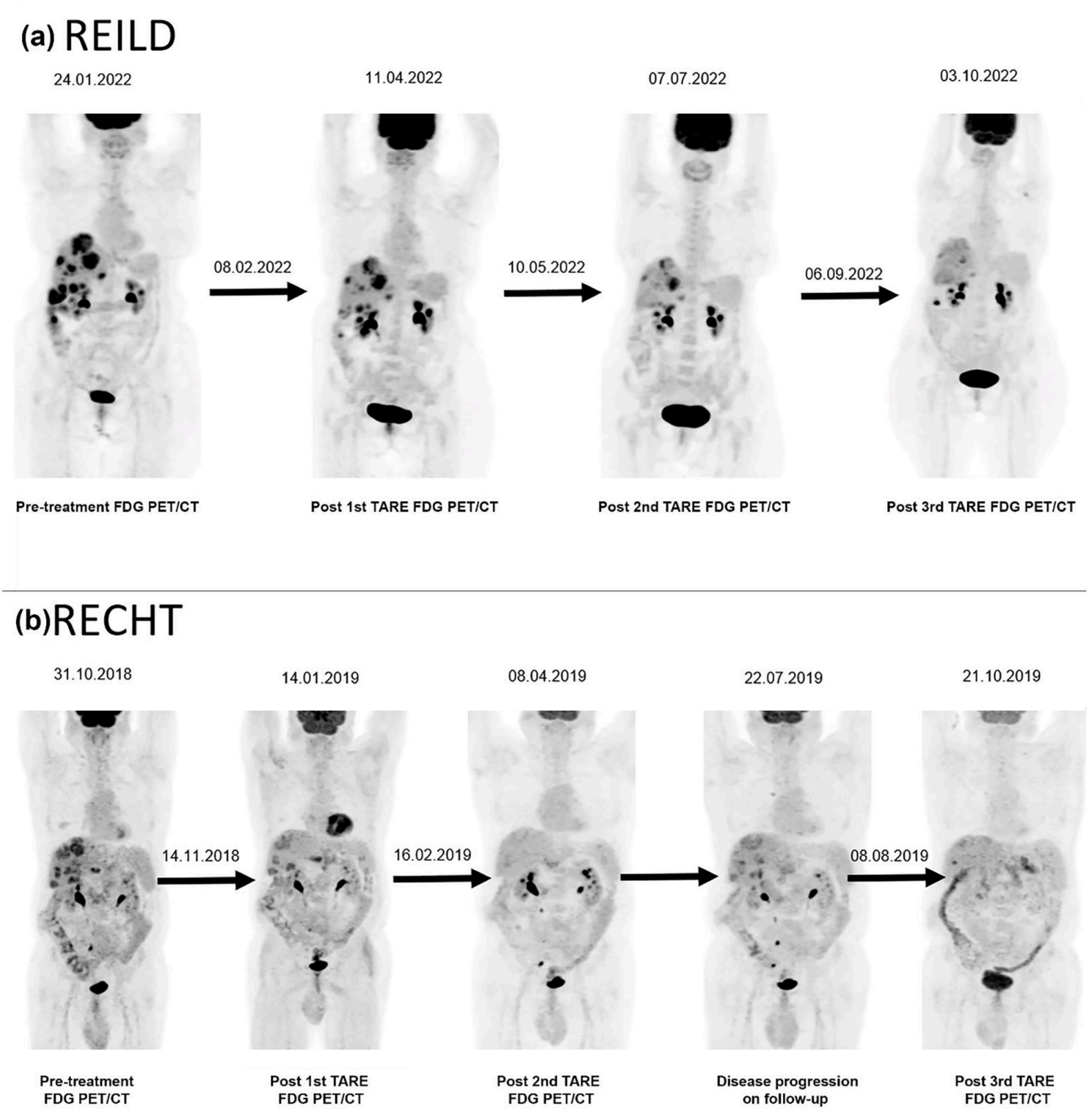


Figure 2

Representative cases of radioembolization-induced liver disease (REILD) and radioembolization-induced chronic hepatotoxicity (RECHT) following TARE with ^{90}Y glass microspheres

Figure Legend 2:

(a) Serial ^{18}F-FDG PET/CT images showing development of REILD after the third TARE session. Progressive deterioration in liver function was observed despite dose reduction in subsequent treatments.

(b) Serial ^{18}F-FDG PET/CT images showing development of RECHT after the third TARE session, with deterioration in liver function.