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Manuscript Title

Quantitative and Volumetric EASL and RECIST: An Improved Method to Assess Tumor Response after Transcatheter Arterial Chemoembolization (TACE)

Manuscript Type

Original Research

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Manuscript Title

Quantitative and Volumetric EASL and RECIST: An Improved Method to Assess Tumor Response after Transcatheter Arterial Chemoembolization (TACE)

Manuscript Type

Original Research

Advance in Knowledge

To better assess tumor response after therapy.

Implications for Patient Care

This work presents an innovative, reproducible, and quantitative way to characterize tumor viability after treatment as measured by changes in volume and image enhancement. This information can then be used to plan future treatments and to compare treatment modalities.

Summary Statement

We present an innovative and reproducible way to assess tumor response following therapy. An improvement upon the current standards of qualitative measures on single axial slices, this method assesses the entire tumor volume quantitatively. It will better help guide future therapies.

ABSTRACT

Purpose: To demonstrate that hepatic tumor quantitative enhancement and volumetric measurements are feasible by 1) using semi-automatic tumor segmentation software to determine tumor volumes (volumetric RECIST, vRECIST), 2) determining image enhancement for the entire tumor volume (quantitative EASL, qEASL), and 3) reporting an exact tumor viability measurement as a % of enhancing tumor volume.

Materials and Methods: This was a single-institution retrospective study (HIPPA compliant and IRB approved) that included patients with hepatocellular carcinoma (HCC) who underwent drug-eluting beads transcatheter arterial chemoembolization (DEB-TACE) for the first time, and had undergone contrast-enhanced MRI before and after DEB-TACE (n=20). Patients with poor image quality (n=3) because of image artifacts were excluded, resulting in a final count of 17 patients. vRECIST (calculated from 3D volumetric tumor segmentation) and qEASL (calculated from image enhancement volumetrically) were measured. Segmentation and processing times were recorded.

Results: Thirty-four scans were analyzed. The time for semi-automatic segmentation was 65±33 seconds with a range of 40-200 seconds (step 1). vRECIST and qEASL of each tumor were then computed (all performed in less than 1 minute) and compared between pre- and post-treatment (step 2). The change in vRECIST after therapy was not statistically significant (p=0.57) but there almost was statistical significance (p=0.06) in qEASL change after therapy.

Conclusion: Semi-automatic quantitative tumor enhancement (qEASL) and volume (vRECIST) assessment is feasible in a realistic time frame. This represents a vast improvement

in tumor assessment over the current time consuming single axial slice, qualitative standard. vRECIST and qEASL can better help the clinician decide future treatment plans.

KEYWORDS

Hepatocellular carcinoma, Transcatheter arterial chemoembolization; EASL; RECIST; Drug-eluting beads; Magnetic resonance imaging.

INTRODUCTION

Multi-phasic contrast-enhanced MRI is accepted as a gold standard for diagnosing liver tumors and assessing treatment response after locoregional therapy, especially following Transcatheter Arterial Chemo-Embolization (TACE). Measuring changes in tumor size (Response Evaluation Criteria in Solid Tumors, RECIST) and enhancement (European Association for the Study of the Liver, EASL) on MRI are the two accepted methods to assess response to TACE (1).

The first criterion, RECIST, evaluates response to treatment based on changes in tumor size (RECIST 1.0 & 1.1 criteria) (2, 3). The second method, the EASL criteria (4), evaluates response to treatment based on changes in tumor enhancement. Although these two methods are widely used, they have some glaring limitations when applied to TACE. TACE induces vascular occlusion and inhomogeneous necrosis, and as a result, tumor enhancement becomes heterogeneous and changes in tumor size are inhomogeneous (5). This makes either method of tumor response assessment difficult after TACE.

Furthermore, the RECIST and EASL criteria are applied to one representative axial slice of the tumor. As a result, different slice selection can lead to a different response assessment using either criterion. Additionally, in the case of RECIST, the measurements comprise the longest and shortest diameters on the specified slice and ignore the volume of the tumor. For EASL, the percent enhancement is made based on visual inspection and often grouped into quartiles (1). This assessment can be particularly inaccurate if the enhancement percentage is at a threshold between two quartiles.

Our hypothesis is that a semiautomatic quantitative tumor enhancement and volume assessment can greatly improve both RECIST and EASL response assessment methods. Our goal is to demonstrate that quantitative enhancement measurement and quantitative volume measurement are feasible by 1) semi-automatic tumor segmentation to determine tumor volumes, 2) determining enhancement for the entire tumor volume rather than on one axial slice, 3) calculating exact enhancement rather than using quartile ranges, 4) reporting an exact tumor viability measurement as a % of enhancing tumor volume. We propose this as quantitative EASL (qEASL) and volumetric RECIST (vRECIST).

MATERIALS AND METHODS

Study Cohort

This single-institution retrospective study was compliant with the Health Insurance Portability and Accountability Act and was approved by our Institutional Review Board. All patients provided written informed consent before inclusion in this study. Eligibility criteria for performing DEB-TACE included a confirmed diagnosis of unresectable HCC by biopsy or typical radiological findings, or an elevated serum alpha-fetoprotein (> 400 ng/mL), Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2, Child-Pugh classification A, B or C, focal or multifocal hepatic malignancy, absent or trace ascites, albumin > 2.5 g/dL, alanine aminotransferase and aspartate aminotransferase < 5 x upper normal limit, total serum bilirubin < 3.0 mg/dL, serum creatinine < 2.0 mg/dL, platelet count ≥ 50,000/mm^3, international normalized ratio (INR) ≤ 1.5, a left ventricle ejection fraction of ≥ 50%, absence of complete occlusion of the portal venous system, and no contraindications to MRI.

Our study group included all patients with HCC who were undergoing DEB-TACE for the first time and who had undergone dynamic contrast-enhanced MR imaging before and 1 month after DEB-TACE. Patients with well-defined and infiltrative tumors were included in the study. From November 1, 2005 to February 8, 2008, 20 patients fulfilled the inclusion criteria. Patients with poor MRI image quality (n = 3) because of severe image artifacts were excluded, resulting in a final count of 17 patients that were used for this study.

DEB-TACE Protocol

All DEB-TACE procedures were performed by an experienced interventional radiologist (J.F.G. 14 years of experience) using a consistent approach. LC Beads (2 mL, BioCompatibles Ltd., Surrey, UK) with a diameter of 100 to 300 µm were loaded with 100 mg of doxorubicin hydrochloride (25 mg/mL, Pharmacia-UpJohn, New Jersey, USA) and mixed with an equal volume of nonionic contrast media (Oxilan 300 mg I/mL, Guerbet LLC, Roissy, France). Access to the common femoral artery was obtained using Seldinger technique, and a catheter was positioned as closely to the tumor vascular network as possible before infusions of the DEBs. This means that every injection was performed in a superselective manner preferably through a microcatheter. DEBs, up to 100mg, were administered by alternating aliquot injections of the beads and contrast, until complete delivery or when the blood flow of the feeding artery slowed down substantially.

MR Imaging Technique

All patients underwent baseline (within 6 weeks prior to initial DEB-TACE) and follow-up (approximately 1 month after the procedure) MR imaging using a 1.5-T MR unit (CV/I, GE Medical Systems, Milwaukee, WI, USA) and a phased-array torso coil. The imaging protocol included: 1) axial T2-weighted fast spin-echo images (TR/TE, 5000/100 msec; matrix size, 256 x 256; slice thickness, 8-mm; interslice gap, 2-mm; receiver bandwidth, 32-kHz), 2) axial single-shot breath-hold gradient-echo diffusion-weighted echo-planar images (TR/TE, 5000-6500/110 msec; matrix size, 128 x 128; slice thickness, 8-mm; interslice gap, 2-mm; *b* value, 500 sec/mm^2; receiver bandwidth, 64-kHz), and 3) axial breath-hold unenhanced and contrast-enhanced (0.1 mmol/kg IV of gadodiamide, Omniscan, General Electric, Princeton, NJ) T1-weighted 3D fat-

suppressed spoiled gradient-echo images (TR/TE, 5.1/1.2 msec; field of view, 320-400 mm^2; matrix size, 192 x 160; slice thickness, 4-6-mm; receiver bandwidth, 64-kHz; flip angle, 15°) in the arterial and portal venous phases (20 and 70 seconds after intravenous contrast administration, respectively). Of interest in this study are the pre-contrast, unenhanced and 20 second post-contrast scans (#3 above).

Semi-automatic Tumor Segmentation

A semi-automatic 3D volume segmentation employing non-Euclidean radial basis functions was used by an experienced interventional radiologist (O.P. 9 years of experience), who did not perform the DEB-TACE procedures, on the 20 second pre- and post-DEB-TACE contrast-enhanced MRIs to segment the tumors (6, 7). Briefly, this method is inspired by front-propagation theory and radial basis functions (mathematically, a function whose value depends only on the distance from the origin). Combined with non-Euclidean distances, this method allows for segmentations that follow 3D image features including straight edges and corners. This method was used because it can accurately segment in 3D, yet needs minimal user interaction. Manual segmentation requires a high level of expertise and incorporates an expert's knowledge with image features to make accurate segmentations. This semi-automatic method provides similar results but only at a fraction of user interaction time. For this study, the segmentation time was recorded.

In practice, the user identifies an initial control point. From there, the user can interactively expand or contract the 3D region of interest. Additional segmentations can be included by placing more control points. Corrections are made in the same volumetric way.

Imaging Data Evaluation – Volumetric RECIST (vRECIST)

vRECIST is an improvement over the current RECIST criteria. The main advantage is that the calculation of volume eliminates potential variability in the assessment based on slice selection. vRECIST was calculated as follows: 1) A semi-automatic 3D tumor segmentation using non-Euclidean radial basis functions was performed as described above on the 20 second contrast enhanced scan. 2) The volume was directly calculated based on this segmentation. The vRECIST therapy response was calculated as the pre- minus post-vRECIST values, so a positive change value in vRECIST indicated a decrease in tumor volume after DEB-TACE. A percent change was also calculated as (pre- minus post-vRECIST) divided by pre-vRECIST. Changes were also compared for each patient using the Paired Student's T-test, where statistical significance was defined as $p < 0.05$.

Imaging Data Evaluation – Quantitative EASL (qEASL)

qEASL was calculated as follows: 1) A semi-automatic 3D tumor segmentation was performed as described above on the 20 second contrast enhanced scan. 2) The pre-contrast scan was subtracted from the 20 second scan to remove background enhancement. 3) The 3D segmented volume region from #1 was applied to #2. 4) From #2, average enhancement values were obtained from 10x10x10 pixels regions of interest (ROIs) representing normal liver parenchyma. 5) Viable tumor was defined as areas in #3 where the enhancement was more than that of the normal parenchyma ROI found in #4. 6) Based on #5, the volume of viable tumor (a subset of what was found for vRECIST total tumor volume) was measured and expressed as

qEASL in cm^3. 7) The viable tumor was also defined as a % of the total tumor volume and expressed as qEASL in %. A color map was overlayed on the 20 second scans to show volumetric and regional tumor enhancement heterogeneity. Colored regions of the segmented tumor are where there is more enhancement than healthy liver tissue. The color map for each patient was normalized to the maximum enhancement in the entire tumor of the pre-DEB-TACE scan. This ensured that the post-treatment color map used the same scale for comparison with the pre-treatment color bar. In the color bar, red represented maximum enhancement (viable tumor) and blue represented minimum enhancement (treated/non-viable tumor). The qEASL therapy responses were calculated as the pre- minus post-qEASL values for viable tumor volume and % enhancement. A positive change value in qEASL indicated a decrease in viable tumor volume or % tumor enhancement after DEB-TACE. A percent change was also calculated as (pre- minus post-qEASL) divided by pre-qEASL. Changes were also compared for each patient using the Paired Student's T-test, where statistical significance was defined as $p < 0.05$.

RESULTS

Patient Demographics

Seventeen patients with unresectable HCC (11 male; 6 female; mean age 61.2 years ±12.8 [range, 40-84 years]) were included in this study. All patients successfully completed both baseline pre- and post-DEB-TACE MRI (34 total MRI examinations). Each patient underwent one selective DEB-TACE session between the pre- and post-MRI. All procedures were performed successfully, without immediate complications. Table 1 summarizes the demographic data for this 17-patient cohort. The majority of these HCC patients had preserved underlying liver function (Child-Pugh class A (13/17, 76.5%). Most patients (14/17, 82.4%) had cirrhosis, and 64.7% were classified as Barcelona Clinic Liver Cancer (BCLC) grade C (A/B/C/D: 2/4/11/0).

Semi-automatic Tumor Segmentation

The time it took to segment each of the 34 MRI examinations (17 pre- and 17-post-DEB-TACE) was 65±33 seconds with a range of 40-200 seconds. Typically, 5-9 mouse button clicks were needed to sufficiently segment a tumor. As seen in the vRECIST and qEASL figures 1–3, the segmented volumes match the tumor boundaries very well.

Volumetric RECIST (vRECIST)

Four representative patients, 8 MRI examinations total (4 pre-DEB-TACE, Figure 1 and 4 post-DEB-TACE, Figure 2), were used to visualize the segmented tumor with a patterned

overlay on a representative axial slice from the 20-second scan. The 3D segmentation allowed for a volume rendering of the tumor (right most column). The time it took for segmenting these 8 MRI examinations was 82±53 seconds (range 40−200 seconds). For these cases, the tumor volumes (vRECIST) were found to be in the range of 15.9–952.0cm^3 and 8.0–1300.0 cm^3 for pre- and post-DEB-TACE, respectively. Specific vRECIST values for these four patient cases (boxed in the table) and the 13 others are shown in Table 2. In 9 (53%) patients, the change in vRECIST after DEB-TACE was found to be a decreasing tumor volume (positive change in vRECIST value), indicative of successful therapy response. Eight (47%) patients did show an increase in tumor volume (negative change in vRECIST value), which is likely due to inflammation following TACE. The change in vRECIST after therapy for all 17 patients as seen on the 1-month post MRI was not statistically significant, $p = 0.57$. The computation time for each patient case using vRECIST was < 1 minute.

Quantitative EASL (qEASL)

Using the same four representative patient cases as above, heterogeneity within tumors can be seen in quantitative color maps (Figure 3). The red areas show increased enhancement and likely represent more viable tumor, while the blue areas likely represent non-viable/necrotic tumor. The majority of the tumor volume for all pre-treatment MRI cases enhanced more than healthy liver tissue. This volumetric enhancement was expressed as a percentage of total tumor volume. For all patients, the pre-treatment cases showed 52.4±33.6% (range 4.0 – 97.0%) of the tumor enhancing more than the healthy background tissue. The post-treatment cases showed 36.8±27.8% (range 2.8 – 93.1%). Specific qEASL values are shown in Table 2. The change in

qEASL after DEB-TACE was found to be a decreasing % tumor enhancement and decreasing viable tumor volume (positive change in qEASL values), indicative of successful therapy response. Six patients did show an increase in tumor enhancement along with viable volume (negative change in qEASL value). The change in qEASL after therapy, as seen on the 1-month post MRI, was not statistically significant in terms of % enhancement ($p = 0.11$). However, qEASL viable tumor volume change was almost statistically significant ($p = 0.06$). It is interesting to note that 4 of the 17 patients showed inverse changes post-therapy in terms of changes in qEASL tumor % enhancement and viable tumor volume. Specifically, one measure was negative while the other was positive. This highlights the benefit of volumetric and quantitative assessment in that the measured values represent the entire tumor volume quantitatively rather than in qualitative brackets at select axial slices. This can help to guide discussion towards improving imaging based response criteria. The computation time for each patient case using qEASL was < 1 minute.

DISCUSSION

An endpoint for assessing cancer treatments is often overall survival. Nonetheless, tumor response as measured by RECIST and EASL, and time to progression (TTP) has been considered a surrogate assessment of treatment efficacy. RECIST (2, 3), mRECIST (8), and EASL (4) criteria have been especially designed for reporting study results in an effort to standardize the results of treatment and to allow comparison between different types of treatment. These criteria are able to convert radiologic image observations into a quantitative and statistically trackable framework for measuring the response to therapy. But, in their current form, these methods utilize analysis of tumors in only one dimension and often times are inaccurate. Despite strict standardized rules, all these methods present numerous drawbacks. With post processing software now able to produce semi-automatic segmentation and measurement in a realistic time-frame, it is "time" to move from anatomic one-dimensional assessment of tumor burden to volumetric anatomical and quantitative assessment. This can be seen in Bonekamp et. al.'s study where they showed association of changes in MR apparent diffusion coefficient and enhancement with tumor size after TACE (9). While the resulting color maps may seem similar, the imaging techniques, software, and goals are different.

The major finding of our study is that it is possible to perform quantitative measurement of tumor enhancement and quantitative tumor volume measurement by a semi-automatic method in a time efficient manner. vRECIST was obtained by hepatic tumor semi-automatic segmentation based on tumor enhancement difference between hepatic healthy tissue and tumor. qEASL was obtained by the enhancement value comparison of segmented tumor volume to the normal parenchymal liver enhancement. Comparison to previous MRI examinations is also possible.

The RECIST criteria's approach is based on assessing changes in tumor size as an indicator of treatment response. Targeted lesions are measured using a single linear summation, and specific attention is given to reproduce all measurements at the same tumor location during follow-up. Tumor enhancement or necrosis is not used in this method to assess treatment efficacy.

One of the crucial steps in RECIST is lesion measurement. While the numerical information tends to appear very precise and quantitative, one cannot determine exactly how they are obtained. In practice, RECIST is very subjective and numerous factors can play a significant role in lesion measurement; as such, it is subject to considerable inter- and intra-observer variability. Suzuki et al. (10) report up to 0.53 (95% CI 0.33 –0.72) inter-observer variability rate and intra-observer variation ranged between 0.76 –0.96. This could be explained by three major reasons: (1) the inability to find the same reference slice during all the follow-up scans, (2) the inability to measure the tumor diameter in the same manner while taking into account tumor modification due to therapy, and (3) tumors may have irregular margins and show heterogeneous enhancement, resulting in potential reader variability (11, 12). Volumetric measurement is a solution because the change in tumor size is better assessed by a change in tumor volume measurement rather than a change in linear measurement (13, 14). Volumetric evaluation provides a more accurate depiction of tumor burden when compared with 1D and 2D measurements (15). Volumetric measurement is also able to depict tumor size changes earlier (16-18). This is a crucial point in patients' follow-up. The ability to observe a positive or negative change earlier may modify the treatment plan. It has already been demonstrated that histopathologic tumor response correlates better with tumor volume than with axial measurements (19-21) and volumetric evaluation of treatment response is also associated with

higher reproducibility (17, 22). Furthermore, tumor volume decrease after treatment has been found to be a predictor of survival (23, 24). vRECIST greatly reduces measurement variability by measuring the entire tumor volume. This is important because one representative axial slice is typically not adequate to assess tumor response. The slice chosen may not be in the largest axial dimension, or the tumor may have changed in other axial slices or directions (asymmetric regression). This can lead to significant inter-observer variability. By calculating and observing changes in the entire tumor volume, this variability is eliminated.

The EASL method, first described in 2000 by the European Association for the Study of the Liver, proposed a more physiological approach especially dedicated to HCC. This is because the main goal of loco-regional therapies for HCC is to achieve tumor necrosis before tumor shrinkage (4). Tumor necrosis is observed shortly after biotherapies or TACE before there is a decrease in lesion size (1, 25, 26). In taking into account tumor necrosis induced by treatment (4), estimation of tumor area viability must use contrast-enhanced radiologic imaging. Viable tumor is defined as areas where there is uptake of contrast agent in the arterial phase of the contrast enhanced MRI. This technique offers a better understanding of response to treatment, especially for hypervascular hepatic lesions, because the degree of hyperenhancement is related to the viability of the tumor (27). Intra-tumoral necrotic areas are used to estimate the change in tumor load. Treatment response is categorized on the basis of the percentage change in the necrotic area from the baseline study to follow-up study, and grouped into quartiles from 0 to 100%. The measurement of lesions according to the EASL criteria is more time consuming than RECIST because four perpendicular diameters need to be recorded to identify the vital and enhancing areas of a lesion. EASL also suffers from subjectivity, especially with heterogeneous enhancement or with infiltrative tumor.

The three benefits of qEASL are: (1) A specific value of tumor enhancement is reported rather than quartiles, (2) Quantification results represent the entire tumor volume rather than a single axial slice, and (3) Tumor viability can be visualized on a regional level as a color map. qEASL eliminates subjectivity in assessing tumor enhancement.

Because RECIST and EASL propose two parallel ways for one tumor evaluation, Lencioni et al. (8) proposed a combination especially for HCC evaluation called modified RECIST (mRECIST). The rationale to change assessment toward mRECIST were: (1) HCC is a hypervascular tumor, (2) all treatment used (including biotherapies and TACE) act directly on tumor vascular supply, and (3) biotherapies and TACE are able to induce necrosis first and then tumor shrinkage later. Tumor enhancement quantification and tumor shrinkage are the two representative expressions of tumor evolution. This specific HCC behavior must be measured to accurately assess tumor response. mRECIST proposes to measure the zone of residual enhancement after treatment. However, mRECIST has the same limitations as RECIST and EASL. Primarily, it still uses one single axial slice for assessment. In addition, mRECIST becomes very inaccurate in those cases of heterogeneous tumor enhancement and multiple tumors. Our specific approach eliminates these limitations with semi-automated whole tumor volume measurement and viable tumor volume measurement. Semi-automatic segmentation techniques and enhancement measurement allow for reliable and reproducible volumetric evaluation of liver lesions. (28).

There were some limitations in this study. It was a retrospective study on a select number of patients. However, we do not feel that this was a major limitation because the purpose of this paper is to describe these new treatment assessment techniques and their feasibility. A further project would be to prospectively evaluate tumor response with vRECIST and qEASL, and

determine the correlation between this response and overall survival. vRECIST and qEASL's reproducibility, sensibility, and specificity must be evaluated in a larger cohort. An area of improving technology development is in MRI. Since the original scans in 2005-2008, the image quality and post-processing has improved and so we anticipate motion artifacts to be less of a concern.

In conclusion, our study showed that a semiautomatic quantitative tumor enhancement (qEASL) and volume (vRECIST) assessment is feasible in a realistic time frame. This software can help the interventional radiologist plan future treatments by demonstrating the shape and location of residual tumor.

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TABLES

Table 1: Patient Demographics Baseline characteristics of patients with hepatocellular carcinoma prior to treatment

Baseline Characteristics	**Value (*n* or mean ± SD)**
Demographics	
No. patients	17
Age (Year)	61.2 ± 12.8 [range 40–84]
Sex ratio (Male/Female)	11/6
Race (White/African-American/Hispanic)	12/4/1
Etiology (Alcohol/HCV/HBV/NASH/ Hemochromatosis/Unknown)	2/6/5/1/1/5
ECOG performance status (0/1/2/3)	7/9/1
Cirrhosis (Present/Absent)	14/3
Type (Unifocal/Multifocal/Diffuse)	11/6/0
Portal vein thrombosis (Yes/No)	3/14
Tumor size* (mm)	7.1 ± 3.8 [range 2.8–16.2]
HCC staging	
Child-Pugh class (A/B/C)	13/4/0
BCLC stage (A/B/C/D)	2/4/11/0
Okuda stage (I/II/III)	11/6/0
Serum tests	
Basal AFP (ng/mL)	701±1151 [range 2–4189]

<10	2
10-200	6
>200	9
Albumin (g/dL)	3.5±0.6 [range 2.6–4.6]
Total bilirubin (mg/dL)	1.0±0.3 [range 0.6–1.6]
AST (U/L)	66.4±30.4 [range 20–125]
ALT (U/L)	66.2±35.3 [range 13–125]
Alkaline phosphatase (U/L)	170.2±74.2 [range 73–305]
INR	1.1±0.1 [range 1–1.3]

Note.–HCV, Hepatitis C Virus; HBV, Hepatitis B Virus; NASH, Non-Alcoholic Steato-Hepatitis; ECOG, Eastern Cooperative Oncology Group; HCC, Hepatocellular Carcinoma; BCLC, Barcelona Clinic Liver Cancer; AFP, Alpha-Feto-Protein; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; INR, International Normalized Ratio.

* One-dimensional measure of the longest dimension as measured by MRI.

Table 2: Tumor segmentation time, vRECIST, and qEASL results of 17 patients before and after DEB-TACE. Images are shown of representative patient cases 1–4 (boxed above).

Patient	Segmentation Time (sec)	vRECIST (cm^3)	qEASL (cm^3)	qEASL (%)	Therapy Response vRECIST	Therapy Response qEASL	
1-Pre	200	952.0	819.9	86.1	-348.0cm^3	261.0cm^3	43.1%
-Post	90	1300.0	558.9	43.0	-36.6% change	31.8% change	50.1% change
2-Pre	90	124.2	115.5	93.0	73.2cm^3	110.6cm^3	83.4%
-Post	50	51.0	4.9	9.6	58.9%	95.8%	89.7%
3-Pre	90	197.8	97.1	49.1	87.9cm^3	65.5cm^3	20.3%
-Post	50	109.9	31.6	28.8	44.4%	67.5%	41.3%
4-Pre	40	15.9	12.2	76.3	7.9cm^3	11.0cm^3	61.0%
-Post	50	8.0	1.2	15.3	49.7%	90.2%	79.9%
5-Pre	90	1370.3	54.5	4.0	-1075.1cm^3	-15.1cm^3	1.2%
-Post	80	2445.4	69.6	2.8	-78.5%	-27.7%	30.0%
6-Pre	40	336.4	201.4	59.9	-16.6cm^3	-65.7cm^3	-15.8%
-Post	50	353.0	267.1	75.7	-4.9%	-32.6%	-26.4%
7-Pre	40	29.6	7.7	26.1	-14.6cm^3	-10.9cm^3	-16.0%
-Post	40	44.2	18.6	42.1	-49.3%	-141.6%	-61.3%
8-Pre	50	52.1	21.2	40.6	20.8cm^3	11.8cm^3	10.5%
-Post	50	31.3	9.4	30.1	39.9%	55.7%	25.9%
9-Pre	40	73.2	14.7	20.0	6.6cm^3	-47.3cm^3	-73.1%
-Post	40	66.6	62.0	93.1	9.0%	-321.8%	-365.5%
10-Pre	40	419.4	407.0	97.0	-157.8cm^3	-28.1cm^3	21.6%
-Post	45	577.2	435.1	75.4	-37.6%	-6.9%	22.3%
11-Pre	60	127.5	5.1	4.0	-15.5cm^3	-5.3cm^3	-3.3%
-Post	40	143.0	10.4	7.3	-12.2%	-103.9%	-82.5%
12-Pre	40	16.5	1.7	10.2	-145.3cm^3	-5.7cm^3	5.6%
-Post	60	161.8	7.4	4.6	-880.6%	-335.3%	54.9%
13-Pre	90	1278.4	370.0	28.9	523.9cm^3	271.7cm^3	15.9%
-Post	120	754.5	98.3	13.0	41.0%	73.4%	55.0%
14-Pre	40	124.5	118.3	95.0	43.3cm^3	101.2cm^3	74.0%
-Post	90	81.2	17.1	21.0	34.8%	85.5%	77.9%
15-Pre	40	33.7	19.2	56.9	-11.5cm^3	-6.7cm^3	-0.3%
-Post	80	45.2	25.9	57.2	-34.1%	-34.9%	-0.5%
16-Pre	90	177.9	170.9	96.1	28.6cm^3	88.0cm^3	40.6%

-Post	50	149.3	82.9	55.5	16.1%	51.5%	42.2%
17-Pre	90	892.8	429.8	48.1	234.6cm^3	93.4cm^3	-3.0%
-Post	70	658.2	336.4	51.1	26.3%	21.7%	-6.2%

FIGURE CAPTIONS

Figure 1: vRECIST pre-DEB-TACE. Note how the semi-automatic tumor segmentation (patterned overlay) aligns well with the actual tumor borders. The quantitative volumes are of the entire segmented tumor.

Figure 2: vRECIST post-DEB-TACE of the same patients as in Figure 1 at similar slice levels. The quantitative volumes are of the entire segmented tumor

Figure 3: qEASL pre- and post-DEB-TACE. Note the heterogeneity in tumor viability as seen on the color maps. Much of the viable tumor (yellow and red) became less enhanced after DEB-TACE and appears as blue in the post-treatment color map. The tumor viability % is a specific quantitative value representing the percent of the entire tumor volume

FIGURES

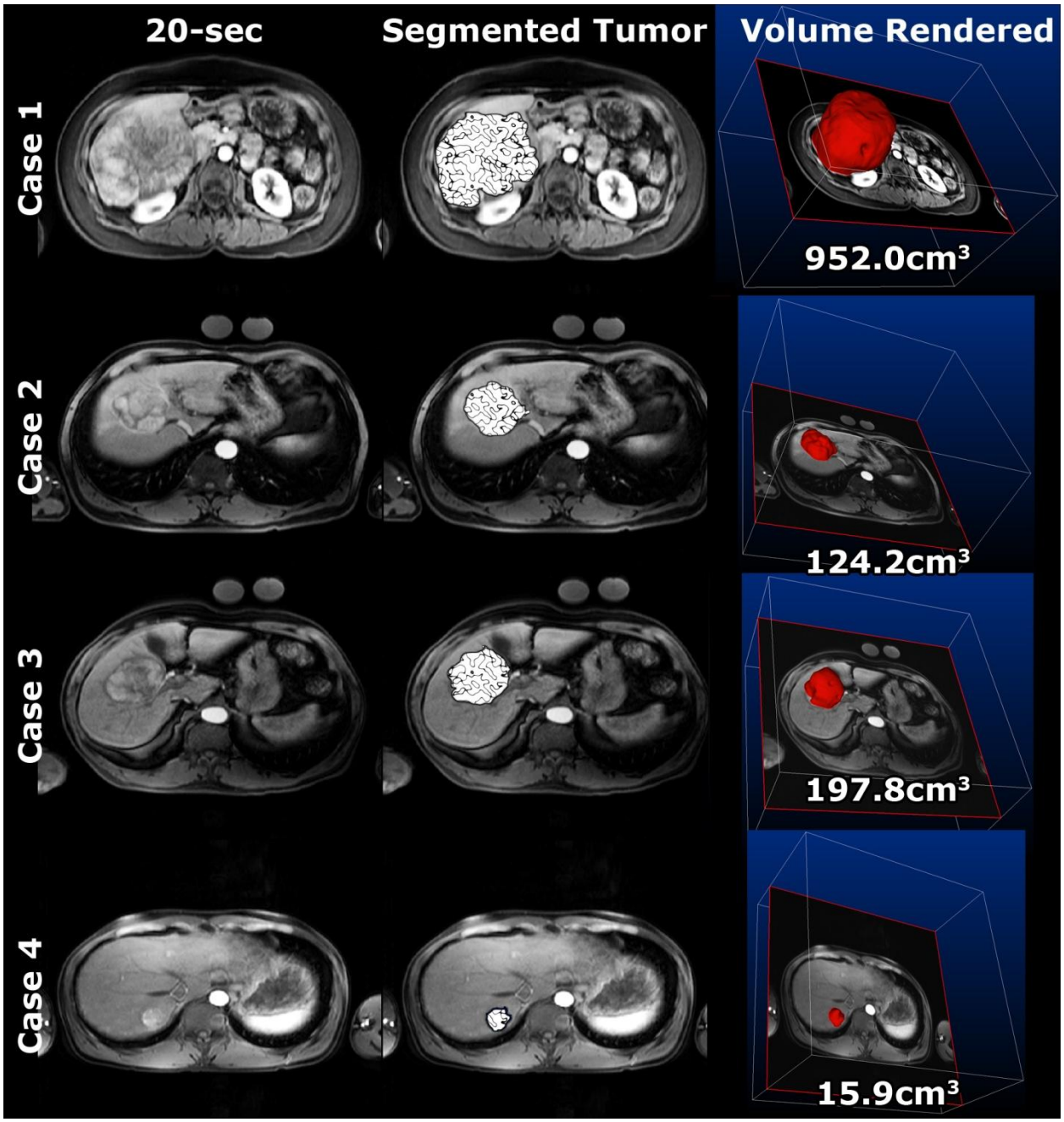

Figure 1: vRECIST pre-DEB-TACE. Note how the semi-automatic tumor segmentation (patterned overlay) aligns well with the actual tumor borders. The quantitative volumes are of the entire segmented tumor.

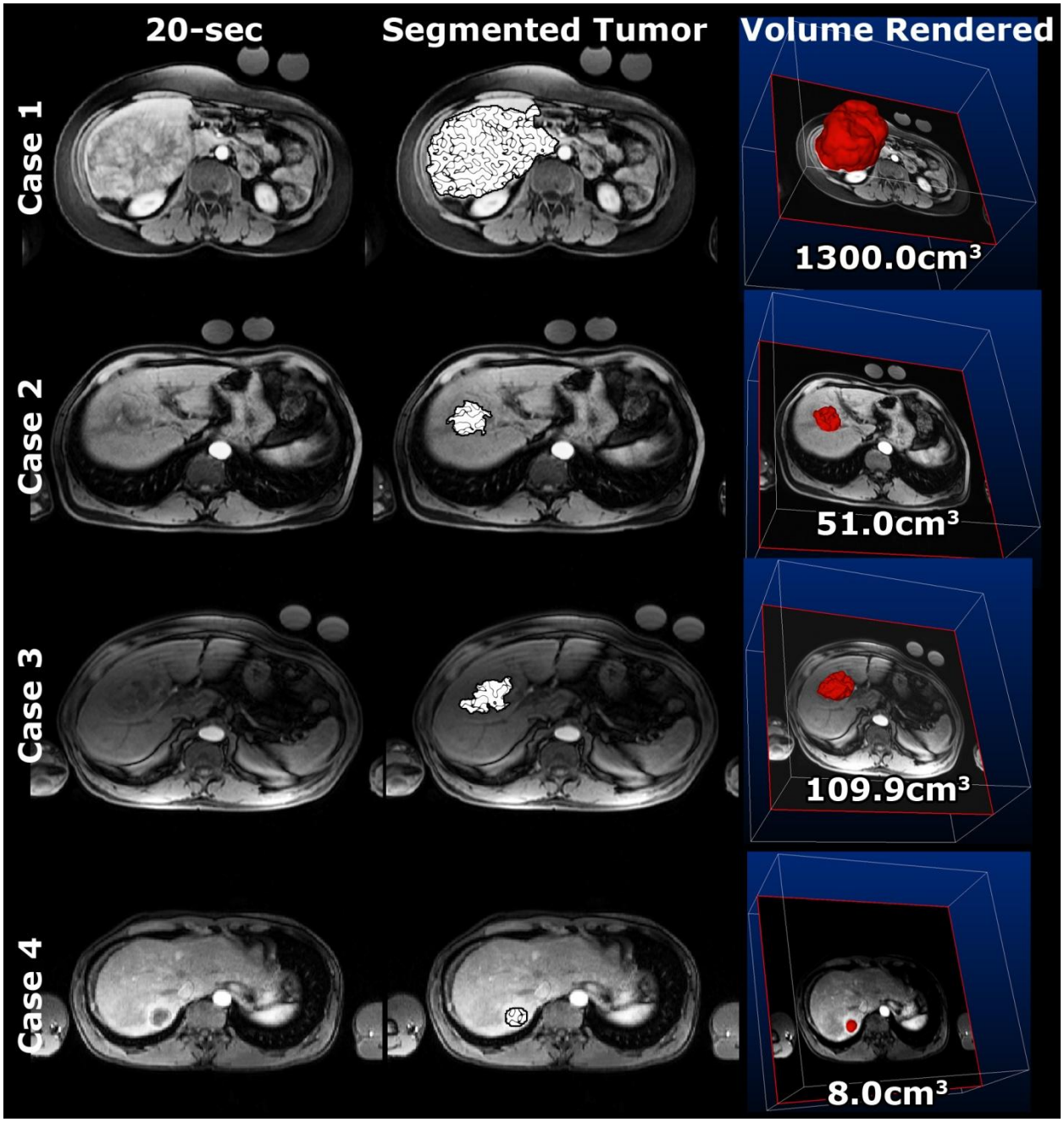

Figure 2: vRECIST post-DEB-TACE of the same patients as in Figure 1 at similar slice levels.

The quantitative volumes are of the entire segmented tumor

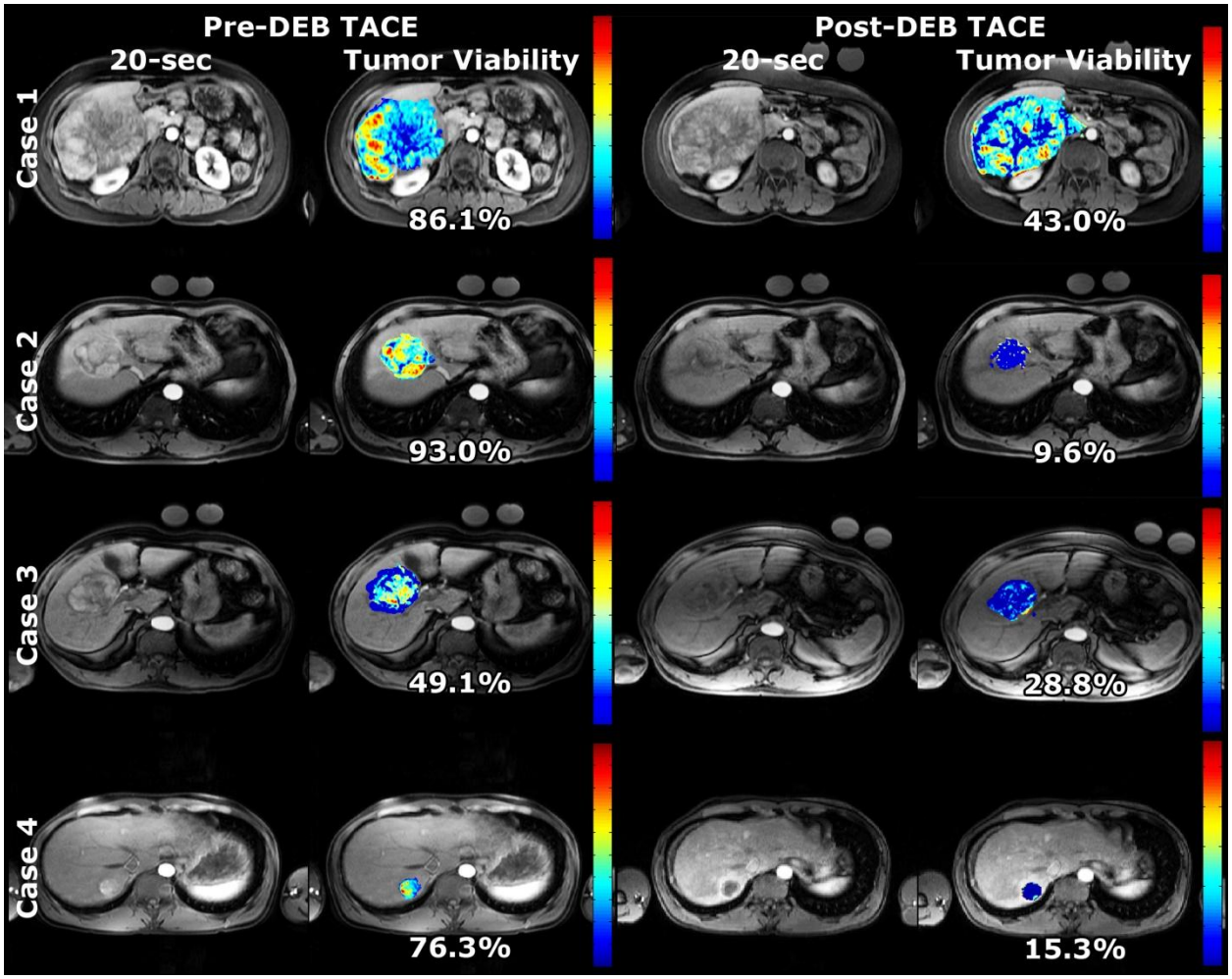

Figure 3: qEASL pre- and post-DEB-TACE. Note the heterogeneity in tumor viability as seen on the color maps. Much of the viable tumor (yellow and red) became less enhanced after DEB-TACE and appears as blue in the post-treatment color map. The tumor viability % is a specific quantitative value representing the percent of the entire tumor volume showing enhancement more than healthy liver tissue. The color bar per patient case is normalized to the maximum enhancement measured in the pre-DEB-TACE tumor volume.