Supplemental Data

1) Tumor Segmentation

To optimize the accuracy of the tumor segmentation, a systematic approach was used to determine the imaging sequence to be used for segmentation. The following describes the approach and then information on the segmentation software itself is provided. A semi-automatic 3D segmentation of the tumor was performed using a multi-phasic contrast-enhanced MR imaging (ceMRI) sequence obtained before TACE. The segmentation was performed on multi-phasic ceMRI that includes arterial (20 sec) and portal-venous (70 sec) phases. For the final analysis, the arterial-phase was chosen over the portal-venous phase because all lesions in the analysis demonstrated much better enhancement in the early phase. The tumor segmentation was performed using an in-house software (Medisys, Philips Research, Suresnes, France). This software uses non-Euclidean geometry and theory of radial basis functions which allows the segmentation of 3D objects with straight edges and corners. The algorithm creates image-based masks located in a 3D region whose center and size is defined by the user, yielding the nomenclature “semi-automatic”. After identifying an initial control point, the user can interactively expand or contract the 3D mask. Adjustments of the overall 3D volume of the mask can be interactively performed by placing additional control points. The shape and the spatial localization of the final 3D segmented mask (Figure 1, a and b) is registered to the coordinates within the MR imaging dataset and – upon image registration – may be applied to other MR imaging scans of the same patient. With the 3D nature of the segmentation, the tumor volume can be directly calculated.

2) Calculation of Enhancing Volume

In order to calculate the volume of the enhancing tumor tissue, the following steps were performed:

1) The pre-contrast MR imaging scan (Figure 1, e and f) was subtracted from the arterial-phase scan in order to remove background enhancement. This step is of particular importance to achieve an accurate assessment of lesions with hemorrhagic necrosis with presence of methemoglobin and/or with melanin as seen in some metastasis of uveal melanoma and helps mitigate false-positive enhancement from contrast-enhancement.

2) The 3D segmentation mask from the arterial-phase ceMRI was transposed onto the subtracted image set from above.

3) A 3D region of interest (ROI, $1cm^3$) was placed into extra-tumoral liver parenchyma of the subtracted image set in order to calculate the relative enhancement values within the tumor volume as a reference for normalization (Figure 1, g and h). Additional information on the selection of ROIs is provided below.

4) A threshold based on image enhancement defined viable tumor tissue as voxels within the 3D mask where the enhancement exceeded the average + 2 standard deviation value of the ROI. Additional information on the calculation of the ROI based threshold is provided below.

5) A normalized color map overlay on the arterial-phase MR imaging scan was used to demonstrate regional tumor enhancement heterogeneity (Figure 1, g and h); with red representing maximum enhancement / viable tumor and blue representing no enhancement, below the threshold / necrotic tumor tissue).

3) Definition of the ROI and Color coding

As opposed to fully automated segmentation techniques, a semi-automated approach allows the combination of software-based image processing with manual adjustments by a radiological reader. The goal of the ROI selection in this study was to achieve an intuitive approach, resembling the gold standard of a radiological reading. Practically, a radiological reader compares enhancement properties of the tumor with the non-tumoral liver tissue rather than extra-hepatic tissue. Several ROI localizations (including extra-hepatic ROIs within non-enhancing soft tissue, e.g. psoas muscle) were considered, however, they appeared to be counter-intuitive and failed to provide consistent results. ROIs were placed within visually non-enhancing tissue on the post-subtraction arterial-phase scan. Furthermore, signal intensity statistics were calculated for every 3D (1cm x 1cm x 1cm = $1cm^3$) ROI with the goal of achieving a maximum of signal homogeneity. This was performed as follows:

1) A $1cm^3$ ROI was placed in a localization as described above (ipsi-lateral liver lobe, non-enhancing extra-tumoral areas)
2) The software provided the minimum and maximum voxel brightness values within the cubic ROI. The numeric output was in patient-specific arbitrary units (AU) for

each ROI. The software furthermore calculated the mean brightness value (MBV), standard deviation as well as the coefficient of variation (CV). Empirically, a CV of less than 30% was seen as acceptable, while a CV greater than 30% was rejected leading to ROI repositioning.

3) The MBV ± 2 standard deviation was selected as a cutoff (threshold) with all values above seen as real contrast enhancement.
4) Based on the selected ROI and the MBV, a patient-specific (normalized) 3D color map was overlaid onto the tumor tissue enclosed by the segmentation mask. The color blue was identified as areas with equal / lower signal intensity as the MBV ± 2 standard deviation, while all signal exceeding this value was coded as an equally distributed histogram of tissue enhancement. The range of enhancement in AU was coded in color shades (aqua yellow – red) with red representing the maximum signal intensity for a particular patient.