**Purpose:**
Image-guidance for HCC suffers from a lack of contrast between tumor and liver parenchyma. To compensate for the inability to directly visualize the radiation target, IGRT strategies have employed liver or diaphragm contour and spine alignment or metallic fiducials as surrogates for optimization of a radiation target’s position. Transarterial embolization (TAE) and transarterial chemoembolization (TACE) are level 1 evidence-based treatments for HCC. While TAE/TACE have been shown to improve survival by several months, local failure occurs in up to 50% of treated lesions within 6 months of a procedure. This lack of durable local control provides a rationale to add a second treatment modality such as radiofrequency ablation (RFA) or focal radiation in a multi-modality treatment approach. If iodine-rich Ethiodol is used as embolizing agent, the treated HCC is stained by this radio-opaque oil. We assessed the quality and durability of Ethiodol tumor stains and their suitability for daily volumetric image-guidance using cone-beam CT (CBCT).

**Methods:**
Fifty-one patients underwent staged TAE/TACE prior to SBRT (50 Gy/5 fx; n=37) or HFxRT (45 Gy/18 fx; n=14). These multi-modality treatments were administered under an institutional protocol. We assessed quality of HCC Ethiodol stains in simulation CT and in cone-beam CTs acquired for daily image-guidance. Quality of Ethiodol stains in simulation CT were graded as excellent (dense stain with mean HU of >350 and diameter >10 mm), good (mean HU of 200-350 or dense stain with diameter <9 mm), fair (mean HU <200 without dense focal retention), and poor (faint or no stain). All CBCT (n=437) were reviewed and suitability of the tumor stain for image-guidance was graded. A stain excellently suited for image-guidance was readily visible on CBCT and did not change in shape during the course of radiation delivery. Good stains provided sufficient image-guidance, but required careful windowing of the CBCT scan. Poor quality was assessed when only punctuate densities were seen, or stains barely provided any imaging-information or were not seen.

**Results:**
Simulation scans showed excellent and good tumor stains in 29, and 11 cases (78%). Fair stains were recorded in 5 CTs, and no Ethiodol was retained in 6 tumors. Mean HU in excellent tumor stains was 698, with densities up to 1276 HU. Mean HCC lesion size was 23 mm (range 6 to 56 mm), and corresponding mean tumor stain was 23 mm (range 4 to 56 mm).

Suitability of the stain for CBCT image-guidance was graded as excellent and good in 26 and 13 cases (76%). Poor quality was assessed in the remaining cases. Four cases showed some loss in Ethiodol stain during the course of treatment; their score changed from excellent in simulation CT to good on CBCT (change was observed from the first day, with no further loss of stain). One case each was graded as good, fair and poor in simulation CT and upgraded to excellent (n=1) and good (n=2) in CBCT review. There was no variability between treatment days in the grading of the CBCT.

**Conclusions:**
TACE or TAE-based Ethiodol tumor stain facilitates volumetric image-guidance for SBRT and HFxRT of HCC. All tumors that showed staining in simulation CT retained that stain for the course of radiation therapy; a minor change in stain density was observed in less than 10% of cases, but was still serviceable for image-guidance. TACE and TAE stains persisted for up to 43 months, the longest imaging follow-up available in the studied population.