

Title: Utilization of 4D-CBCT in lieu of Intra-Hepatic Fiducial Markers for Tumor Localization in Liver SBRT – Description of a Novel Technique and Clinical Outcomes in a Retrospective Cohort

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Background:

Stereotactic body radiation therapy (SBRT) is a safe, effective, and non-invasive treatment for primary and metastatic liver malignancies. As liver malignancies are typically not well defined on cone beam CT, best practices for liver SBRT involves placement of intra-hepatic fiducial markers (IHFMs) prior to treatment. However, many patients decline IHFM placement or are ineligible due to coagulopathy or tumor location, highlighting the need for alternative localization strategies. This study describes a novel technique using four-dimensional computed tomography (4D CT) for volume delineation and 4-dimensional cone beam CT (4D-CBCT) for treatment alignment without IHFMs and reports clinical outcomes.

Methods:

Patients underwent simulation using an alpha cradle, with both three-dimensional (3D) and 4D CT imaging acquired. Planning images were fused with diagnostic PET/CT and/or MRI for target delineation. Organs at risk (OARs), gross tumor volume (GTV), and normal liver were contoured on the average scan of the 4D CT, which also served as the planning CT. A liver internal target volume (Liver-ITV) was created. Liver motion due to respiration in the anterior-posterior, cranial-caudal, and left-right dimensions was determined by careful analysis of the 4D-CT. An internal gross tumor volume (IGTV) was created by expanding the GTV asymmetrically in the anterior-posterior, cranial-caudal, and left-right directions according to liver motion. A PTV was created by expanding the IGTV by 5–6 mm. Treatment was delivered using volumetric modulated arc therapy to a median dose of 50 Gy in 5 fractions, prescribed to the PTV. Dose constraints to OARs were identical to those used routinely done for IHFM-directed liver SBRT. 4D-CBCT was used for image guidance, aligning to the Liver-ITV with a six-degree of freedom couch. Toxicities and outcomes were recorded on an institutional database.

Results:

Twenty-one patients (median age 68 years [range 53 – 91]; 52% female) with 26 liver lesions (2 hepatocellular carcinomas, 24 metastases: 14 gastrointestinal, 5 breast, 4 lung primaries) were treated. The median tumor size was 1.9 cm (range: 0.5–4.9). With a median follow-up of 14 months, local control was achieved in 92% of cases. No severe acute or chronic treatment-related toxicity was observed. Most patients (62%) experienced mild (grade 1) acute gastrointestinal toxicity, including nausea, vomiting, and right upper quadrant (RUQ) discomfort, with one grade

2 RUQ pain, all of which resolved by 1-month post-treatment. Late toxicities were minimal, with only one patient developing grade 2 chest wall myositis around 9 months post-treatment.

Conclusion:

For patients who decline or are ineligible for IHFM placement, we describe a novel, non-invasive technique for liver tumor localization via 4D-CBCT which, in this institutional cohort, provides high local control rates and a favorable toxicity profile.