論 文 内 容 要 旨

Functional image-guided stereotactic body radiation therapy planning for patients with hepatocellular carcinoma

（肝細胞癌に対する機能画像を用いた体幹部定位放射線治療計画）

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Introduction: Recent technological advances in the planning and delivery of stereotactic body radiotherapy (SBRT) have provided the means to treat hepatocellular carcinoma (HCC) in safer, and more effective than previously. However, challenges of HCC treatment include limited liver function in some patients; in previous studies, non-classic radiation-induced liver disease (RILD) was more common in patients with poor liver function (hepatitis B infection and Child–Pugh classes B and C) . Therefore, SBRT to the liver should be cautiously planned to prevent RILD. Moreover, the incidence of RILD is strongly correlated with irradiated liver volumes and mean liver doses. Hence, precise assessments of the current level of liver function are critical in the radiation treatment (RT) of HCC to minimize irradiate volumes and mean doses to functional liver tissues. Functional imaging techniques are used during RT planning and treatment to minimize irradiated volumes and mean doses to functional tissues while delivering highly conformal doses to the tumor. Recent studies have suggested that gadoxetate disodium (EOB; EOB Primovist; Bayer Yakuhin Ltd., Osaka, Japan)–enhanced magnetic resonance imaging (EOB-MRI) is effective for detecting hepatic lesions and may indicate hepatic function. Therefore, we believe that the EOB-MRI–guided liver functional imaging modality can be applied to SBRT for liver cancer to spare the functional liver region using intensity modulated radiation therapy (IMRT) technique and lead to safer and more efficacious treatment.

Purpose: The present simulation study aimed to evaluate the ability of EOB-MRI–guided SBRT planning by using IMRT technique in sparing the functional liver tissues during SBRT for HCC.

Methods: In this study, 20 patients with HCC were enrolled and EOB-MRI was performed before planning. Functional liver tissues were defined according to quantitative liver–spleen contrast ratios $\geq$ 1.5 on a hepatobiliary phase scan. Functional images were fused with the planning computed tomography (CT) images, which were obtained during the arterial phase, in the treatment planning system. Gross tumor volumes (GTVs) were defined as those carrying residual lipiodol from transarterial chemoembolization and early enhancement during the arterial phase of dynamic CT. A clinical target volume (CTV) margin of 0–5 mm was added to the GTV for subclinical invasions, and a planning target volume (PTV) margin of 5–8 mm was added to the CTV based on the reproducibility of respiratory motions and setup errors. Eight ports were selected in all patients, including four coplanar and four non-coplanar static beams, which were established in directions that avoided the stomach, intestine, gall bladder, and

spine if possible. The total prescribed dose was 48 gray (Gy) in four fractions; the prescription dose comprised 95% of the PTV. The following two SBRT plans were designed using a "step-and-shoot" static IMRT technique for each patient: 1) an anatomical SBRT plan (plan A) optimization uses based on the total liver; and 2) a functional SBRT plan (plan F) based on the functional liver. Dosimetric parameters of plan A and plan F were investigated by: 1) doses to 95% of PTV (PTV $D_{95\%}$) and mean PTV dose; 2) calculating mean doses to total and functional liver minus GTVs (MLD and fMLD) ; 3) expressing percentages of total and functional liver volumes, which received doses from 5 to 30 Gy [V5 to V30, fV5 to fV30]; 4) calculating mean doses, doses to 0.5cc and to 5cc volumes (D0.5cc and D5cc) of stomach, duodenum and intestine; and 5) calculating monitor units.

Results: Dosimetric parameters including PTV $D_{95\%}$ (mean: plan A, 48.0; plan F, 48.0 Gy; $p = 0.78$) and mean PTV doses (mean: plan A, 54.6 Gy and plan F, 54.8 Gy; $p = 0.11$) did not differ significantly between the two plans. Compared with anatomical plans, functional image-guided SBRT plans reduced MLD (mean: plan A, 5.5 Gy and plan F, 5.1 Gy; $p < 0.0001$) and fMLD (mean: plan A, 5.4 Gy and plan F, 4.9 Gy; $p < 0.0001$), as well as total and functional liver V5 to V30 and fV5 to V30. Mean dose, D0.5cc and D5cc of stomach (***mean:*** plan A, 0.82 Gy; plan F, 0.78 Gy; $p = 0.19$; ***D0.5cc:*** plan A, 6.0 Gy; plan F, 5.8 Gy; p=0.34 ; ***D5cc:*** plan A, 4.5 Gy; plan F, 4.4 Gy; p=0.36), duodenum (***mean:*** plan A, 0.59 Gy; plan F, 0.62 Gy; $p = 0.09$; ***D0.5cc:*** plan A, 2.2 Gy; plan F, 2.4 Gy; p=0.07 ; ***D5cc:*** plan A, 0.96 Gy; plan F, 0.98 Gy; p=0.4) and intestine (***mean:*** plan A, 0.68 Gy; plan F, 0.66 Gy; $p = 0.29$; ***D0.5cc:*** plan A, 4.5 Gy; plan F, 4.7 Gy; p=0.36 ; ***D5cc:*** plan A, 3.1 Gy; plan F, 3.1 Gy; p=0.45) were not significantly different between the two plans. However, monitor units (mean: plan A, 2437; plan F, 2495; $p = 0.01$) and conformity indexes (mean: plan A, 0.99; plan F, 1.01; $p = 0.003$) differed significantly between the two plans.

Conclusions: This simulation study demonstrates the ability of functional imaging with EOB-MRI for SBRT planning in patients with HCC. EOB–MRI-guided SBRT planning using the IMRT technique may improve functional liver preservation in patients with HCC.