Increasing radiation dose for better hepatic cancer control from radiation therapy (RT) is limited by the development of radiation-induced liver disease (RILD). Clinical syndrome of RILD occurs typically 2 weeks to 4 months after completion of RT. In severe cases, RILD can lead to liver failure and death. Using the Lyman-Kutcher-Burman NTCP model, the likelihood of developing RILD can be estimated based on the planned dose on the normal liver [1]. However, the models solely based on dose distribution which ignores individual liver sensitivity to RT that may allow safe delivery of higher radiation dose on some patients. Imaging can quantitatively assess normal tissue response to RT, and thereby it may be able to characterize individual liver tolerance to radiation and provide surrogates to early predict the development of RILD.

RILD is a veno-occlusive disease characterized with hepatic congestion from thrombosis in the central veins of the liver. Therefore, hepatic portal venous perfusion imaged by dynamic contrast enhanced imaging (DCE) may have potentials to predict radiation-induced liver dysfunction. A study used DCE-CT to investigate portal venous perfusion changes of 10 patients with intrahepatic cancer treated with high-dose focal RT [2]. The study showed the reduction in the regional venous perfusion one month after the completion of RT was linearly related to the local accumulated dose and change in the regional venous perfusion after approximate 45 Gy. This finding indicates DCE imaging may allow construction of an individual portal venous perfusion-dose response function to characterize individual sensitivity to radiation. In addition, the study showed the dose ranging from 42.4 to 67.8 Gy with a median dose of 54.4 Gy decreased portal venous perfusion to 20 mL/(100g min)-a critical point where the liver dysfunction occurred [3]. Most importantly, there was a significant correlation between indocyanine green (ICG) clearance rate and the mean portal venous perfusion in the normal liver parenchyma. ICG clearance rate is a clinical surrogate of liver function. Therefore, the results suggested that spatially resolved portal venous perfusion could be an indicator of overall liver function. However, the CT-based hepatic perfusion imaging was spatially limited to a 2- cm slab in the cranial-caudal direction. To image the hepatic venous perfusion of whole liver, DCE-MRI was used in a recent study [4]. The study acquired whole liver volumetric MRI in a time step of 2.4 secs for a total of 2 mins after MRI contrast agent administration. DCE-MRI of 17 patients undergoing 3D conformal RT or SBRT was acquired prior to, during and 1 month after RT. A significant correlation between ICG clearance rate and the mean portal venous perfusion of a whole liver excluding tumors was found. The results showed regional portal venous perfusion measured during RT was a significant predictor for venous perfusion 1 month after RT. Interestingly, hepatic venous perfusion assessed by DCE-MRI demonstrated that hypervenous perfusion or reperfusion in low-dose regions occurred post-RT in 3 patients. This study further indicated that hepatic venous perfusion derived from DCE imaging has the potential to assess individual sensitivity to radiation and to predict toxicity of RT in liver.

Although these studies showed DCE imaging held great potential for better radiation therapy for liver cancer, DCE-MRI and DCE-CT have not been evaluated as a surrogate for assessment and/or modification of radiation therapy in any prospective phase III clinical trial. In addition, there are no standards for DCE image acquisition and quantification, which hinders interpretation and utilization of the published information. More evaluation and clinical trials are needed for adoption of these imaging techniques in routine clinical care.

References

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