Value of dynamic contrast enhanced MRI in predicting outcomes of HCC receiving radiotherapy

Masatoshi Kudo

Received: 10 February 2015 / Accepted: 17 February 2015 / Published online: 7 March 2015
© Asian Pacific Association for the Study of the Liver 2015

Radiotherapy (RT) is an emerging treatment option for advanced hepatocellular carcinoma (HCC). RT is effective and confers a survival benefit in selective cases [1], but it is not recommended in most HCC treatment guidelines such as AASLD [2], EASL-EORTC [3], APASL [4], or JSH [5, 6]. An imaging biomarker that predicts the outcome of RT is urgently needed.

Dynamic contrast-enhanced magnetic resonance imaging (DCEMRI) is a routine radiological modality that is frequently used to evaluate treatment response in the clinical setting. In particular, DCEMRI is used to evaluate changes of vascularity or hemodynamics in HCC nodules, similar to dynamic CT. A feature of DCEMRI that is different from dynamic CT is its ability to precisely measure the properties of the microcirculation using special analytic methods. In this issue of *Hepatology International*, Liang et al. [7] attempted to calculate semiquantitative perfusion parameters, such as initial first-pass enhancement slopes (Slope) and peak enhancement ratios (Peak), which represent microcirculation and permeability to contrast medium in the evaluation of treatment response to RT. Slope is more closely related to the vascular density of the tissue, whereas Peak represents a complex process involving blood flow, transit, and permeability that affect the contrast media concentration in the total extracellular space. This study aimed to answer three questions: (1) Does concomitant use of the anti-angiogenic agent, thalidomide, with RT enhance the treatment response? (2) Can Slope and Peak of the tumor be used as imaging

biomarkers to predict treatment outcome such as progression free survival (PFS) or overall survival (OS)? (3) Can Slope and Peak of the non-tumor liver parenchyma be used as imaging biomarkers to predict treatment outcome such as PFS or OS?

For the first question, the authors clearly showed that concomitant use of thalidomide did not improve treatment response or survival compared with RT alone, although modification of dosage and schedule of thalidomide use might result in different outcomes.

With respect to the second question, baseline Peak and Slope of the tumor at day 14 of RT correlated well with the response rate assessed with RECIST, but surprisingly, the perfusion parameters did not correlate with PFS or OS. Therefore, the answer to question 2 remains unknown. It is also unclear why RT increases the perfusion parameters of HCC nodules after 2 weeks of RT.

For the third question, only the increased Slope of liver parenchyma at 14 days after RT was independently associated with shorter PFS on multivariate analysis. In addition, multivariate analysis showed that elevated Peak of liver parenchyma one month after RT predicts shorter OS.

Correlation of the elevated perfusion parameters of the liver parenchyma surrounding the tumor, but not the tumor itself, with shorter PFS and OS is very surprising. The authors reasoned that the well-perfused and oxygenated microenvironment of non-tumor liver parenchyma favors tumor progression regardless of the tumor response. If this is true, why was RT performed? In other words, it is not clear why RT was associated with shorter PFS and OS even though a tumor response was obtained. It was suggested that RT is not the choice of treatment for the heavily treated HCC patient group because these phenomena are caused by RT. RT might shorten PFS and OS in these patients.

M. Kudo (✉)
Department of Gastroenterology and Hepatology, Kinki
University School of Medicine, Osaka, Japan
e-mail: m-kudo@med.kindai.ac.jp

Since this is a phase II single-arm trial, a phase III trial to examine the survival benefit of RT by comparing RT with best supportive care using Slope and Peak data is awaited.

In any case, this study using DCEMRI to establish an imaging biomarker that correlates with PFS or OS is a promising and relevant approach in the treatment of advanced HCC by RT or targeted agents. More extensive studies are warranted to demonstrate its utility.

Compliance with ethical requirements and Conflict of interest Masatoshi Kudo declares that he has no conflict of interest.

References

1. Lee DS, Seong J. Radiotherapeutic options for hepatocellular carcinoma with portal vein tumor thrombosis. *Liver Cancer* 2014;3:18–30.
2. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. *Hepatology* 2011;53:1020–1022.
3. Llovet JM, Ducreux M, et al. EASL-EORTC clinical practice guidelines: Management of hepatocellular carcinoma. *J Hepatol* 2012;56:908–943.
4. Omata M, Lesmana LA, Tateishi R, Chen PJ, Lin SM, Yoshida H, et al. Asian pacific association for the study of the liver consensus recommendations on hepatocellular carcinoma. *Hepatol Int* 2010;4:439–474.
5. Makuuchi M, Kokudo N, Arii S, Futagawa S, Kaneko S, Kawasaki S, et al. Development of evidence-based clinical guidelines for the diagnosis and treatment of hepatocellular carcinoma in Japan. *Hepatol Res* 2008;38:37–51.
6. Kudo M, Matsui O, Izumi N, Iijima H, Kadoya M, Imai Y, et al. On behalf of the liver cancer study group of Japan: JSH consensus-based clinical practice guideline for the management of hepatocellular carcinoma: 2014 update by the liver cancer study group of Japan. *Liver Cancer* 2014;3:458–468.
7. Liang PC, Ch'ang HJ, Hsu C, Chen LT, Shin TTF, Liu TW. Perfusion parameters of dynamic contrast enhanced magnetic resonance imaging predict outcomes of hepatocellular carcinoma receiving radiotherapy with or without thalidomide. *Hepatol Int* 2014. doi:[10.1007/s12072-014-9557-1](https://doi.org/10.1007/s12072-014-9557-1).