



Improving detection combined with targeted therapy for small hepatocellular carcinoma

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Surgery remains the best treatment option for cure in patients with hepatocellular carcinoma (HCC). However, the majority of patients with localised HCC are unfit for curative resection or transplantation. Currently, several modalities are available for non-surgical liver directed therapy including radiofrequency ablation (RFA), microwave ablation, cryo-ablation, ethanol injection, laser ablation, and irreversible electroporation. The choice of these modalities is largely determined by institutional experience and preference. RFA has been shown to be an effective method of treating small HCCs (<5 cm). Large series showed a response rate of 99% with 5 and 10 years tumour progression rates of 3% (1,2). Smaller lesions are thought more likely to respond well to RFA due to the size of the ablation field (3). Although small HCCs can be diagnosed by computer tomography (CT) and magnetic resonance imaging (MRI), only one third of HCCs ≤ 1 cm are detected by conventional ultrasonography (US) (4). This low pickup rate has limited the feasibility of image-guided percutaneous RFA to sub-centimetre HCCs thus far. Fusion imaging techniques utilise electromagnetic tracking to synchronise real time US with CT or MRI images in order to enhance the detection of liver lesions (5-7). Song *et al.* assessed the feasibility of US/MRI fusion imaging to plan and guide RFA for sub-centimetre HCCs (8).

Song *et al.* retrospectively reviewed the ability of fusion US/MRI to detect HCC nodules between 5–10 mm and evaluated the efficacy and safety of percutaneous RFA of these nodules. The rationale for treatment was that most

of these lesions progressed to overt HCC in a year (9). US/MRI fusion imaging was used to assess the feasibility of RFA of sub-centimetre HCCs. The feasibility criteria for RFA were determined by experienced radiologists with over 10 years experiences in HCC management.

Two hundred and ten sub-centimetre HCCs were included in the study. Fifty-one (24%) were not conspicuous on MRI/US fusion imaging. The detection rate was much higher compared to those reported in previous studies using US alone. Based on their RFA feasibility criteria, 65% of 210 HCCs detected were feasible for RFA with 60% ultimately undergoing ablation. The baseline characteristics between feasible and non-feasible groups were similar apart from the proportion of patients receiving antiviral treatment and the location of the tumours. There was a higher proportion of the lesions feasible for RFA in the right lobe of the liver (72%) compared to 50% of lesions in the left lobe ($P=0.01$). The average body mass index (BMI) for the patients was 24.

Of the lesions feasible for RFA, the technique efficacy and technical success rate was 98.4%. The complication rate was 2.5%. There were 2 cases of intra peritoneal bleeding and 1 case of thermal injury to the colon. At 3 years, tumour progression occurred in 7.3% of lesions successfully treated with RFA.

The detection of small HCCs using conventional ultrasonography is limited and operator dependant. The dynamic nature of US allows it to be used to for guidance for ablative therapy for liver lesions. However, US requires

the user to mentally register anatomical information from other imaging modalities such as CTs and MRIs. Fusion imaging eliminates this requirement. It helps the operator to characterise conspicuous lesions more confidently and allows them to conduct interventions for more challenging target lesions. Song *et al.* convincingly demonstrated that in experienced hands, US/MRI fusion imaging was able to accurately detect sub-centimetre HCCs and target them for RFA with a high efficacy.

Some key questions remain to be answered. First, the therapeutic benefit of targeting sub-centimetre HCC nodules remains to be seen. Particularly as histological confirmation of these lesions were not obtained prior to treatment in this study. Second, the generalisability of the results can only be assessed when fusion imaging is used in less experienced hands. Lastly, whether fusion imaging can overcome other known limiting factors for percutaneous ablative therapy, such as depth of the lesions and body habitus of the patients, needs to be evaluated with large-scale prospective studies.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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