Guidance and monitoring of radiofrequency liver tumor ablation with contrast-enhanced ultrasound

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Abstract

Radiofrequency (RF) treatments of non-resectable hepatic tumors are generally guided with real-time sonography, which, however, cannot differentiate necrotic changes from viable tumor. To achieve complete treatment of hepatic tumors, accurate imaging techniques are needed for close treatment follow-up. Usually contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) are used; however, they can be performed only at the end of treatment sessions. In this field, contrast-enhanced ultrasound (CEUS) has shown to improve the sensitivity of plain ultrasonography. Recently, further developments of contrast-enhanced US technique have significantly increased its clinical utility. Continuous mode, low MI scans performed with harmonic imaging and contrast specific software appears as a very useful technique for the visualization of both macro- and microcirculation with depiction of tumor vascularisation.

In our hospital, we have been employing contrast-enhanced sonography with sulphur hexaflouride microbubbles (SonoVue®, Bracco, Italy) before, during and immediately at the end of RF ablation procedures to monitor and assess the therapeutic result prior to closing the treatment session. The results obtained in a group of 109 patients with hepatocellular carcinoma (HCC) in liver cirrhosis (192 lesions) and in 53 patients with liver metastases (97 lesions) undergoing a single session of percutaneous RF tumor ablation, showed that the sensitivity of CEUS for the detection of residual tumor was almost equivalent to that of contrast-enhanced helical CT. More importantly, since the introduction of intraoperative CEUS the rate of partially unablated tumors has dropped from 16.1 to 5.9%. Cost-effectiveness and reduction of patients’ discomfort related to the need of re-treatment are the two most outstanding advantages of CEUS in this field.

Keywords: Radiofrequency tumor ablation; Contrast-enhanced ultrasound; Liver; HCC; Metastases

1. Introduction

Radiofrequency (RF) ablation is currently by far the most used technique for both hepatocellular carcinoma and liver metastases and the number of treated patients is steadily increasing. Several large series demonstrated its safety and effectiveness and pointed out its significant advantages, including feasibility in non-surgical candidates, the possibility of repeated treatment sessions if local recurrence or new lesions develop, lower morbidity and mortality compared to surgical resection, and markedly reduced treatment costs and hospital stays [1–4]. It is nowadays widely accepted that patients with liver metastases from colorectal or other primary cancers may reasonably undergo RF ablation with curative intention if a maximum of four to five lesions, each of them smaller than 4-cm are present. Similarly, in patients with chronic liver disease, hepatocellular carcinomas (HCCs) and dysplastic lesions can undergo RF ablation as only treatment when no more than four to five nodules are detected and each of them does not exceed 5–6 cm, in absence of portal thrombosis and liver function decompensation. Hepatocellular carcinomas of larger size are usually non-invasively treated by means of combined therapies (chemoembolization, ethanol injection, laser, radiofrequency).

The ultimate goal of all ablative treatments is the disruption of tumor vascularity. The best way to non-invasively...
Fig. 1. Single HCC (2.5 cm) at segment 4, adjacent to distended gallbladder, in cirrhotic patient, depicted with B-mode sonography (A), CEUS in arterial phase (B) and contrast-enhanced CT (C). Note how the internal areas of hypovascularity are equally demonstrated by CEUS and CT. Immediately after RF ablation with cool-tip electrode, CEUS in arterial phase shows a large area of hypovascularity replacing the treated tumor (D). Complete necrosis is confirmed with 24 h contrast-enhanced CT (E). Note the presence of a dilated vein between gallbladder and tumor, which represents a pericholecystic venous shunt related to chronic liver disease.
assess the efficacy of any percutaneous ablation is the demonstration of blood supply disruption inside and at the periphery of the tumor by means of imaging methods. Diagnostic imaging is of paramount importance not only in the assessment of immediate therapeutic results but also in detection of lesions and selection of patients for treatment, in targeting of lesion(s) with optimal positioning of the energy applicator and in long-term follow-up.

1.1. Detection of lesions for selection of patients and targeting of the lesion

Early detection and accurate assessment of the extent of neoplastic liver disease at the time of diagnosis or during the course of treatment is crucial for optimal patient management. Imaging modalities such as multiphasic contrast-enhanced helical computed tomography (CT) and dynamic gadolinium-enhanced magnetic resonance imaging (MRI) provide convenient staging of hepatic and extra-hepatic neoplastic involvement. Unenhanced B-mode sonography represents the most widely available low-cost imaging modality for the screening of liver disease; but is less accurate than CT and MRI for the detection of focal lesions, particularly of smaller ones. However, with the introduction of real-time imaging techniques and second-generation contrast agent, contrast-enhanced ultrasound (CEUS) pre-treatment evaluation of patients and real-time guidance of needle positioning has shown in our experience the potential of significantly improve detection and staging of liver tumors and the precise targeting of the lesion.

1.2. Evaluation of RF ablation treatment effect and follow-up

The most important imaging finding that suggests complete treatment of a focal liver tumor is the disappearance of any previously visualized vascular enhancement on contrast-enhanced images [5]. Either biphasic helical CT or dynamic gadolinium-enhanced MRI, although more expensive and less immediate than US, is useful in the assessment of therapeutic efficacy for both hepatoma and metastatic lesions. As shown during clinical studies [6], CT and MRI findings can predict the extent of coagulative necrotic area to within 2–3 mm. However, contrast-enhanced CT or MRI studies cannot be performed in the interventional (either surgical or sonographic) room, and usually they are performed within 1 week following the RF ablation session and results compared with baseline examinations to differentiate between ablated regions and residual viable tumor requiring additional treatment [6].

Since the introduction of first-generation US contrast agents, color Doppler (CD) and power Doppler (PD) modalities have been used to evaluate the response of hepatocellular carcinoma to interventional treatments, including RF ablation. Initial experiences addressing the usefulness of CEPD after RF ablation of hepatoma demonstrated the possibility of detecting hypervascular tissue consistent with residual viable tumor with complete specificity and 90% sensitivity [7–9]. Similarly, our group studied patients with liver metastases immediately after ablation and demonstrated that CEUS in CD and PD modes could help to differentiate perfused from non-perfused tissue and detect residual tumor, enabling additional treatment sessions in some, but not all cases [10]. More recently, the superiority of pulse inversion CEUS over CEPD (sensitivity 23.3% versus 9.3%) in the detection of residual HCC after 4 months of RF ablation was demonstrated in a paper by Meloni et al. [11]. In all these experiences, helical CT was the “gold standard” and specificity was considered complete (100%) for visible hepatoma when foci of persistent hypervascularity were observed.

1.3. Our experience using CEUS with second-generation contrast agent

According to our protocol, pre-treatment CEUS examination was performed as initial step of the RF session, during the induction of anesthesia, in order to reproduce mapping of lesions as shown on CT/MRI examinations and to allow real-time lesion targeting [12,13]. Images and/or movie clips were
Fig. 2. A 1.5 cm colorectal metastasis in the right lobe of the liver, studied in portal phase, after bolus injection of 2.4 ml of SonoVue® (A). The lesion has hypovascular pattern, as confirmed by contrast-enhanced helical CT in portal phase (B). Few minutes after finishing percutaneous radiofrequency ablation with cool-tip electrode (Radionics, Tyco, Burlington, USA), after second bolus injection of SonoVue®, a large (3 cm × 2.1 cm) oval-shaped, irregularly margined hypoechoic, non-enhancing zone is seen in the area of treatment (C). The diagnosis of complete necrosis is confirmed by 24-h post-ablation contrast-enhanced CT (D).
digitally stored to be compared with immediate post-ablation study.

In particularly difficult cases, needle insertion was performed during the specific phase in which the maximum lesion conspicuity was observed: in arterial phase for hypervascular lesions such as HCCs and hypervascular metastases, in portal or equilibrium phases for hypovascular metastases.

Immediate post-ablation evaluation using CEUS was performed 5–10 min after the assumed completion of the RF session, with the patient still under general anesthesia. As depicted on contrast-enhanced CT and MRI, a thin and uniform enhancing rim is usually visible along the periphery of the necrotic area, which should not be mistaken for tumor.

Comparison of immediate post-ablation images with stored pre-ablation scans is mandatory. Residual viable hepatoma is suspected when a portion of the original lesion maintains hypervascularity in the arterial phase (Fig. 1). As with helical CT, residual untreated metastatic lesions sometimes appear indistinguishable from necrosis in the portal and equilibrium phases: on CEUS, evaluation of the early phase is important since viable tumor shows weak but perceptible enhancement (Fig. 2). If even questionable residual tumor foci with enhancement or vascular supply are depicted, immediate CEUS-guided targeted re-treatment is carried out. Treatment is stopped only when complete avascularity is demonstrated.

Over a period of 26 months, a group of 162 patients, 109 with HCC and 53 with liver metastases, underwent a single session of percutaneous RF tumor ablation. CEUS was performed using sulphur hexafluoride microbubbles (SonoVue®, Bracco, Italy) before, during and immediately at the end of RF ablation procedures to monitor and assess the therapeutic result prior to closing the treatment session.

Contrast-specific software (coherent contrast imaging (CCI) and contrast pulse sequencing (CPS), Siemens Acuson, USA; ECI, Siemens, Germany; contrast tuned imaging (CTi), Esaote, Italy) in continuous mode with very low mechanical index (0.01–0.1) was employed for all the examinations [12,13].

In 238 of 289 liver malignancies treated, no residual tumor was found on CEUS of these, CT depicted residual foci only in 12/238 cases (5.0%), all of them of very small size (0.8–1.7 cm). On the other hand, in the remaining 51 tumors, single or multiple (1.0–2.2 cm) residual foci were detected and immediately submitted to additional RF application in the same session until no further residual enhancement was detectable: only in 5/51 cases (9.8%) a 1.2–1.9 cm residual tumor was depicted at post-ablation CT. In the group of patients with metastases, using CEUS as routine pre-treatment imaging modality, increased conspicuity (versus contrast-enhanced helical CT) for tiny hypovascular metastases was obtained in 12% of patients: this led to a significant modification of treatment strategy, since 38% of these patients, initially enrolled for RF ablation were excluded due to the unexpectedly large number of metastases detected.

2. Conclusions

In our experience, the use of CEUS represents a significant improvement in each of tumor ablative treatment steps and may be useful to achieve optimal patients’ management and treatment results. With the routine adoption of CEUS, we obtained a rate of partial necrosis of 5.9% (17/289), in comparison with a 16.1% rate achieved from 1994 to August 2000 (prior to the introduction of CEUS for the real-time management of ablations) for 429 hepatocellular and metastatic lesions. Furthermore, this approach reduces the costs by decreasing both the number of RF procedures (25 treatment sessions saved in our series) and follow-up examinations.

References
