Cardiovasc Intervent Radiol (2011) 34:852–856
DOI 10.1007/s00270-010-9966-z

TECHNICAL NOTE

Stereotactic Radiofrequency Ablation

Reto Bale · Gerlig Widmann · Marion Haidu

Received: 25 June 2010 / Accepted: 27 July 2010 / Published online: 24 August 2010

Abstract
Purpose To describe the technique of percutaneous stereotactic radiofrequency ablation (SRFA) and its application in a patient with an unresectable multifocal intrahepatic cholangiocarcinoma (ICC).
Materials and Methods A 72-year-old man presented with two nodules of an ICC with a maximum diameter of 10 and 4 cm, respectively. To produce overlapping ablation areas and cover the entire tumor volume, 18 paths for the placement of radiofrequency ablation (RFA) probes at multiple locations were planned on 2D and 3D reconstructions of the computed tomographic (CT) data. The 15-gauge coaxial needles were advanced through the aiming device to the preplanned depth. A control CT fused to the planning CT data confirmed correct needle placements. RFA was performed with an impedance-based multiple-electrode RFA system. Fusion of the contrast-enhanced control CT with the planning CT showed an appropriate zone of ablation.
Results Besides a mild asymptomatic pleural effusion, no complications occurred. Twenty-seven months after the first RFA, two new small distant liver metastases were successfully treated by SRFA. Currently, 38 months after diagnosis and 36 months after the first SRFA, the patient is free of detectable disease.
Conclusion SRFA seems to offer an effective treatment option in selected patients with even unresectable ICC.

Keywords Radiofrequency ablation · Cholangiocarcinoma · Navigation · Liver tumor · 3D-planning · Treatment · Stereotaxy

Introduction

Cholangiocellular carcinoma is the second most common primary hepatobiliary malignancy, and approximately 8% of all cholangiocellular carcinomas arise from the intrahepatic bile ducts [1]. At present, only surgical resection of intrahepatic cholangiocellular carcinoma (ICC) is associated with improvement in long-term survival [1–3]. Prognosis for patients with unresectable ICC is poor: survival is less than 1 year without treatment, and treatment alternatives are few [4]. Percutaneous image-guided radiofrequency ablation (RFA) is a minimally invasive technique that uses high frequency alternating current to heat tissue to the point of coagulation with the aim of local curation [5, 6]. The use of RFA for solitary ICC has been reported in a limited number of small case series and case reports [7–10]. To our knowledge, there is no report about the use of RFA in multifocal ICC ($n > 1$) or in ICC larger than 7 cm.

Here we provide what is to our knowledge the first report on stereotactic RFA (SRFA) and its application in a patient with a large unresectable multifocal ICC located close to major vessels. Evaluation of the patient data was approved by the institutional review board.

R. Bale and M. Haidu contributed equally to this work.

R. Bale · G. Widmann · M. Haidu (✉)
Department for Microinvasive Therapy (SIP),
Medical University Innsbruck, Anichstr. 35,
6020 Innsbruck, Austria
e-mail: marion.haidu@i-med.ac.at

R. Bale · G. Widmann · M. Haidu
Department of Radiology, Medical University Innsbruck,
Anichstr. 35, 6020 Innsbruck, Austria

Material and Methods

A 72-year-old man underwent a routine blood check and was found to have a high level of γ-glutamyl transpeptidase of up to 166 U/l (reference range 10–71 U/l). The patient did not exhibit any symptoms except mild abdominal pain. Contrast-enhanced abdominal computed tomography (CT), magnetic resonance imaging, and ultrasound revealed a tumor 10 cm in maximum diameter involving liver segments I, V, VI, VII, and VIII and extending from the diaphragm to the lower surface of the caudate lobe. The tumor encased the right and middle major hepatic vein and had broad contact to the caval and portal veins (Fig. 1A, B).

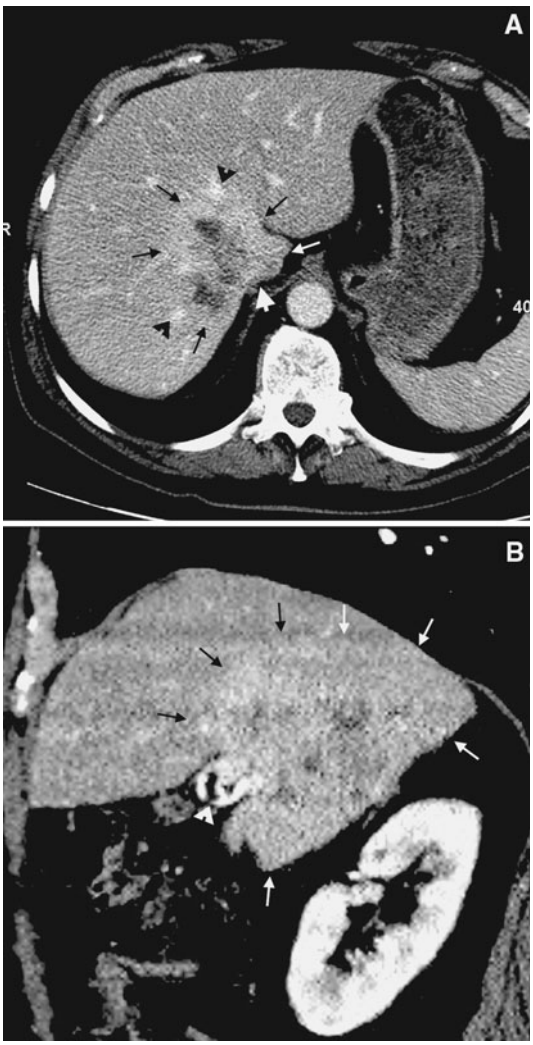
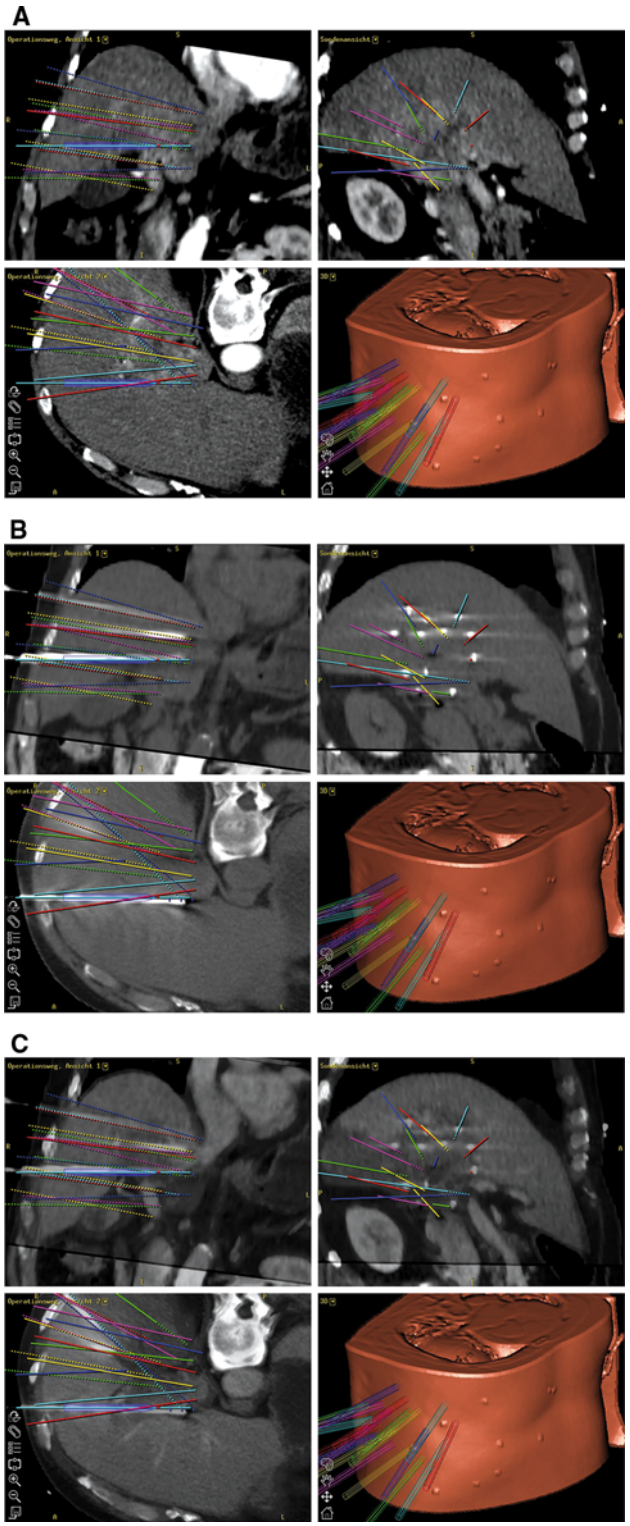


Fig. 1 Contrast-enhanced CT showing a contrast-enhancing lesion with 10 cm in maximum diameter (*small white and black arrows*), encasing the right and middle major hepatic veins (*black arrowheads*) and having broad contact to the caval vein (*large white arrow*) with compression. Note also the vicinity of the portal structures (*white arrowhead*) to the tumor. **A** Axial view, **B** Sagittal view

Furthermore, an intrahepatic satellite tumor 4 cm in diameter was detected in segment VII subcapsular. Ultrasound-guided core needle biopsy of the tumor was performed, and histopathologic and immunohistochemical analysis revealed a moderately differentiated tubular adenocarcinoma. Cytokeratin-7 was strongly positive, consistent with a primary bile duct tumor. Laboratory tests revealed normal tumor markers (including α-1-fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19-9). The patient had not received any previous treatment at the time of diagnosis. Positron emission tomography and whole-body CT revealed no evidence of metastatic disease. The patient had no other relevant medical history. Because of the extension, size, and location of the tumor and the expected morbidity after surgical resection, SRFA was considered treatment of choice. Two consecutive RFA sessions were planned to achieve complete ablation, the first for ablation of the large tumor and the second for ablation of the smaller nodule located in segment VII. The first RFA session was performed in May 2007 and the second in June 2007. In each case, written informed consent was obtained 1 day before the intervention. The treatments were performed while the patient was under general anesthesia. On the day of the RFA procedure, the patient received prophylactic periprocedural systemic single-shot antibiotic therapy (1.5 g cefuroxime).

The entire SRFA procedure [11, 12] was performed in the interventional CT suite. The patient was immobilized in a BodyFix double-vacuum fixation system (Medical Intelligence, Schwabmünchen, Germany) [13], and fiducial markers were attached to the patient's skin for image-to-patient coordinate transformation (that is, registration) [11]. A 3-mm contrast-enhanced multidetector CT (Siemens Sensation Open) scan of the upper abdomen was obtained in maximal expiration and immediately sent to the optical navigation system (Treon; Medtronic, Louisville, CO) via the hospital's internal network.

The optical navigation system consists of an optical localization system, a workstation, a monitor, and various trackable instruments equipped with active (infrared light emitting) or passive (infrared light reflecting) markers. To produce overlapping ablation areas and cover the entire tumor volume, paths for the placement of radiofrequency probes at multiple locations were planned on 2D and 3D reconstructions of the CT data (Fig. 2A). After sterile draping and registration, where the fiducials on the real patient are touched with the optically tracked probe and linked to the corresponding points in the image data, the Atlas aiming device (Medical Intelligence) of the navigation system was adjusted according to the surgical plan. It enables the 3D-navigated alignment of linear instruments according to a virtual plan. The device can be rotated around two centers of rotation, allowing for exact



◀**Fig. 2** Screenshots of the navigation system showing multiplanar reconstructions and a 3D reconstruction of the patient's CT data set with the planned needle pathways. The *upper* and *lower left quadrant* reflect two perpendicular reconstructions along the planned trajectory (trajectory 0 and 90). The *upper right quadrant* shows a plane perpendicular to the planned trajectory (probe's-eye view). In the *lower right quadrant* a 3D reconstruction of the skin of the patients with the markers and the trajectories is visualized. **A** Definition of 18 trajectories on planning CT data set. **B** Superposition of control CT on the planning CT, with the pathways showing precise placement of all needles with a maximum deviation of 3 mm. **C** Superposition of contrast-enhanced control CT (with remaining coaxial needles) after RFA with planning CT showing the large necrotic area

orientation of the central axis according to the planned path. Brackets with an adjustable concentric aperture allow the use of needles with different calibers. The 15-gauge coaxial needles are advanced manually to the depth displayed by the navigation system. Afterward, the brackets are opened and the needle is left in place.

Eighteen coaxial needles were placed in the 10-cm tumor and six in the 4-cm nodule, respectively, with an interelectrode spacing of 1.5–2 cm. Care was taken not to damage large vessels, bile ducts, and adjacent organs. After needle placement, a control CT without contrast media was performed and fused to the planning CT data by Treon's ImMerge software. After confirmation of correct needle placement (Fig. 2B), RFA was performed with an impedance-based multiple-electrode RFA system with cooled-tip electrodes (Covidien, Boulder, CO) [14]. This system consists of a 470-kHz radiofrequency generator, a switching controller, three 17-gauge cooled-tip probes with an active uninsulated tip length of 3 cm, and four large grounding pads. Power was automatically switched from one electrode to the other depending on the impedance, and the system was activated for 16 min for each ablation cycle. In total, 18 ablation cycles (54 probe positions) where required for the large lesion and three for the small lesion (three probe positions), respectively, resulting in a total ablation time of 288 min for the large ICC and 48 min for the smaller ICC. Contrast-enhanced control CT performed immediately after RFA and fusion with the planning CT (Fig. 2C) showed that the coagulation zone covered the entire tumor volume, including a safety margin of 5 mm at the minimum. Afterward, hot probe withdrawal was performed. Except for a minimal pleural effusion, no side effects or complications were observed.

Results

No immediate or late major complications occurred. After the first session, the patient experienced postablation syndrome [15] as a result of the large coagulation zone. An increase of C-reactive protein up to 23 mg/dl (reference range 0–0.7 mg/dl), aspartate aminotransferase up to 2246 U/l (reference range 10–50 U/l) and alanine aminotransferase up to 2071 U/l (reference range 10–50 U/l) were observed. To prevent infection, the patient received systemic broadband antibiotic therapy for 2 weeks. The C-reactive

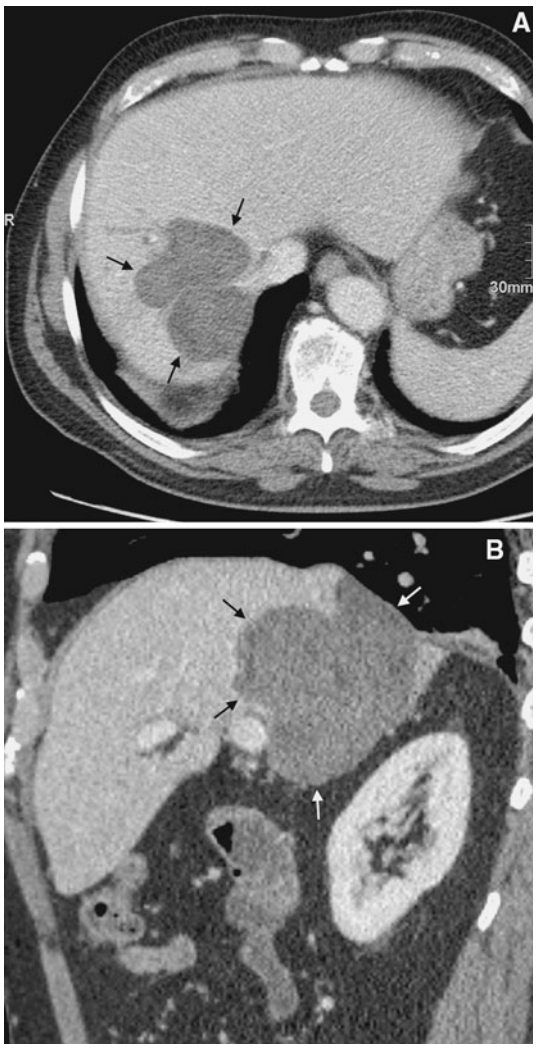


Fig. 3 Contrast-enhanced CT 19 months after RFA showing the large RFA-induced necrosis without evidence of recurrent tumor. **A** Axial view, **B** sagittal view

protein, aspartate aminotransferase, and alanine aminotransferase levels decreased to normal values within 2 weeks, and the pleural effusion resolved without the need for percutaneous drainage. Three weeks later, the second RFA session was performed, and except for minimal asymptomatic pleural effusion, no side effects or complications occurred. Follow-up examinations (CT and magnetic resonance imaging scans) (Fig. 3) were performed every 3 months. At 26 months after the first RFA, two new distant liver metastases with a diameter of 1 cm each (segments III and V) appeared, which were successfully treated by SRFA 1 month later. Currently, 38 months after diagnosis and 36 months after the first SRFA, the patient is still in good physical condition and free of detectable disease, as confirmed by contrast-enhanced whole-body CT. The maximum size of the ablation necrosis decreased from 12 to 9 cm.

Discussion

Currently, surgical resection offers the best opportunity for improving long-term survival in patients with ICC [1]. Unfortunately, most patients are unsuitable candidates for surgery at the time of diagnosis as a result of advanced tumor stage [3], and response to systemic chemotherapy is poor [1, 2, 16]. Median survival for patients with unresectable ICC was reported to be only 3–6 months without treatment, and effective treatment remains a major challenge [4]. Recently, transcatheter arterial chemoembolization has been associated with a survival benefit for patients with unresectable ICC, with the median survival ranging from 10 to 13 months [17, 18]. The effectiveness of radiation therapy remains unclear [2].

RFA has the potential to irreversibly destroy tumor cells. It was demonstrated to be effective in the treatment of unresectable liver malignancies by means of improving disease-free and overall survival [5, 6]. Its advantages compared to other local ablative techniques have been reported in several studies [5, 19]. With conventional image-guided RFA techniques, tumor size larger than 5 cm, proximity to large intrahepatic vessels, and subcapsular location are factors that usually lead to insufficient ablations and significantly influence outcome [20].

Recently, two successful case studies of RFA have been reported for the treatment of solitary ICC smaller than 4 cm in diameter [7, 9]. Slakey reported that after previous resection, a recurrent ICC measuring 2 cm in diameter was ablated percutaneously under ultrasound guidance with no evidence of disease 10 months after RFA [7]. In second case reported by Zgodzinski and Espat, the patient underwent open-surgical biopsy and RFA for treatment of a tumor 4 cm in diameter that unexpectedly turned out to be an ICC. That patient was free of recurrent tumor after a follow-up of 24 months [9].

Chiou et al. reported the treatment effect after percutaneous ultrasound-guided RFA of ten solitary ICCs [8]. The maximum tumor size was 6.8 cm, and no tumor was located adjacent to major vessels. Treatment success strongly depended on the tumor size. Complete ablation after 12 RFA sessions was achieved in all five tumors with a diameter smaller than 3 cm, in two of three tumors with a diameter of 3–5 cm, and in one of two tumors with a diameter larger than 5 cm [8].

In this case study, application of stereotaxy allowed for successful ablation of the tumor despite its large size and unfavorable location as a result of surrounding major vessels.

Perfusion-mediated tissue cooling influences thermal ablation. However, stereotaxy permits precise positioning of multiple RFA probes directly adjacent to the vessel wall. Thus, heat dissipation is so fast that conduction does not play a major role, as compared to focused ultrasound.

By means of stereotaxy, additional transarterial (chemo)-embolization before RFA is not necessary, thus requiring only one treatment session per tumor. Furthermore, injury of vital structures such as the central bile ducts and neighboring organs was successfully avoided, thanks to precise prepuncture path planning.

To our knowledge, this is the first report of the use of stereotactic RFA and its applications in a patient with primary unresectable large multifocal ICC. Disease-free survival at 3 years after RFA treatment in this case suggests that SRFA may be a reasonable approach for effective therapy in selected patients with even unresectable ICCs. However, the encouraging results of this initial case must be confirmed by larger patient studies. This report suggests that SRFA may also have the potential for minimally invasive local curation of large and even unresectable liver tumors of other origin.

Conflict of interest The first author is a co-inventor of the Atlas aiming device and the BodyFix double-vacuum immobilization system and a co-shareholder in their financial returns.

References

1. de Groen PC, Gores GJ, LaRusso NF et al (1999) Biliary tract cancers. N Engl J Med 341:1368–1378
2. Khan SA, Thomas HC, Davidson BR, Taylor-Robinson SD (2005) Cholangiocarcinoma. Lancet 366:1303–1314
3. Aljiffry M, Abdulelah A, Walsh M et al (2009) Evidence-based approach to cholangiocarcinoma: a systematic review of the current literature. J Am Coll Surg 208:134–147
4. Anderson CD, Pinson CW, Berlin J, Chari RS (2004) Diagnosis and treatment of cholangiocarcinoma. Oncologist 9:43–57
5. Lau WY, Lai EC (2009) The current role of radiofrequency ablation in the management of hepatocellular carcinoma: a systematic review. Ann Surg 249:20–25
6. Gillams AR, Lees WR (2009) Five-year survival in 309 patients with colorectal liver metastases treated with radiofrequency ablation. Eur Radiol 19:1206–1213
7. Slakey DP (2002) Radiofrequency ablation of recurrent cholangiocarcinoma. Am Surg 68:395–397
8. Chiou YY, Hwang JI, Chou YH et al (2005) Percutaneous ultrasound-guided radiofrequency ablation of intrahepatic cholangiocarcinoma. Kaohsiung J Med Sci 21:304–309
9. Zgodzinski W, Espat NJ (2005) Radiofrequency ablation for incidentally identified primary intrahepatic cholangiocarcinoma. World J Gastroenterol 11:5239–5240
10. Rai R, Manas D, Rose J (2005) Radiofrequency ablation of recurrent cholangiocarcinoma after orthotopic liver transplantation—a case report. World J Gastroenterol 11:612–613
11. Bale R, Widmann G (2007) Navigated CT-guided interventions. Minim Invasive Ther Allied Technol 16:196–204
12. Bale R, Widmann G, Stoffner DI (2010) Stereotaxy: breaking the limits of current radiofrequency ablation techniques. Eur J Radiol 75:32–36
13. Nevinny-Stickel M, Sweeney RA, Bale RJ et al (2004) Reproducibility of patient positioning for fractionated extracranial stereotactic radiotherapy using a double-vacuum technique. Strahlenther Onkol 180:117–122
14. Laeseke PF, Sampson LA, Haemmerich D et al (2006) Multiple-electrode radiofrequency ablation creates confluent areas of necrosis: in vivo porcine liver results. Radiology 241:116–124
15. Goldberg SN, Grassi CJ, Cardella JF et al (2005) Image-guided tumor ablation: standardization of terminology and reporting criteria. Radiology 235:728–739
16. Cunningham SC, Choti MA, Bellavance EC, Pawlik TM (2007) Palliation of hepatic tumors. Surg Oncol 16:277–291
17. Kim JH, Yoon HK, Sung KB et al (2008) Transcatheter arterial chemoembolization or chemoinfusion for unresectable intrahepatic cholangiocarcinoma: clinical efficacy and factors influencing outcomes. Cancer 113:1614–1622
18. Aliberti C, Benea G, Tilli M, Fiorentini G (2008) Chemoembolization (TACE) of unresectable intrahepatic cholangiocarcinoma with slow-release doxorubicin-eluting beads: preliminary results. Cardiovasc Intervent Radiol 31:883–888
19. Shiina S, Teratani T, Obi S et al (2005) A randomized controlled trial of radiofrequency ablation with ethanol injection for small hepatocellular carcinoma. Gastroenterology 129:122–130
20. Veltri A, Sacchetto P, Tosetti I et al (2008) Radiofrequency ablation of colorectal liver metastases: small size favorably predicts technique effectiveness and survival. Cardiovasc Intervent Radiol 31:948–956