Multipolar radiofrequency ablation of large hepatic metastases of endocrine tumours
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Radiofrequency ablation (RFA) is a reliable method of creating thermally induced coagulation necrosis. Local recurrence after RFA of hepatic metastases is directly dependent on tumour size related to the free margin of ablation. To produce larger coagulation volumes a bipolar radiofrequency device was developed that allows the simultaneous activation of three active needles. This technique was used at laparotomy in a patient with liver metastases of an endocrine tumour. Coagulation size up to 12 cm in diameter could be created. The postoperative recovery of the patient was uncomplicated. No local recurrence was seen after 13 months of follow-up with computed tomography scan. The use of simultaneously operated multiple radiofrequency electrodes in a multipolar mode expands the treatment options for patients with large and unresectable intrahepatic metastases.

Introduction
Despite advances in cancer therapy the treatment of liver metastases remains a challenge. Most patients are poor candidates for surgical resection, only 20% are suitable for surgery [1–3]. New minimally invasive techniques for the ablation of unresectable tumours have gained increased attention as effective treatment alternatives [4,5]. Radiofrequency ablation (RFA) is a promising method to ablate tumours focally. This technology involves the delivery of a radiofrequency current with a frequency of 375–500 kHz direct to tissue to cause resistive heating as a result of the movement and vibration of the ions. Once cells are heated above 50°C, cellular proteins become denaturized, lipid bilayers melt, DNA and RNA are destroyed, and irreversible cell death occurs [6]. The volume of the heated region depends on different factors such as applied energy, probe geometry, the duration of heat exposure, fluid content of tissue, blood perfusion rate, blood vessel density, and others [7]. Several strategies have been developed to improve tissue–energy interactions for thermal ablation therapy with the goal of increasing the target lesion. The first RFA systems with monopolar devices, which require grounding pads on the thighs in order to close the electrical circuit, resulted in lesion sizes up to 1.6 cm in diameter [8]. Technical developments with electrode design, optimized ablation algorithms, more powerful generators and bipolar techniques have resulted in more effective ablation with lesions up to 4 cm in diameter.

Bipolar technologies in which the radiofrequency current flows between the two electrodes at the tip of the probe are safe and gentle on the patient in contrast to monopolar radiofrequency applications in which current flows through the patient’s body. A new concept has recently been developed applying bipolar devices in a multipolar mode, i.e. all the possible electrode pairs are activated automatically one after the other for a short period of time (Fig. 1) [9]. In addition, larger coagulation volumes can be achieved with internally liquid-cooled bipolar applicators. Both strategies were used in combination to achieve even larger coagulation volumes. We report a case in which liver metastases were successfully ablated with the use of RFA in a multipolar mode.

Case report
A 63-year-old man with multiple endocrine neoplasia syndrome type 1 (MEN1) was referred to our hospital with asymptomatic unresectable liver metastases from a locally advanced endocrine pancreatic tumour. A computed tomography (CT) scan of the liver showed a metastasis in segment V of 3.6 cm in diameter with a satellite lesion of 1.0 cm in diameter, a metastasis in segment VII of 7.4 cm in diameter and seven small lesions of 1–2 cm in diameter diffusely distributed throughout the liver (Fig. 2a). RFA was performed at open abdominal surgery under ultrasound guidance. Ultrasound analysis during surgery revealed larger metastases; the metastasis in segment V was 4.0 cm in diameter and the metastasis in segment VII was 8.8 cm in diameter. The metastasis in
segment V was ablated using three bipolar coagulation electrodes simultaneously, 4 cm active length, 3 cm distance between probes in a triangular formation with a 140 W power setting and an applied energy of 150 kJ (34 min of exposure; ProSurge electrodes and LabPower generator; Celon AG Medical Instruments, Germany). At the beginning of the RFA procedure, portal and hepatic artery inflow occlusion (Pringle manoeuvre) was applied for 15 min. Track ablation was performed in the bipolar mode for each probe separately with 40 W of power and disabled resistance control.

Second, the metastasis in segment VII was ablated using four bipolar coagulation electrodes simultaneously, 4 cm active length, 3.5–4 cm distance between probes in a rectangular formation with a 180 W power setting and an applied energy of 180 kJ (33 min exposure). The Pringle manoeuvre was applied for 15 min during this application. Then all four electrodes were withdrawn 2 cm and another 130 kJ were administered at the same power setting and during another 15 min of the Pringle manoeuvre (23 min exposure). All four bipolar coagulation electrodes were removed using track ablation. Finally, two lesions in segment IV (both 2 cm in diameter) were ablated simultaneously with a single bipolar coagulation electrode in each lesion, 4 cm active length with 25 kJ each without the Pringle manoeuvre.

The patient withstood surgery well and was discharged on the eighth postoperative day. A CT scan one week after RFA demonstrated a sharply demarcated zone of coagulation necrosis of 7.3 cm in diameter in segment V and in segment VII a coagulation necrosis of 12 cm in diameter (Fig. 2b). A CT scan 13 months postoperatively demonstrated no local recurrence despite the appearance of several new small metastases (0–1 cm) that were seen throughout the liver.
Discussion

In recent years, local tumour ablation by RFA has become the most frequently used technique for local tumour destruction. An analysis of local recurrence after RFA of hepatic metastases revealed the tumour size to be a key factor [10,11]. For tumours less than 3 cm in diameter the post-RFA recurrence rate is 6.6%, whereas for tumours greater than 3 cm in diameter approximately 56% appear to recur [12]. As an alternative to RFA, other local ablation techniques such as interstitial laser coagulation are used to clear the liver from metastatic tumour lesions [13,14]. We have recently demonstrated that interstitial laser coagulation with the use of multiple water-cooled fibres applied simultaneously, together with hepatic inflow occlusion, can produce large lesions of up to 8.6 cm in diameter. In the case report presented here we demonstrate that next-generation bipolar RFA is able to produce even larger coagulation lesions up to 12.0 cm in diameter.

Local ablation is a well-established treatment for unresectable hepatocellular carcinomas [15] and liver metastases from colorectal carcinomas [16]. A few series have also shown good local tumour control, with a satisfactory duration effect on symptoms after RFA in hepatic metastases of endocrine tumours [17–19]. In metastases of endocrine tumours, the goal is to reduce the tumour mass with the preservation of surrounding normal hepatic tissue. There is a tendency to destroy metastases early in the course of disease, thereby postponing or eliminating the surgically untreatable stage. Patients with hepatic metastases of endocrine tumours treated with RFA showed symptom relief in 95%, with significant or complete symptom control in 80% for a mean of 10 months [17]. Even in patients with extrahepatic disease, liver metastases ablation may provide symptom relief [17]. The complication rate is 5–10% and the mortality rate is low [5,20]. Although we produced large lesions, the tumour lysis syndrome was not observed. The tumour lysis syndrome describes the metabolic derangements that occur upon cellular disruption leading to acute renal failure [21]. RFA as well as laser-induced thermotherapy cause heat fixation of the tissue [22] without the release of circulating cellular compounds. Therefore, local ablation techniques are especially suitable for repeated treatment in patients with hepatic metastases of endocrine tumours in which new metastases develop during follow-up.

Possible contraindications to this new RFA system are comparable to those of other ablative therapies, depending on the location of the tumour. Tumours adjacent to large vessels are difficult to treat, because the blood flow in the vessels cools the heating process, potentially leading to residual viable tumour cells against the blood vessel. Tumour adjacent to major branches of the portal vein are particularly problematical, because the ablation is likely to cause obstruction of the associated bile duct. Careful selection of patients is obviously required to avoid complications.

RFA may be applied through a percutaneous, laparotomic or laparoscopic route [23]. Mulier et al. [24] found in their meta-analysis that a surgical open approach yielded statistically significantly superior results compared with a percutaneous approach, independent of the size of the tumour. The surgical approach provides for bipolar RFA in a multipolar mode the best degree of freedom for inserting the electrodes.

The newly developed RFA system consisted of electrodes that were constructed using bipolar technology and energy applied in a multipolar mode. As energy is concentrated at the point of interest, the bipolar electrode produces larger and more homogeneous thermal lesions than the monopolar saline-enhanced electrode method [25,26]. In addition, relative contraindications to monopolar RFA, such as the presence of a pacemaker, surgical clips or other metallic structures are not valid any more, because the electrical circuit does not involve the whole body. Besides, skin burns caused by undersized grounding pads cannot occur.

Previous investigators have shown that the simultaneous operation of multiple applicator needles for tissue coagulation is significantly more effective compared with the same number of sequentially applied applicators with the same amount of energy [27]. Consequently, larger coagulation volumes can be achieved with multiple simultaneous electrodes. In the patient in this case report we used four bipolar electrodes simultaneously and withdrew them two times, which resulted in a coagulation lesion of 12 cm in diameter. Even larger coagulation lesions can be thus achieved by the repositioning of the electrodes along their axis.

The size of the coagulation volume depends not only on the set power, but also on the delivered energy and therefore on the duration of the application. Higher power levels quickly induce evaporation of the cellular water content in the immediate vicinity of the probe, and thus lead to desiccation of this region of tissue. The rise in tissue resistance impedes the further input of energy and any increase in the coagulation volume. If lower power is applied, the desiccation process takes place later. A greater amount of energy can be applied to the tissue and a larger coagulation volume can be achieved. This process is supported by the additional effect of thermal conductivity.

In conclusion, bipolar RFA in a multipolar mode is an exclusive technique able to produce large coagulation lesions in patients with intrahepatic metastases.
Acknowledgement
The authors would like to thank A. Roggan for his technical support and his comments on this manuscript.

Conflict of interest
None of the authors has any economic, political or any other conflict of interest in the work.

Authors’ contributions
L.M. Veenendaal and R. van Hillegersberg were responsible for the conception, drafting and final approval of this article. I.H.M. Borel Rinkes contributed to the conception, revising and final approval of this article.

References
7 Pereira PL, Trubenbach J, Schmidt D. Radiofrequency ablation: basic principles, techniques and challenges. Rofo 2003; 175:20–27.