RADIOFREQUENCY ABLATION OF LARGE SIZE LIVER TUMOURS USING NOVEL PLAN-PARALLEL EXPANDABLE BIPOLAR ELECTRODES: INITIAL CLINICAL EXPERIENCE

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ABSTRACT

Objective: Although radiofrequency ablation (RFA) is a promising method for local treatment of liver malignancies, with conventional monopolar systems recurrence rates for large size tumours (≥ 3.5cm) remain high. The objective of this study was to evaluate the safety, feasibility and local effectiveness of a novel bipolar plan-parallel expandable system for these larger tumours.

Materials & Methods: Eight consecutive patients with either unresectable colorectal liver metastases (CRLM) (6 patients), carcinoid liver metastases (1 patient) and hepatocellular carcinoma (HCC) of ≥ 3.5cm were treated with bipolar RFA during laparotomy with ultrasound guidance. Early and late, major and minor complications were recorded. Local success was determined on 3-8 months follow-up CT scans of the upper abdomen.

Results: Nine CRLM, one carcinoid liver metastases and one HCC (3.5–6.6cm) were ablated with bipolar RFA. Average ablation time was 16 minutes (range 6-29 min.). Two patients developed a large liver abscess which required re-laparotomy. In both cases bowel surgery during the same session probably caused bacterial spill. There were no mortalities. The patients were released from hospital between 5 and 29 days after the procedure (median 12 days). The 6-12 months follow-up PET-CT scans showed signs for marginal RFA-site tumour recurrence in two patients with CRLM (2/11 lesions).

Conclusions: Preliminary results suggest bipolar RFA to be a relatively safe, fast and feasible technique which seems to improve local control for large size hepatic tumour ablations.
INTRODUCTION

Currently, the most widely used tumour ablative technique for treatment of liver malignancies is radiofrequency ablation (RFA). In patients with unresectable hepatic tumours RFA has proven to be safe and feasible. Furthermore, RFA has been suggested to improve both short and long term survival. Unfortunately, 8-40% of treated patients have local RFA-site tumour recurrence, especially in tumours ≥3.5cm in diameter.

In conventional “monopolar” RFA an active electrode is placed within the tumour. To complete an electrical circuit grounding pads attached to the patient’s thighs function as neutral electrodes. An alternating current between these electrodes, which flows through the body of the patient, induces conductive heating around the active electrode with temperatures 50-100°C leading to tumour cell death and thermal coagulation necrosis. Besides possible skin burns and collateral damage by uncontrolled electrical current pads, the most important limitation of this technique is the poor local effectiveness in large size tumours. Although electrodes such as expandable electrodes, multi-probe arrays (cluster electrode) and cooled-tip electrodes (to avoid carbonization around the electrode) have shown to increase the sizes of the ablation zone, many overlapping ablations are often necessary for tumour sizes ≥3.5cm especially if you want tumour free margins of at least one centimetre to be ablated. Furthermore, it is very difficult and often even impossible to determine regions of remaining vital tumour tissue which need to be treated with overlapping ablations, on either ultrasound or CT directly after the first ablation.

Novel “bipolar” radiofrequency systems in which both electrodes are located on one application instrument separated by an insulator have been recently developed to overcome these problems of monopolar RFA, and have already demonstrated their safety and effectiveness in experimental studies. A multipolar RFA concept which allows up to three radiofrequency probes to be placed simultaneously within the tumour has also shown to be feasible.

The aim of the present study was to demonstrate the first experiences with a new bipolar expandable system in which two separate electrodes are placed not within the tumour tissue but marginal to the tumour, plan-parallel and opposed to each other (InCircle™, RFA Medical Inc., Fremont, USA) and to evaluate safety, feasibility and effectiveness.
MATERIALS & METHODS

Patient selection:
Between November 2007 and November 2008 eight consecutive patients with 11 large size liver malignancies were considered suitable for treatment with the bipolar RFA system (InCircle, RFA Medical Inc., Fremont, USA) (Table 1): 9 colorectal liver metastases (CRLM), 1 large size carcinoid liver metastasis and one hepatocellular carcinoma (HCC) ≥3.5cm. Inclusion criteria for performing bipolar RFA were (1) tumour diameter 3.5 – 8cm; (2) no evidence of extra-hepatic metastases; (3) complete ablation of all liver metastases technically possible; (4) functional or technical irresectability of the tumour(s). The definitive decision against resection was made intra-operatively. All patients were treated during laparotomy under general anaesthesia using ultrasound guidance. All tumours present in a patient were treated in one session. Additional irresectable tumours <3.5cm were treated with conventional monopolar RFA (LeVeen umbrella electrode and RF3000 generator, Boston Scientific, USA). The study was approved by the institutional ethical committee and all patients gave written informed consent. The procedures carried out on humans followed were in accordance with the ethical standards of the world medical association (Declaration of Helsinki).

RFA procedure:
An epigastric transverse laparotomy was performed for optimal liver exposure. The abdominal cavity was explored in order to exclude extra-hepatic tumour manifestations.

Based upon pre- and postcontrast (2.4ml Sonovue iv, Altana Pharma, Konstanz, Germany) intraoperative ultrasound (Prosound Alpha10; 10.0 MHz linear intraoperative probe and 5.0/1.25 MHz convex probe, Aloka, Tokyo, Japan) a decision for bipolar RFA was made in case of irresectable metastases of 3.5 – 8cm. At the start of the procedure, the expandable needle electrodes were placed one at a time, parallel to each other on two opposite sides directly adjacent to the centrally positioned tumour by an experienced interventional radiologist in close collaboration with the surgical oncologist performing the laparotomy. The presented bipolar unit does not require the use of grounding pads. The electrodes were connected to a well known and compatible commercially available RF generator (RF3000, Boston Scientific, USA). Based upon the shape and size of the tumour two somewhat differently shaped electrodes were used: the “rectangle” expandable electrode (4.0, 5.0 or 7.0cm with 14 gauge trocar; InCircle, RFA Medical Inc., Fremont, USA) which creates cubic, box-shaped or at least parallelogram-shaped ablation zones and the “ellipsoid” expandable electrode (5.0 or 7.0cm with ellipsoid trocar; InCircle, RFA Medical Inc., Fremont, USA) which consist of two triangular-prism shaped electrodes placed anti-parallel to each other,
Table 1 Overview of patients treated with bipolar RFA: tumour and procedure characteristics, outcome and complications

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex, age</th>
<th>Primary tumour</th>
<th>Lesion</th>
<th>Segment</th>
<th>Size</th>
<th>Position</th>
<th>Approximant large vessel</th>
<th>Number of needle (re)-positionings</th>
<th>Needle shape</th>
<th>Needle size (cm)</th>
<th>Ablation size (cm)</th>
<th>Number of local recurrence</th>
<th>Follow-up (month)</th>
<th>Complications</th>
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<td>Rectangle</td>
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<td>Colon</td>
<td>VIII</td>
<td>2</td>
<td>4.1</td>
<td>Superficial</td>
<td>−</td>
<td>1</td>
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<td>3.7</td>
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<td>2</td>
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a Before primary (at least two increases in tissue impedance (roll-off) with an interablation delay of 30 s and a fully hyperechoic tumour including a tumour-free margin of at least one centimetre on intraoperative ultrasound) and secondary endpoints (absence of enhancement of tumour tissue on contrast-enhanced intraoperative ultrasound) were reached.

b Maximum non-enhancing ablation zone diameter on 2–4 week post-procedure CT scan of the upper abdomen.

c Based upon the presence/absence of either lesion growth between 2–4 weeks post-procedure versus 3–6 month follow-up liver CT scans, focal abnormalities at the margin of the post-RFA lesions and/or pathological tracer uptake on F18-FDG PET.
therefore surrounding the lesion without traversing through tumour tissue (Fig. 1 and Fig. 2). In all cases the bridge connector between the two electrodes was removed before needle placement. The electrodes were manually placed into opposing positions, directly adjacent to the tumour, one by one. The rationale for this was the ability to create a more exact ablation zone for every tumour shape and the fact that the bridge connector fixes the electrodes at 5cm distance which is too little to create tumour free ablation margins of at least one centimetre in tumours $\geq 3.5$cm. For both the rectangle and ellipsoid shaped electrodes we used the same ablation protocol: starting with a generator power of 100Watts for 5min we increased the power to 135 Watts after 5min. Primary endpoints for a technically successful ablation were at least two increases in tissue impedance (roll-off) with an interablation delay of 30 seconds and a fully hyperechoic ablation zone including a tumour-free margin of at least one centimetre on intraoperative ultrasound (IOUS). If necessary the needle electrodes were repositioned for one or more overlapping ablations. The final endpoint of a successful ablation was the absence of enhancement of tumour tissue on contrast-enhanced intraoperative ultrasound (CE-IOUS).

Fig. 1: Figure showing both the “rectangle” expandable electrode (4.0, 5.0 and 7.0cm with 14 gauge trocar) which creates cubic, box-shaped or at least parallelogram-shaped ablation zones (A) and the “ellipsoid” expandable electrode (5.0 or 7.0cm with ellipsoid trocar) which consists of two triangular-prism shaped electrodes placed plan-parallel to each other, therefore surrounding the lesion without traversing through tumour tissue (B).

Ablation time, delivered energy at the time of roll-off and the number of electrode repositionings were noted. Early and late, major and minor, direct and indirect procedure related complications, according to the classification by Rhim et al., were carefully assessed as was the length of hospital stay. Local success was determined comparing
a 1-4 weeks post-procedure CT with a six month follow-up F18-FDG PET-CT scan. An experienced abdominal radiologist and nuclear physician reviewed the examination for the presence or absence of local RFA-site recurrence in consensus with the interventional radiologist who performed the procedure.

RESULTS

Technical results:
In all patients the bipolar RF ablation was considered technically successful based upon the primary and final endpoints (Table 1). Average ablation time was 16 minutes (range 8-29 minutes). The power at time of primary roll-off was 135W in all cases and 118W on average for the secondary roll-off (range 100-135W). In 5/9 tumours the electrodes were re-positioned once and in 2/9 tumours the electrodes were re-positioned twice before reaching an adequate hyperechoic and non-enhancing ablation zone. In one case the post-procedural CE-IOUS clearly showed a central artery coursing through the tumour with surrounding enhancement probably caused by the so called heat-sink-effect: continuous cooling of tumour tissue during the ablation caused by large vessels coursing through or approximate to the ablation zone. After re-ablation the artery was still patent but the adjacent tumour tissue did not show any enhancement anymore [Fig. 2].

Complications:
Two patients developed a large liver abscess. In both cases a surgical procedure of the bowel during the same session probably caused bacterial spill and contamination of the liver RFA-site. In one of these two patients (Subject 4) RFA was performed in a single session together with colonic reconnection surgery and left portal vein occlusion to enable a possible future extended hemihepatectomy. In the other patient (Subject 6) the intestinal primary carcinoid tumour was excised in the same session with liver RFA. Surgical re-laparotomy with abscess drainage and excision of the infected and necrotic liver tissue was performed in both cases. One patient (Subject 3) developed a large asymptomatic biloma [Fig. 3]. A fourth patient (Subject 5) with dyspnoea had subsegmental pulmonary embolism. There were no mortalities. The patients were released from hospital between 5 and 29 days after the procedure (median 12 days).
Fig. 2: Trans-axial PET-CT slices of a simple hepatic cyst (asterisk) and a 4.0cm CRLM (arrows), before (A) and after RFA (C). IOUS before RFA (D), during RFA (E-H) and post-procedural CE-IOUS before and after re-ablation (I,J) showing a central artery coursing through the tumour (arrowhead) with some residual surrounding tumour tissue enhancement probably caused by the so called heat-sink-effect (white box): continuous cooling of tumour tissue during the ablation caused by large vessels coursing through or approximate to the ablation zone.

Local control:
Two patients (Subject 3 and 5) showed marginal RFA-site tumour recurrence, 3-6 months after the procedure. In one of these patients recurrence was present marginal to 2/3 post-RFA lesions (Subject 3) [Fig. 3]. Both patients were recently re-treated with conventional monopolar RFA for the recurrence. In all other patients the follow-up PET-CT scans of the upper abdomen after at least 6 months did not reveal any signs for marginal recurrence such as PET avidity, tumour growth or focal abnormalities at the margin of the post-RFA lesions. Therefore local success was considered 81.8% (9/11 lesions).
DISCUSSION

The first available single needle monopolar electrodes generated cylindrical shape coagulation volumes with a diameter of only 1.6cm². To create larger volumes of coagulation necrosis several systems were developed, many of which are now commercially available. The most well known systems nowadays use expandable electrodes and/or internal applicator cooling or perfusion electrodes. Expandable monopolar RF applicators featuring an umbrella-shaped array generates more spherical-shaped tumours. Internal and/or external cooling of the RF probe by circulating saline solution removes heat closest to the electrode and prevents early tissue charring. A greater deposition of energy can thereby be achieved. Perfusion electrodes using fluids other than saline such as acetic acid or alcohol have also shown to enable ablation of larger volumes. However, the unpredictable fluid distribution after injection remains a major drawback of this technique. In general, monopolar RF systems require the use of larger neutral electrodes to close the electric circuit, which are usually attached to the patient’s thighs. Due to the RF energy passing through the body, a body temperature increase can be induced. Furthermore, skin burns may occur because of a mismatch between applied energy and the size of the neutral electrodes. The use of monopolar multiprobe arrays led to larger coagulation volumes but requires the correct positioning of all probes. Moreover, the use of multiple RF probes is associated with multiple punctures of the liver, which could increase the risk of complications. Bipolar RFA using single needle systems (either non-expandable or expandable with two electrodes on one needle separated by an insulator) and multipolar non-expandable cluster electrode systems have recently proven to create larger ablation zones. Furthermore, the Pringle manoeuvre in which both the hepatic artery and the portal vein are temporarily
occluded has shown up to a fivefold volume increase of the ablation zone due to a diminished heat sink effect. For the percutaneous approach de Baere showed a local control for tumours smaller than 35mm that abut vessels 4mm or larger, equivalent to tumour control of the same-size tumours away from vessels using a temporary portal and/or hepatic vein balloon occlusion. However, balloon occlusion did not seem to affect the results of RF ablation for tumours 35mm or larger.

The present study is the first to report clinical experiences using a novel commercially available bipolar RFA system. It shows the feasibility to create larger ablation zones larger than 10cm using a relatively safe and fast bipolar system with an improved local control for liver tumours ≥3.5cm. Skin burns on patient’s thighs or collateral damages by uncontrolled electrical current paths will not occur since grounding pads are unnecessary. Furthermore, the number of necessary electrode repositionings for large hepatic tumours will decrease compared to monopolar RFA. The bipolar electrodes eliminate the need for physical contact with the centre of the target area as is required with monopolar systems. The potential of tumour seeding during placement or retraction of the device therefore will decrease. However, the system also has some important disadvantages. First, the large needle thickness of at least 14 gauge for the rectangle probe and even more for the ellipsoid shaped trocar increases the risk of haemorrhage and bile duct trauma. This makes a percutaneous approach more dangerous compared to smaller gauge monopolar systems. Furthermore, ultrasound guided needle placement is more difficult since the electrodes are not placed within the centre of the tumour but into adjacent normal appearing liver tissue. Although we did not use track ablation, the manufacturer recently described the possibility of track ablation by applying 50 Watts of RF energy while the device is slowly removed from the tissue. The system, in our opinion, demands an operator with at least a large expertise in ultrasound guided interventions and a hepatobiliary surgeon who can intervene directly in case of needle tract haemorrhage after needle retraction. We recommend not combining these large size liver RF ablations with bowel surgery in the same session, because of the risk for liver abscess formation.

To conclude the preliminary results suggest bipolar RFA to be a relatively safe, fast and feasible technique which seems to improve local control for large size hepatic tumour ablations. Future hardware developments should try to decrease needle size-thickness and enable track ablation, which would make a percutaneous approach with the presented bipolar system less invasive and therefore more safe and feasible.
REFERENCES

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