BIPOLAR RADIOFREQUENCY ABLATION FOR SYMPTOMATIC GIANT (>10 CM) HEPATIC CAVERNOUS HAEMANGIOMAS: INITIAL CLINICAL EXPERIENCE

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ABSTRACT

Aim. To describe initial clinical experience with bipolar radiofrequency ablation (RFA) for symptomatic giant hepatic haemangiomas.

Materials and methods. Four consecutive patients with a large-volume, symptomatic hepatic cavernous haemangioma of >10 cm were treated with bipolar RFA during laparotomy with ultrasound guidance. Complications were carefully noted. Clinical and radiological effectiveness were evaluated comparing baseline with 3 and 6 months follow-up of symptom assessments and upper abdominal magnetic resonance imaging (MRI) or computed tomography (CT).

Results. RFA was successfully performed for all four giant haemangiomas. No major complications were observed. Peri-procedural shrinking was remarkable and intermediate-term volume reduction ranged from 58-92% after 6 months. Symptom relief after 6 months was complete in two patients and considerable in the other two.

Conclusion. Preliminary results suggest intra-operative bipolar RFA to be a safe, feasible, and effective technique for treatment of giant symptomatic hepatic cavernous haemangiomas.
INTRODUCTION

Haemangioma is the most common benign solid liver tumour. The lesions, which may be single or multiple, are thought to represent vascular malformations that enlarge by means of ectasia rather than neoplastic growth. Lesions >4 cm have been referred to as giant haemangiomas. Although most haemangiomas are asymptomatic and can be managed safely with observation alone, larger lesions may produce a variety of symptoms and signs, including pain (abdominal, back, or shoulder), fullness, early satiety, nausea, vomiting, and fever. Kasabach-Merritt syndrome, with thrombocytopenia secondary to platelet trapping within the haemangioma, and spontaneous haemorrhage are rare but may occur and treatment may be indicated. The primary treatment is surgical resection, but hepatic arterial ligation, transarterial embolization, radiation therapy, and the use of a vascular endothelial growth factor (VEGF) inhibitor have also been reported. Unfortunately, surgical resection is associated with morbidity up to 27% and low risk of mortality.

Radiofrequency ablation (RFA) has shown promising results in the recent literature for treatment of malignant lesions. It is a procedure with a relatively low complication rate (less than 10%, mostly minor complications, often unnecessary to treat) and a very small risk of death (<1%), notably when compared to resection. It is proven to be a safe and effective treatment for primary and metastatic neoplasms of the liver. Little has been published on the treatment of benign liver tumours such as haemangiomas with RFA; most data are based on case reports from groups using monopolar (single or multiple electrode) devices creating ablation zones up to 5 cm, which may be too small to treat haemangiomas large enough to cause symptoms. Only two studies (one case report and one larger series in which only five lesions exceeded 10 cm) describe ablation of haemangiomas larger than 10 cm using multiple overlapping monopolar ablations. The recent introduction of a novel bipolar RFA system enables high-volume ablations with coagulation zones up to 10 cm. The objective of the present study was to evaluate the safety, feasibility, and local effectiveness of bipolar “InCircle” RFA for these large (>10 cm), symptomatic tumours.

MATERIALS AND METHODS

Patient selection

Between September 2009 and May 2011, four consecutive patients with large size hepatic haemangiomas (>10 cm) were treated with bipolar RFA (InCircle, RFA Medical, Fremont, California USA). Inclusion criteria for performing bipolar RFA were
(1) definite diagnosis of a giant cavernous haemangioma (GCH) >10 cm based on the typical enhancement pattern on contrast-enhanced multiphase computed tomography (CT) or magnetic resonance imaging (MRI); (2) clinical symptoms typically caused by the giant haemangioma present for at least 1 year, excluding the presence of other hepatobiliary or gastrointestinal disorders on ultrasound, MRI, or CT examinations and gastroduodenoscopy. The study and procedures were approved by the local ethical committee. Patients gave written informed consent and all procedures carried out were in accordance with the ethical standards of the world medical association (Declaration of Helsinki).

**RFA procedure**

Under general anaesthesia an epigastric transverse laparotomy was performed for optimal liver exposure. Based upon intra-operative ultrasound (IOUS; Prosound Alpha10; 10.0 MHz linear intra-operative probe and 5/1.25 MHz convex probe, Aloka, Tokyo, Japan) the definite decision against surgical resection and for RFA was made. The technique of the InCircle bipolar RFA unit (7 cm needles with 8x14 gauge trocar; InCircle) has been extensively described (for large malignant liver tumours) in a previous report. After removing the bridge connector (Fig 1) the expandable needle electrodes were placed and deployed parallel to each other within the margins or directly adjacent to the GCH, at approximately 7 cm distance, by an experienced interventional radiologist in close collaboration with the surgeon performing the laparotomy. To enhance shrinking the electrodes were manually pressed towards each other, squeezing the GCH during ablation. The electrodes were connected to a compatible and commercially available RF generator (RF3000, Boston Scientific, Natick, Massachusetts, USA). Generator power was set at 100 W for 5 min and increased to 135 W after 5 min. Primary endpoints for a technically successful ablation were at least two increases in tissue impedance (roll-off) with an inter-ablation delay of 30 s or a fully hyperechoic ablation zone on IOUS and an ablation time of at least 20 min. If necessary, the needle electrodes were repositioned for one or more overlapping ablations. 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.
Radiological and clinical effectiveness

Radiological effectiveness (considerable volume reduction of >50%) was determined comparing a pre-procedural contrast-enhanced breath-hold MRI or CT examination with similar 3 and 6 month follow-up examinations. Tumour volume was calculated using the perimeter calliper method (drawing perimeters around the haemangioma on every CT section and multiplying the automatically calculated lesion-area by the reconstruction increment; lesion-volume is then defined as the sum of all section-volumes).

To assess clinical effectiveness, a single visual analogue symptom (VAS) score sheet (ranging from 0-10) for pain (and/or other debilitating symptoms) was used at baseline, and at 3 and 6-months after RFA.
Case 1
A 42-year-old woman presented with no relevant medical history and chronic but progressive complaint of abdominal pain and dyspepsia. Ultrasound revealed a 14.5 cm large lesion in the left liver lobe. There were two additional hepatic lesions: one in segment IV, with a maximum diameter of 1 cm and one in segment VII with a maximum diameter of 2 cm. All three lesions showed the typical characteristics of haemangioma on MRI (Fig 2). Preoperative antibiotics were given. At surgery, the tumour was considered unresectable because of its extent into the caudate lobe and its close relation to the inferior vena cava and hilar structures. Debulking bipolar RFA (not treating the most central part of the lesion) was performed with the “rectangle” expandable electrode with one repositioning. A remarkable shrinking was observed during ablation (IOUS-based lesion length decreased to 8.5 cm). Baseline, 3, and 6 month follow-up tumour volumes were 793, 106, and 106 cm³ (volume reduction of 87%). Also, there was reduced mass effect on the intrahepatic inferior vena cava (Fig 2). There were no direct procedure-related complications. Total length of hospital stay was 4 days. The patient was free from abdominal pain and discomfort after 3 and 6 months (VAS scores 7, 0, and 0, respectively).

![Figure 2. Female patient with a symptomatic 14.5 cm giant cavernous haemangioma (white arrows) in the left liver lobe before (a) and after (b) treatment with bipolar RFA (avoiding the most central part of the lesion). Tumour volume decreased by 87% and the patient was free from symptoms after 6 months.](image)

Case 2
A 53-year-old woman presented with chronic but slowly progressive stabbing pain in the right upper abdomen, night sweats, fever, weight loss, and diarrhoea. Ultrasound revealed a giant haemangioma later confirmed on MRI (Fig 3). The lesion had a maximum diameter of 10.6 cm. No other lesion or disease was found. Preoperative
antibiotics were given. At surgery the large lesion was treated with bipolar RFA using the “ellipsoid” expandable electrode. After one reposition, sonographically complete ablation (lesion fully hyperechoic) was achieved with a remarkable shrinking during ablation (IOUS-based lesion length decreased to 5.9 cm). Baseline, 3, and 6 month follow-up tumour volumes were 370, 62, and 30 cm$^3$ (volume reduction of 92%). The patient developed self-limiting postprocedural pain lasting for 6 days. Length of hospital-stay was 9 days. Clinically, haemangioma-induced symptoms were slightly decreased after 3 months and considerably after 6 months (VAS scores 9, 4, and 2, respectively). She also clearly gained weight, although she continued to have diarrhoea.

![Figure 3](image-url)

**Figure 3.** Another female patient with a symptomatic 10.6 cm giant cavernous haemangioma (white arrows) in the right liver lobe before (a) and 6 months after (b) bipolar RFA. Tumour volume decreased by 92% and the symptoms were considerably diminished.

**Case 3**

A 44-year-old woman presented with long-lasting, slowly progressive, and invalidating pain in the upper abdomen, right flank, and back with nausea, not being able to walk or cycle even minor distances. Ultrasound and subsequent CT revealed a giant haemangioma of 12.9 cm involving segments V, VI, and VII of the right liver lobe (Fig 4). Debulking bipolar RFA (avoiding the most central part of the lesion) was performed with the “rectangle” expandable electrode followed by three additional 5 cm monopolar RFAs for non-hyperechoic regions of the tumour (Fig 1a). Again, a remarkable shrinking was observed during ablation (Fig 1b; IOUS-based lesion length decreased to 7 cm). After the procedure some macroscopic haematuria was present lasting for 24 h, which may have been caused by collateral damage to the adjacent right-sided kidney or by an inserted urinary catheter. An ultrasound examination did not reveal any
renal abnormalities. Total length of hospital stay was 5 days. Baseline, 3, and 6 month follow-up tumour volumes were 820, 180, and 180 cm³ (volume reduction of 78%). The patient was completely free from abdominal pain and nausea after 3 and 6 months (VAS scores 8, 0, and 0, respectively).

Figure 4. A third female patient with a symptomatic 12.9 cm giant cavernous haemangioma in the right liver lobe (white arrows) before (a) and 6 months after (b) bipolar RFA. Tumour volume decreased by 78% with full symptom relief after 6 months.

Case 4
A 40-year-old female presented with slowly progressive and disabling pain and discomfort in the right flank and back. Ultrasound and subsequent CT revealed a giant haemangioma of 11.4 cm involving segments VI, VII, and VIII of the right liver lobe (Fig 5). Bipolar RFA was performed with the “rectangle” expandable electrode (IOUS-based lesion length decreased to 8.6 cm). Total length of hospital stay was 3 days. Baseline, 3, and 6 month follow-up tumour volumes were 820, 382, and 344 cm³ (volume reduction of 58%). After 3 and 6 months the pain had largely disappeared, although some discomfort remained (VAS scores 7, 4, and 3, respectively).
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Figure 5. A fourth female patient with a symptomatic 11.4 cm giant cavernous haemangioma in the right liver lobe before (a) and 6 months after (b) bipolar RFA. Tumour volume decreased by 58% with considerable symptom relief after 6 months.

DISCUSSION

Cavernous haemangiomas of the liver are benign, usually small (<4 cm) lesions, but when they are larger than 4 cm in diameter they are classified as giant cavernous haemangiomas.

They arise from the mesoderm and are composed of blood-filled cavernous spaces of varying size, lined with a single layer of flat endothelial cells, which may be separated by fibrous septa of variable thickness. In most cases they are accurately diagnosed by non-invasive radiological imaging techniques.

Giant haemangiomas can be symptomatic and present with pain (abdominal, back, or shoulder), fullness, early satiety, nausea, vomiting, and fever. Severe complications such as abscess formation, heart failure, jaundice, Kasabach-Merritt syndrome, and rupture (either after biopsy, trauma, or spontaneous) are rare. Interventional procedures should be performed only in cases of symptomatic haemangiomas: haemangiomas that grow progressively or haemangiomas at high risk of bleeding. In symptomatic patients, the causal relation of the haemangioma for the development of symptoms must be established. In the authors’ service, typical symptoms that have been present for at least 1 year together with the absence of any other hepatobiliary or upper gastrointestinal abnormality on ultrasound, upper abdominal contrast-enhanced CT, and gastro-duodenoscopy, are considered affirmative to appoint the giant haemangioma as the most likely cause.

To the authors’ knowledge, this is the third report describing RFA for lesions >10 cm and the first using bipolar RFA. The observed peri-procedural shrinking was highly remarkable in all cases, as was the radiological and 6 month clinical response.
The mechanism of action of RFA in treating hepatic haemangiomas has yet to be determined, but it may involve its thrombogenic effect, as damage to the layer of the endothelial lining in the vascular structures promotes thrombosis. The fact that haemangiomas have a non-solid nature and contain a lot of fluid is probably the reason for the enormous size reduction of the tumour during “squeezed” ablation.

One important disadvantage of the bipolar RF system used is the needle-electrode diameter (asymmetrical axis of 8x14 gauge), which makes an even less invasive percutaneous approach with this system relatively unsafe. For this reason the authors preferred an open approach, despite the formation of a laparotomy scar and possible consequent complications involved with these kinds of open procedures. Although surgical resection has long represented the primary treatment modality for symptomatic hepatic haemangiomas, in the authors’ opinion a natural shift to treatment with the less invasive RFA for difficult or large resections seems only logical. Especially as the main argument against resection is the need to submit a patient with a benign disease to such major surgery.

Over the last decades several therapeutic options for the treatment of symptomatic haemangiomas are described. Hepatic arterial ligation (of the proper, left, or right hepatic artery) has long represented a reasonably effective alternative therapy for lesions judged hazardous to resect, which seems logical as its blood supply is predominantly derived from the hepatic artery. Radiation therapy provides partial reduction in haemangioma size and relief of symptoms, but has certain risks including radiation hepatitis, veno-occlusive disease, and the development of hepatomas. Transarterial embolization (TAE) has also been reported to be an effective treatment of symptomatic haemangiomas, but may result in severe complications including ectopic embolizations and destructive biliary damage. Furthermore, described size-decrease and symptom relief are modest at most. According to one report, trans-arterial embolization is only effective if the haemangioma is a lesion with a clear (macroscopically visible) arterial blood supply. If not, this procedure can lead to the aggravation of symptoms. The trans-arterial embolization may be associated with KasabacheMerritt syndrome. Use of the VEGF-inhibitor, bevacizumab, is incidentally described for enlarging lesions. High VEGF-expression leads to increased angiogenic activity in cavernous haemangiomia endothelial cells. The use of specific antibodies directed against VEGF abolishes this vascular endothelial growth-promoting activity in vitro.

To conclude, bipolar RFA seems to represent a promising technique for the treatment of symptomatic large-volume giant haemangiomas of the liver and should be considered an alternative to surgical resection.
REFERENCES


