Radiofrequency for the Treatment of Liver Tumours

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Introduction

Resection should still be considered the gold standard for many liver tumours. However, resection is not possible because of the ill-located position of the tumour(s) or widespread extension of the lesions within the liver. In a well-defined subgroup of these patients, local tumour ablative procedures may be indicated. During the past few years, techniques on tumour ablation by radiofrequency (RFA) have evolved significantly. This development has resulted in an increasing use of RFA over Europe. Although the technique has been proven to be safe, the precise impact on survival of RFA therapy in patients with different types of liver tumours is still unclear. This article will give a global overview of the results thus far.

Technique and Devices

The basic idea behind local tumour ablation is to selectively destruct tumour tissue (including a rim of normal tissue around the tumour) without significant damage to vascular structures in the remaining liver and hence consequential loss of large areas of normal liver tissue [1]. During RFA a small electrode is placed within the tumour to deliver RFA energy to the tissue. RFA current generates ionic agitation, which is converted into frictional heat. As tissue temperatures increase between 60 and 100°C, there is insta-
taneous induction of irreversible cellular damage with breakdown of proteins and cell membranes referred to as coagulation necrosis.

Several electrode designs are available. One principle is based on water-cooled electrodes and is available as one stiff electrode of 19G or three parallel electrodes forming a cluster needle (Tyco Healthcare, Burlington, Mass., USA). Two other systems show an expandable design. The expandable electrodes are introduced collapsed within a hollow needle (14–15 G). Once positioned within the tumour, multiple prongs are deployed resulting in a final umbrella-like configuration (RITA Medical Systems, Fremont, Calif., USA and Radiotherapeutics, Natick, Mass., USA). A fourth system, using stiff needles, combines high-frequency energy with needle fluid perfusion (Berchtold, Tuttlingen, Germany). A fifth system uses several different shapes of electrodes all with a bent thermistor to monitor tissue temperature (Mirax, Medimex, Hamburg, Germany). In a recent study, Mulier et al. [2] analyzed the performance of several probes. They concluded that the size and geometry of the hepatic lesions induced by the different devices was quite variable. Moreover, with normal blood flow, the diameter of the lesions was often smaller than suggested and lesions were rarely perfect spheres but either ellipses or flattened spheres. Distortion of RFA lesions nearby vessels was common but could partially be prevented by a Pringle manoeuvre. From their data it can be stated that physicians should be well familiar with the accurate size and geometry of the RFA lesions in order to perform optimal tumour destruction.

Approach

In the beginning, RFA ablation was positioned within the field of radiology. Due to the small diameter of the electrodes, the technique was well suited for percutaneous treatment of liver lesions. Later on, surgeons started to use RFA in order to increase the number of patients who might benefit from liver resection. In these cases, RFA was used in addition to resection in order to treat some unresectable lesions that are left over after resection of the main tumour mass. In addition, a laparoscopic route for RFA was introduced [3–14].

Generally the approach used is dependent on the profession of the clinician. The percutaneous approach is least invasive, carries a low morbidity and can be performed as an outpatient procedure under conscious sedation or general anaesthesia dependent on the extent of disease [15]. In contrast, laparoscopy with supplementary laparoscopic ultrasonography will give additional information on small and superficial liver lesions as well as on extrahepatic disease. For example, in a study by Rahusen et al. [16], 25% of patients with colorectal liver metastases showed additional findings to conventional work-up during laparoscopy and laparoscopic ultrasound. Moreover, the laparoscopic approach can be advantageous when tumour is adherent to structures that can be damaged by thermal ablation such as colon and stomach. Laparotomy is indicated in those cases where resection is the principal way of treatment and some additional unresectable lesions are suited for RFA. Moreover, the approach may be advantageous in those lesions situated at the dome of the liver. No reliable data are available comparing these three approaches directly. However, in a recent literature review by Mulier et al. [17], a local recurrence rate of 3,224 liver tumours was analyzed after RFA treatment. Amongst others the series comprised hepatocellular carcinoma (2,369 lesions), unspecified lesions (1,046) and colon cancer metastases (763 lesions). In a multivariate analysis, both size ($p < 0.001$) and approach ($p = 0.005$) had a significant and independent impact on the local recurrence rate (table 1). The authors concluded that RFA by laparoscopy or laparotomy results in superior local control, independent of tumour size. According to their opinion, the short-term benefit of less invasiveness for the percutaneous route does not outweigh the higher risk on local recurrence. The surgical route either by laparoscopy or laparotomy should be the first choice for any patient who can tolerate surgery. Moreover, they concluded that especially large lesions, requiring multiple probe insertions with overlapping treatment zones, are often insufficiently treated resulting in a high local recurrence rate.

<table>
<thead>
<tr>
<th>Lesion size</th>
<th>Percutaneous</th>
<th>Laparoscopy/laparotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 cm</td>
<td>16%</td>
<td>4%</td>
</tr>
<tr>
<td>3–5 cm</td>
<td>25.9%</td>
<td>21.7%</td>
</tr>
<tr>
<td>&gt;5 cm</td>
<td>60.0%</td>
<td>50%</td>
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Table 1. Approach of RFA and local recurrence [data taken from 17]

Monitoring Radiofrequency

During the Procedure

Online monitoring of the ablative procedure is crucial in order to obtain complete tumour destruction. During laparotomy or a laparoscopic approach, monitoring is generally limited to direct vision for superficial lesions and ultrasonography for all other lesions. During RFA a hypechoic area is formed around the tip of the electrode due to the formation of bubbles from evaporated water. The precise boundaries of this hypechoic area, however, do not automatically correlate with the coagulative damage. So, ultrasonography provides only a rough estimate of the size of the ablation. Both CT and MRI imaging have been reported to be more reliable in this regard. After thermal treatment, CT shows a round or tear-drop-shaped hypoenhancement area which is sharply demarcated from normal liver tissue and which allows accurate monitoring of the treatment effect. Also, MRI may allow accurate monitoring of the treatment effects [18]. Selected sequences during MRI can monitor temperature elevations in the tumour and surrounding tissue which increases treatment efficacy. Nevertheless, also for the percutaneous approach of thermal ablation, ultrasonography is still the most common method used mainly because of its real-time capabilities, availability, speed, and low cost.

Follow-Up

After RFA, close follow-up of the treated lesions may be important in order to perform re-treatment in case of inadequate ablation. Tumour markers such as CEA and d-fetoprotein are only a reliable parameter for successful treatment in those patients with elevated levels at the time of tumour ablation. In these patients a normal level of tumour markers may be indicative for successful treatment. However, in general, tumour markers are only a very rough estimate for evaluating local treatment efficacy. Most often, contrast-enhanced CT scan is used for follow-up of the treated lesions. In case of tumour recurrence, a faint, irregular, hypoenhanced area becomes visible around the margins of the ablated tissue that in-
creases in size on follow-up scans. Comparable images may be obtained by MRI. More recently, FDG-PET scan has been used to follow up local ablative treatment of colorectal liver metastases (fig. 1) [19]. After successful treatment, metastatic lesions become photopenic. Persistent activity after local tumour treatment is highly suspicious for inadequate treatment. Moreover, the reappearance of activity in photopenic areas is strongly indicative for tumour recurrence. In a recent study, 104 lesions treated by RFA (68 lesions) or cryosurgery (36 lesions) were followed by FDG-PET and CT scan directly after tumour ablation (within 3 weeks) and every 3 months thereafter. CT scans within 3 weeks after local tumour ablation showed hypodense treatment areas of all lesions without any evidence of tumour remnants. During further follow-up examinations the mean time point of detection of local recurrence by CT was 9 months. In contrast, FDG-PET scan within 3 weeks after tumour ablation showed increased focal activity at the edge of the treatment zone in 8 lesions. Seven of these 8 patients turned out to develop local recurrence during further follow-up, 1 patient appeared to develop an abscess in the treated area, leading to a false-positive FDG-PET scan. Immediate imaging by FDG-PET within 3 weeks after local tumour ablation showed a negative predictive value for the detection of local recurrence of 99%, the positive predictive value for the detection of local recurrence was 88%. In an earlier study by the same group it was demonstrated that FDG-PET also showed tumour recurrence outside the treated area considerably earlier than CT [20].

Results

Colorectal Liver Metastases

In the literature there is general consensus that the application of RFA in colorectal liver metastases should be limited to unresectable disease. However, despite many reports on the use of RFA in this patient category, it remains difficult to define the results of RFA in colorectal liver metastases [3–14]. First of all, RFA ablation is aiming for local tumour control, while the main issue in colorectal liver metastases is to control systemic disease and prolong overall survival. Both issues are often not necessarily identical or even overlapping. Moreover, results published so far are often confusing by reporting overall treatment results of a wide variety of different tumour types ranging from highly malignant lesions such as colorectal liver metastases and melanoma to borderline malignancies such as endocrine tumours or even benign lesions. Also additional treatments by chemotherapy often obscure the primary effect of RFA treatment.
Local Tumour Recurrence after RFA for CRC Liver Metastases

Two series were initially reported on the use of RFA during laparotomy. Wood et al. [3] reported on 84 patients with 231 lesions of which 70 lesions were of colorectal origin. 71% of the cases were treated by laparotomy. Overall a local recurrence rate of 6.5% on a lesion basis and 18% on a patient basis were reported. Curley et al. [4] reported in a comparable group of 123 patients, of which 61 patients with colorectal metastases, a local recurrence rate on a lesion basis of 2 and 2.5% on a patient basis. The median diameter of the lesions in both studies was 2 and 3.4 cm, respectively. In a more recent study by Pawlik et al. [13], RFA was used in addition to resection. This series comprised 350 lesions (72% colorectal liver metastases) with a median diameter of 2 cm. Local recurrence rate was 8% on a patient basis and 2.3% on a lesion basis. Local recurrence usually presented within the first year after RFA ablation in all series.

Later studies also included patients treated by laparoscopic approach [7, 9, 10]. These studies observed a local recurrence rate on a lesion basis between 3 and 12%, while local recurrence on a patient basis varied between 7 and 26%. Median diameter of the lesions treated in these studies varied from 2 to 3 cm. Results vary significantly for the percutaneous approach. De Baere et al. [5] treated 86 patients with 121 lesions of which 76 patients had colorectal liver metastases. The median diameter of the lesion was 1.9 cm. Local recurrence on a lesion basis in this series was 9%, and 16% on a patient basis. Solbiati et al. [6], however, showed significantly higher local recurrence rates in 117 patients with 179 colorectal liver metastases. In this series with a median diameter of the lesion of 2.6 cm the local recurrence rate on a lesion basis was as high as 39%. Local recurrence was even 68% for lesions >4 cm in diameter. This finding was in agreement with Wood et al. [3] and Bilchick et al. [9] who reported on local recurrence rates for tumours >3 cm of respectively 33 and 38%.

In a review study on local recurrence after RFA for colorectal liver metastases, Mulier et al. [17] reported an overall local recurrence rate of 14.7% on a lesion basis. Results were dependent on the size of the lesions as well as the approach used for RFA.

In conclusion, the literature shows that for lesions up to 3 cm, RFA is effective and can result in definite local tumour control in >90% of the lesions treated. For lesions >3 cm, local recurrence rates at the site treated are still high and have been reported to be over 30%. For these larger lesions, multiple probe insertions are necessary to obtain a treatment zone large enough to include all tumour tissue. It seems that the efficacy of these overlapping treatment zones is still unreliable resulting in high local recurrence rates. Moreover, the different series give a slight indication that laparoscopic RFA and RFA performed during open surgery is more reliable than percutaneous RFA. During these approaches the surgeon has the opportunity to reduce the heat sink effect by the large vessels by clamping the portal ligament. Furthermore, superficial lesions as well as lesions in the dome of the liver are more easily accessible by the open approach compared to the percutaneous approach.

Effect of RFA on Disease-Free Survival

The efficacy of local tumour ablation in terms of effect on survival is still hard to assess because most reports include different patient selection criteria, different treatment protocols and sometimes even different types of tumour (table 2). Moreover, the extent of metastatic disease treated in the different series varies considerably which directly influences data on disease-free and overall survival.

Most series, however, show a disease-free survival of 1 year or less [6, 10, 13, 14]. Depending on the indications and the extent of liver disease at the time of RFA ablation, disease-free survival varies between 7 and 12 months. For >90% of the cases, recurrent disease occurs outside the treated area, either within the liver or at extrahepatic sites. For this reason many centres favour the use of chemotherapy after RFA treatment. Since in patients with unresectable colorectal liver metastases the effect of RFA on disease-free survival is limited, the ultimate effect of RFA on overall survival may at least be questionable. In this regard no data from randomised clinical trials are available and data on overall survival are limited to phase II studies.

Effect of RFA Ablation on Overall Survival (Phase II Studies)

One-year overall survival after RFA ablation of unresectable colorectal liver metastases varies generally between 80 and 93%, 2-year overall survival is reported between 50 and 75% [3–14, 20]. In the patient populations selected in the different studies the number and diameter of lesions is generally low. In most studies the mean number of metastases is <2, while most lesions treated are <3 cm. Between the studies there are significant differences between these figures, which indeed may reflect differences in resectability criteria. The way RFA was applied also varies considerably between the different studies. Most series include an open approach as well.
as the percutaneous or laparoscopic approach. Although the way in which RFA was applied clearly affected the local recurrence rate, it does not seem to affect overall survival. This finding can easily be explained by the fact that recurrent disease generally occurs outside the treated area.

In a retrospective study (1992–2002) by Abdalla et al. [14], overall survival after RFA for unresectable disease was directly compared to a more or less comparable group of patients treated by chemotherapy only as well as to a group of patients with comparable tumour characteristics treated by resection. Four-year overall survival of patients treated by resection, resection plus RFA and RFA only was 65, 36 and 22%, respectively. For patients treated by chemotherapy only, 4-year survival was 10%. Although a survival advantage for RFA over chemotherapy was found, the survival curves are clearly converging towards 5 years. The authors concluded that RFA alone or in combination with resection for unresectable disease does not provide survival data comparable to resection, and provides survival only slightly superior to non-surgical treatment. Whether this modest effect on survival will also sustain after a randomised patient selection and with the use of newer chemotherapy regimens with improving outcomes is very doubtful.

Altogether, several studies on RFA for unresectable colorectal liver metastases have shown median overall survival times of >30 months. These results have been claimed to be superior to standard treatment of chemotherapy, which nowadays can result in a median survival of 24 months. The superior results of local ablative therapy compared with chemotherapy may certainly be due to patient selection. Especially since patients selected for aggressive local treatment show only a limited number of liver metastases (in most studies a median number of approximately ≤4), while patients as reported in chemotherapy series may show more widespread liver involvement or even extrahepatic disease.

| Group (first author) | Patients | Lesions | Patients Lesions | n | Lesions per patient | Approach | Mortality % | Additional therapy | Median follow-up months | Local recurrence, % | Liver Extrahepatic DFS at median follow-up Overall survival |
|---------------------|----------|---------|------------------|---|---------------------|---------|-------------|-------------------|-------------------|------------------|-------------------|-----------------------------|
| Wood 2000 [3]       | 84/231   | 37/11   | Lesions: 70/18/143 | 36 | 1–9 median 2/NG NG | Perc 29%/28% | NG           | Resection | 9/18 | 6.5/50% | 26% | 74% at median follow-up |
| Curley 1999 [4]     | 123/169  | 61/48   | 1–12 median 3.4 | 14 | 1–4/1–5 | Perc 25%/69% | Open 75%/31% | Resection | 15/14 | 2/9 | NG | 73% | NG |
| Pearson 1999 [8]    | 92/138   | 46/34   | 1–12 median 3.8 | 12 | 1–5/5 | Perc 69%/24% | Open 31%/38% | Resection | 15/12 | 2.5/3 | NG | NG | NG |
| De Baere 2000 [5]   | 86/121   | 76/10   | <4.5 median 1.9 | <5 | <4/3 | Perc 58%/24% | Open 35%/14% | Resection | 14/12 | 9/7 | NG | 50% | 1 year 81% |
| Bilchik 2000 [9]    | 68/181   | 30/9    | 1–9 median 2    | 29 | 1–13/3 | Perc 24%/80% | Resection | 13/7 | NG | 52% | 1 year 80% |
| Sobolati 2001 [6]   | 117/179  | 117/117 | ~<9.5 median 2.6 | <4 | 1.5 | Perc 100% | Open 38%/38% | Resection | 12/3 | 3 | NG | 1 year 49% | 2 years 35% |
| Bowles 2001 [7]     | 76/328   | 39/25   | 1–18 median 3   | 12 | 1–14/4 | Perc 58%/11% | Open 34%/8% | Resection | 15/12 | 9/7 | NG | 33% | 1 year 80% | 2 years 50% |
| Bleicher 2003 [10]  | 153/447  | 59/21   | 1–13.5 median 2.5 | 73 | 1–13/7 | Perc 51% | Open 35%/14% | Resection | 11/7 | 9/7 | NG | 29% | 1 year 61% |
| Adam 2002 [12]      | 33/43    | NG/18   | <5 median 2.8   | 1 | 1.3 | Perc | Open 16/18/16 | Resection | 16/12 | 51% | 27% | 1 year 58% |
| Pawlik 2003 [13]    | 172/737  | 124/5   | 1–12 median 2   | 43 | 2–21/3 | Open | Resection | 21/21 | 8/8 | 79% | 98% | 2 years 75% | 3 years 53% |
| Abdalla 2004 [14]   | 57/101   | 57/1    | median 2.5      | 1 | 1–8/1 | Open | NG | NG | 21/9 | 52% | 48% | 1 year 40% | 3 years 6% |

NG = Not given.

Effect of RFA on Overall Survival (Phase III Study)

In order to determine the place of local ablative therapy, controlled clinical trials are highly needed. One trial would concern patients with unresectable colorectal liver metastases in which aggressive local treatment of the metastases with RFA plus chemotherapy is compared to the standard treatment of chemotherapy alone. Such a trial (CLOCC) is at the moment running as a multicentre intergroup trial by the European Organisation for Research and Treatment of Cancer, the Arbeitsgemeinschaft für Leber Metastasen in Germany, and the NCRI colorectal cancer group in the UK (information bme@eortc.be). Another study would concern the place of RFA in the treatment of resectable colorectal liver metastases. Until the results of these studies are available, local tumour ablation for colorectal liver metastases should be considered experimental and should mainly be performed within well-controlled clinical trials.

Current Practice in the Netherlands

The technique was introduced in the Netherlands in 1999. Initial experience with the technique was described in 50 patients, mainly with colorectal liver metastases [21]. Eleven tumours (7 patients) were resected after prior treatment with RFA ablation. All tumours demonstrated non-viable tumour. At a median follow-up of 11 months, 26 patients developed disease recurrence of which 3 at the ablation site. In the Netherlands this technique is at present mainly used within a clinical trial (CLOCC).

Hepatocellular Carcinoma (HCC)

The treatment of HCC, being one of the most common malignant tumours in man worldwide, occurs mostly in cirrhotic livers. The loss of liver function in cirrhotic livers limits the option of resection in many cases. Liver transplantation has been demonstrated to be the best treatment that can be offered for smaller HCCs, but only a relatively low number of patients with HCC can be treated in this way. Even with the extension of transplant programs by living related liver donation, such as recently started in the Netherlands, the problem of the shortage of donor organs remains unresolved. Therefore, alternative treatments such as RFA have to be explored.

Place of RFA Ablation in HCC

To evaluate whether RFA may have a place in the treatment of HCC, the outcome should be compared to that of other local treatment modalities such as partial liver resection and percutaneous ethanol injection (PEI).

It is widely accepted that partial liver resection can offer local control of primary liver cancer if complete removal of the tumour can be achieved and no extrahepatic disease can be demonstrated. Five-year survival rates vary from 18 to 51% and depend on the size of the tumour, the number of nodules, vascular ingrowth and the underlying disease. In patients without underlying liver disease, 5-year survival rates up to 80% may be achieved with complete removal of the primary process, even in case of larger HCCs [22].

Local destruction of tumour cells can be achieved by injecting ethanol into a tumour nodule; through a combination of cellular dehydration, coagulative necrosis and vascular thrombosis tissue ischemia is induced [23]. Homogeneous distribution of the injected alcohol is essential for a successful procedure and multiple treatment sessions may be necessary to achieve complete tumour destruction. PEI can be done as an outpatient treatment with local anaesthesia. It is accepted to perform PEI for HCC nodules up to 3 cm. About 70% of patients with HCC <3 cm show complete tumour necrosis according to histopathological studies [24, 25]. PEI is generally contraindicated in the presence of ascites, thrombocytopenia, portal thrombosis or extrahepatic disease.

The side effects of PEI are mild and the complication rate is low. Leakage of alcohol into the abdominal cavity may cause abdominal pain [25, 26]. Tumour seeding along the needle tract after PEI for HCC has been reported with an incidence of 1% [27, 28].

The reported 5-year survival rate after PEI varies from 24 up to 59% and is dependent on liver function, tumour size and number of nodules [29–31]. Livraghi et al. [25] described in a large series of PEI for small HCCs (<5 cm) a 5-year survival rate of 47% for Child A patients, 29% for Child B and 0% for Child C patients.

In most reports on RFA in HCC the tumour nodules that can be treated successfully are <3 cm, but complete necrosis of larger tumours has been described [32–38]. RFA is generally contraindicated in the presence of ascites and decompensated liver functions. RFA can be performed percutaneously, laparoscopically or via laparotomy.

The complication rate is low and includes temporary pain, fever and pleural effusion. Tumour seeding along the needle tract has been described [35, 36]. Studies with 5-year survival rates of 33% [37] and 40% [38] have been reported. In the Netherlands there is only a limited expe-
experience with RFA in the treatment for HCC and the technique is used predominantly to control tumour growth for those awaiting liver transplantation.

**Liver Transplantation**

Total hepatectomy followed by liver transplantation seems to be the ideal treatment for patients with a HCC in a cirrhotic liver. Not only is the HCC nodule removed but also the precancerous liver tissue that may be present in the remnant liver is resected. However, it should be noted that vascular ingrowth and the presence of extrahepatic disease should be excluded before a liver transplantation can be considered. As for resection it has been demonstrated that the outcome of surgery is dismal when patients with extrahepatic disease or vascular ingrowth are accepted for transplantation. The Dutch protocol is in line with the internationally accepted criteria for transplantation: patients with decompensated cirrhosis and a single nodule <5 cm or multinodular disease (three nodules <3 cm) can be offered liver transplantation as the first choice of treatment [39, 40].

The benefits of liver transplantation should be outweighed against the risks of serious morbidity and mortality due to the procedure. Hepatic graft dysfunction up to 6% has been described in a large series of 14,282 patients. Morbidity may be related to hepatic arterial complications including thrombosis (6%) necessitating retransplantation, and biliary complications (14%). The reported operative mortality varies from 0 up to 6%.

The yearly recurrence has been estimated at 20% with a range of 15–30% [41]. Vascular ingrowth has been demonstrated to be the main prognostic independent factor for recurrence [42]. Larger tumours (>5 cm) are more often found to invade vessels. Without vascular invasion 5-year recurrences of 4% have been reported, with vascular invasion the recurrence rate may be as high as 65% [41]. In general, the reported 5-year survival varies from 44 to 75%. In well-selected patients (small, single nodules) 5-year survival rates of 92% have been described [43]. The introduction of living related liver transplantation may help to improve the outcome as the waiting time for transplantation may be reduced from about 400 days to 50 [44, 45].

**Current Practice in the Netherlands**

All treatment modalities available for HCC can be offered in the Netherlands. The criteria for surgical resection and liver transplantation as well as the outcome of these procedures can meet international standards. The experience with local ablative techniques for the treatment of HCC is limited to a few centres and the numbers are too low to allow proper analysis for the outcome. Single-centre reports suggest that RFA may be used successfully to control HCC in those patients awaiting liver transplantation.

**Miscellaneous Liver Tumours**

Except for the more common liver tumours like colorectal liver metastases and HCC, more rare tumours can be treated with RFA. This can be done as an addition to partial hepatectomy to make the patient tumour-free, as a debulking procedure in order to prolong life in patients with slow growing tumours or as a treatment of patients with symptoms of tumours with endocrine activity. In the University Medical Center Groningen, 50 patients were treated with RFA, of which 10 procedures were performed for miscellaneous diagnoses such as medullary thyroid carcinoma metastases (n = 2), gastrointestinal stromal tumours (n = 2), follicular thyroid carcinoma metastasis (n = 2), hepatoblastoma (n = 1), Grawitz metastasis (n = 1), neuroendocrine metastasis (n = 1) or liver adenomatosis (n = 1). Six of these procedures were performed either by CT guided percutaneously or laparoscopically. The decision to perform local ablation for these less frequent indications is based on the effectiveness and possibility of alternative treatments, prognosis, aim of the ablation (cure or palliation) and expected complication rate. In this paper, only liver metastases of neuroendocrine tumours and liver adenomatosis will be discussed.

**Neuroendocrine Liver Metastases**

Surgical treatment of liver metastases from neuroendocrine tumours varies from such large procedures as liver or multivisceral transplantation, or partial liver resection to less invasive procedures like percutaneous ablation. Transplantation, although a potentially curative procedure, is restricted to a small minority of highly selected patients with favourable prognostic tumour characteristics [46, 47]. An important issue for determining which treatment should be offered is the often indolent course of these tumours. It is therefore essential to critically appraise the expected effect of treatment on the natural course of these tumours. On the other hand, an aggressive surgical approach is often justified to relieve severe hormone-related symptoms. Unfortunately the occurrence of widespread and bilobar metastases often precludes a curative treatment by resection alone. Therefore...
the combination of partial liver resection and local ablation is necessary to obtain as much tumour debulking as possible. For more localised metastases the minimally invasive approach of percutaneous CT guided ablation is attractive.

Three reports present the results of RFA for neuroendocrine liver metastases [48–50]. Symptomatic relief after RFA was obtained in about 70% of the patients [49, 50]. Furthermore, the complication rate using the minimally invasive approach of either laparoscopy or percutaneous ablation was remarkably low [49, 50]. Because of heterogeneity in diagnosis and the limited number of patients, an effect on survival is difficult to judge from these data. Additionally, one has to bear in mind that many patients referred for RFA had already had several previous treatment modalities, and also had extrahepatic metastases. This results in a negative selection of patients because of widespread disease and the selection and survival of more therapy-resistant cell lines. In patients undergoing RFA, adequate measures should be taken to block hormone secretion because during RFA the release of hormones can possibly result in systemic complications [51].

In the multimodality treatment of neuroendocrine metastases, local ablation deserves a place for either intention to cure (rare) or debulking with the aim of reduction of symptoms or prolongation of life. Real evidence for the role of RFA in this challenging type of diseases is still lacking, and is probably difficult to obtain because of the low incidence and the heterogeneity of the disease.

Liver Adenomatosis

Adenoma of the liver is a benign tumour occurring in women usually with (a history of) the use of oral contraceptives. When several (by some defined as >10 lesions) of these tumours are present in an otherwise healthy liver (not associated with glycogen storage disease), the entity is called liver adenomatosis [52]. Although it is a rare condition, it is worthwhile identifying because of its associated risk of bleeding, infarction or rupture. Because of the frequent bilobar distribution of these adenomas, RFA can have a definite role during surgical procedures. Generally, resection of the adenoma which caused the symptoms (usually the largest) combined with ablation of the smaller ones is the procedure of choice. This is especially relevant because increased tumour growth in the remnant liver, which is probably associated with liver regeneration, is a well-known complication which has been described in adenomatosis [52, 53].

Conclusion

RFA ablation of liver tumours is an evolving technique. In the Netherlands this technique is used for several types of liver tumours. In case of colorectal metastases, the technique is only used for unresectable lesions. However, also in these situations the effect of the technique is still controversial and RFA ablation is mainly used within a clinical study design (CLOCC study). The experience with local ablative techniques for the treatment of HCC is limited to a few centres. Single-centre reports suggest that RFA may be used successfully to control HCC in those patients awaiting liver transplantation. Within the multimodality treatment of neuroendocrine metastases, local ablation may deserve a place for either intention to cure (rare) or debulking with the aim of reduction of symptoms or prolongation of life.

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