University of Groningen

Radiofrequency Ablation of Hepatic Metastases from Thyroid Carcinoma

Wertenbroek, Marieke W. J. L. A. E.; Links, Thera P.; Prins, Ted R.; Plukker, John T. M.; van der Jagt, Erik J.; de Jong, Koert P.

Published in:
Thyroid

DOI:
[10.1089/thy.2008.0080](https://doi.org/10.1089/thy.2008.0080)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2008

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Wertenbroek, M. W. J. L. A. E., Links, T. P., Prins, T. R., Plukker, J. T. M., van der Jagt, E. J., & de Jong, K. P. (2008). Radiofrequency Ablation of Hepatic Metastases from Thyroid Carcinoma. *Thyroid*, 18(10), 1105-1110. <https://doi.org/10.1089/thy.2008.0080>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Radiofrequency Ablation of Hepatic Metastases from Thyroid Carcinoma

Marieke W.J.L.A.E. Wertenbroek,¹ Thera P. Links,² Ted R. Prins,³ John T.M. Plukker,⁴
Erik J. van der Jagt,³ and Koert P. de Jong¹

Background: Radiofrequency ablation (RFA) is performed for various types of liver tumors. It might also have a role in the palliative treatment of liver metastases from thyroid carcinoma.

Summary: Three patients with liver metastases of thyroid carcinoma were retrieved from our database of 125 patients who had been treated with RFA for liver tumors. In all three patients, the metastases were a sign of widespread disease, and several other treatment modalities had been performed earlier. Two patients had metastases from medullary thyroid carcinoma and had severe diarrhea. The third patient had a rapidly progressive metastasis of a follicular thyroid carcinoma. The aim of the treatment was cytoreduction with amelioration of symptoms ($n = 2$) and debulking with increased sensitivity for subsequent ^{131}I treatment. The ablation was performed via laparotomy ($n = 1$), laparoscopically ($n = 1$), or percutaneously ($n = 1$). One patient experienced superficial burn wounds after a long-lasting RFA procedure. Severity of symptoms was reduced significantly after RFA for a prolonged period of time. RFA induced partial tumor necrosis because of hypervascularization of the tumor in one patient. After arterial embolization the second RFA treatment induced total tumor necrosis. Local recurrences at the site of the ablated liver metastases were not encountered during follow-up.

Conclusions: RFA is a useful treatment modality in patients with liver metastases from thyroid carcinoma. It should be considered an adjunct to other types of treatment or for those patients in whom more regular treatment modalities are not effective or possible or are associated with increased risks.

Introduction

THYROID CARCINOMA ENCOMPASSES only about 1% of all malignant tumors. Of the well-differentiated thyroid cancer, follicular carcinoma (FTC) is the second most common malignancy of the thyroid after papillary carcinoma (PTC). The other forms of thyroid cancer, including medullary thyroid cancer (MTC), are less frequent.

The initial presentation with distant metastases (usually in lungs or bones) occurs in 4–23% of patients with differentiated thyroid cancer (1–3). Distant metastases from MTC occur initially in about 14% of patients (4). Liver metastases from thyroid cancer are mostly a sign of widespread disease and are difficult to diagnose by radiological imaging techniques because they are frequently small and multiple.

The incapacitating symptoms of the metastatic disease are predominantly functional, like diarrhea in MTC patients or palpitations associated with high free thyroxine (FT_4) serum levels, which can occur in patients with metastatic papillary or follicular cancer. Current management strategy for the

treatment of well-differentiated thyroid cancer is surgery, followed by ^{131}I treatment. In the primary treatment for MTC only surgery is curative. In cases of persistent disease, chemotherapy, radiotherapy, radioactive metaiodobenzylguanide (MIBG), and interventional radiological procedures can be used, but these are not daily clinical practice.

Radiofrequency ablation (RFA) is a thermal ablation technique that induces tumor necrosis by creating ionic agitation resulting in frictional heat. RFA has been described as treatment for locally recurrent thyroid malignancy (5).

We describe our experience with the use of RFA in the palliative treatment of patients with liver metastases of thyroid carcinoma.

Patients and Methods

Three patients with thyroid liver metastases were retrieved from our prospective RFA database. One hundred twenty-five RFA procedures for liver tumors were performed in the University Medical Center Groningen between July 2000 and January 2008. About 50% of these procedures were done

¹Department of Surgery, Division of Hepato-Pancreatico-Biliary Surgery & Liver Transplantation; ²Department of Internal Medicine, Division Endocrinology; ³Department of Radiology; ⁴Department of Surgery, Division of Surgical Oncology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands.

percutaneously under computer tomographic (CT) guidance. RFA was performed using the RF 3000 TM Radio Frequency Ablation System (Boston Scientific, Boston, MA). Depending on the diameter of the tumor a LeVein needle of 2, 3.5, 4, or 5 cm diameter was used. The RFA needle is placed in the center of the tumor under ultrasonography or CT guidance. RFA was applied according to the protocol of the manufacturer and consisted of heat induction until the rise in tissue impedance halted the generation of radiofrequency waves. Large tumors were treated by several overlapping positions of the deployed RFA needle.

The follow-up scheme consisted of physical examination with biochemical tests, and MRI or multiphase CT every 3 months during the first 2 years and every 6 months thereafter. This was done to identify local recurrence of the ablated tumor or new lesions elsewhere. The follow-up lasted until June 2007.

Plasma calcitonin levels (reference values 0.3–12 ng/L) were measured by enzyme-linked immunosorbent assay (Sangui Biotech Inc., Santa Ana, CA). Plasma carcinoembryonic antigen (CEA) levels (reference values 0.5–5 (g/L) were measured by chemiluminescent microparticle immunoassay (Abbott Laboratories, Abbott Park, IL). Serum thyroglobulin level was measured by radioimmunoassay (Cis Bio International, Gif-sur-Yvette, France) with a detection limit of 1.5 ng/mL.

A literature search was done using MEDLINE and EMBASE using the search terms “thyroid”, and/or “metastasis”, and/or “ablation”, and/or “medullary”, and/or “liver”, and/or “differentiated”. Cross references in the retrieved literature were also included. Only reports published in English between 1980 and 2007 were included.

Patient 1

In 1973, at the age of 22, a woman with a family history of multiple endocrine neoplasia 2a, was diagnosed with MTC for which total thyroidectomy with mediastinal lymph node dissection and thymectomy was performed. In 2001, at the age of 50, metastatic lesions were seen in the liver and the iliac bone on the MIBG-scan, for which she was treated with ^{131}I -MIBG and local radiotherapy at the iliac bone. However, the complaints of diarrhea and weight loss were persistent. Three spots in the liver were then treated with RFA during laparotomy; one 7-cm large metastasis in the right liver lobe and two lesions with a diameter of 3–4 cm in the left lobe. Because of the size and hypervascularity of the lesions, the procedure took 10 hours to complete. She developed superficial burn wounds on the legs, at the site of the grounding pads. Two months after treatment, the calcitonin level decreased from a pre-operative value of 40,000 ng/L to 9000 ng/L post-RFA and the symptoms of weight loss and diarrhea resolved (Fig. 1A). We have no explanation for the single irreproducible high calcitonin level in 2002. In the beginning of 2005 widespread metastatic disease was detected for which she was treated again with ^{131}I -MIBG and local radiotherapy. The ablated liver tumors did not show signs of progression. In February 2007 she died due to disseminated disease.

Patient 2

A 61-year-old man with a sporadic MTC was treated in 1997 with total thyroidectomy and lymph node dissection of

FIG. 1. Course of serum tumor markers in the three patients. (A) Patient 1, (B) Patient 2, (C) Patient 3. CEA, carcinoembryonic antigen.

the neck and mediastinum and postoperative external radiotherapy of 64.5 Gy/36 fractions. Five years later, he complained of diarrhea, nightly sweat attacks, and pain in the right shoulder, and multiple bilobar liver lesions were detected on CT. Laparoscopic RFA treatment of three lesions (3-, 4-, and 7-cm diameter) was done in 2002 with the goal of achieving tumor debulking and reduction of symptoms. The postoperative course was uneventful and his complaints subsided to a significant extent, despite the fact that hardly any change in CEA and calcitonin levels was detected (Fig. 1B). Since mid-2004 until April 2007 he was treated with imatinib, a tyrosine kinase inhibitor, because of recurrent symptoms, rising tumor markers, and progression of newly developed liver and bone metastases. This treatment resulted in another period of stabilized tumor progression. This treatment was

stopped because of leukopenia and edema, which resulted in progression of the disease in bone and diffuse liver metastases. However, the RFA-treated tumors did not reveal signs of progression until February 2008. Currently, 10 years after his initial diagnosis and 6 years after RFA of his liver metastases, he has a reasonable quality of life.

Patient 3

In 1997, at the age of 60 years, a woman presented with a FTC which had metastasized to the fourth lumbar vertebra (L4). Treatment consisted of total thyroidectomy, followed by multiple treatments with ^{131}I , transarterial embolization of the metastasis in L4, radiotherapy, and finally corpectomy of L4 and spondylodesis of L3 to L5. In 2004, on PET and CT scan a 3.8-cm lesion was detected in the liver without signs of other metastases. Rapid increase in diameter of the liver lesion led us to perform a CT-guided percutaneous RFA procedure with the aim of halting progression and prolonging her life expectancy (Fig. 2A, 2B). A percutaneous biopsy taken before the RFA confirmed the diagnosis of FTC. After six cycles and an ablation time of 90 minutes the procedure had to be stopped prematurely because of hyperthermia of the patient. The RFA treatment was considered inadequate, which was confirmed by CT showing a still partially vascularized tumor with a hypodense central part, suggestive of partial necrosis (Fig. 2C). Subsequently a selective, transarterial embolization of the metastasis was performed (Fig. 2D, 2E). During this procedure three new suspicious lesions were detected in the liver, which were not seen on the prior multiphase CT. After selective embolization, the larger metastasis was successfully treated with RFA (Fig. 2F), resulting in a decrease in serum thyroglobulin levels (Fig. 1C). Additional systemic treatment with radioactive iodine was started because of the newly discovered liver metastases. The cumulative activity of ^{131}I radioiodine was 900 mCi. Six months later she died due to septic shock in association with a bone marrow insufficiency probably related to a myeloproliferative disorder.

Discussion

Thermal ablation of liver tumors was initially performed by freezing (cryoablation). For several reasons most liver surgeons nowadays favor tumor destruction by heating, using RFA (6). RFA is a generally accepted technique for treatment of liver tumors with low morbidity and mortality, especially when using a percutaneous or laparoscopic approach. (7,8). The overall complication rate of RFA of hepatic malignancies amounted to 9%, and the reported mortality rate is below 1% (8–10). As with many new techniques the rate of success is highly dependent on the experience of the operator (11,12).

We describe the treatment and follow-up of three patients with liver metastases of thyroid carcinoma, in whom RFA was one of the treatment modalities. In none of our patients was local recurrences at the ablation site encountered on repeated imaging during follow-up.

In our literature search (summarized in Table 1) only 10 patients were encountered in whom RFA was performed for liver metastases of thyroid carcinoma (13–26). The efficacy of RFA treatment in these patients is difficult to judge, however, because they were described in larger series of patients with various other diagnoses for which RFA was performed.

The need for multimodality treatment of this type of patients is exemplified in patient 3. RFA is less effective in highly vascularized tumors because the blood flow cools down the treated tumor, the so called “heat sink effect.” After selective transarterial embolization of the tumor a decrease in the blood supply enhances local heat generation by RFA and complete tumor necrosis can be obtained.

In patient 1 the quality of life greatly improved by reduction of her severe diarrhea. RFA of the liver metastases in patient 2 also resulted in a reduction of diarrhea although no effect on CEA and calcitonin levels was found. In patient 3 the first RFA, although incomplete, already caused tumor necrosis as reflected by the hypovascular (necrotic) central part of the tumor visible on the CT scan (Fig. 2C). However, as an illustration of tumor debulking, serum thyroglobulin levels decreased only after a second RFA procedure that was performed after selective arterial embolization.

The aim of RFA of liver metastases of thyroid carcinoma is palliation because liver metastases are a manifestation of widespread disease. Nevertheless, these patients can have considerable life expectancy and obtaining a good or reasonable quality of life is worthwhile. Additionally, tumor bulk reduction enhances the effectiveness of radioactive iodine. This has been demonstrated for the combination of embolization and radioiodine in the treatment of bone metastases (27).

RFA should be considered as another cytoreductive modality besides resection, radioactive iodine, radiotherapy, or transarterial (chemo) embolization. In our opinion RFA can have a role in reducing tumor bulk and thus increase efficacy of ^{131}I treatment. Furthermore, it should also be considered in those patients in whom the metastases have low or no ^{131}I uptake, which in one series occurs in nearly 30% of the patients (28). This might be explained by the degree of tissue differentiation. Well-differentiated thyroid tissue has the capability to take up iodine but is metabolically inactive, while less-differentiated thyroid cancer tissue loses its capability to trap iodine and becomes metabolically more active. This complementary uptake of FDG and radioiodine is called the “flip-flop” phenomenon (29) and makes FDG-PET scanning valuable for the detection of ^{131}I -negative metastases of differentiated thyroid cancer (30,31). RFA can also be an option in patients who already had several ^{131}I treatments in the past and in whom the risk of developing myeloproliferative disorders or a secondary malignancy is increasing with the cumulative activity of ^{131}I administered (32,33).

Transarterial chemoembolization (TACE) is a successful technique in the treatment of various liver tumors; however, variations in hepatic arterial anatomy, the presence of arteriovenous shunting, and tortuosity or stenosis of hepatic arteries can sometimes make TACE impossible (reviewed by Liu *et al.* [34]). The rate of major complications after TACE is rather low (5%) but the postembolization syndrome is reported in up to 90% of patients (35). This syndrome consists of fever, abdominal pain, nausea, and vomiting and is the main reason for prolongation of hospital stay after TACE. In our opinion both techniques are supplementary with the advantage of RFA of a very effective local tumor treatment with a low complication rate and the advantage of TACE of a more diffuse effect on either a part or to the whole liver, albeit with a higher complication rate (24,26).

Although it is claimed that RFA is less effective in larger tumors (e.g. >5 cm) patient 1 shows that even large tumors

FIG. 2. Combined treatment of transarterial embolization and radiofrequency ablation induces total tumor necrosis in patient 3. First incomplete radiofrequency ablation (RFA) (A, B, C) followed by arterial embolization (D, E) and second complete RFA (F). (A) Computed tomography (CT) during arterial phase showing a hypervascular lesion (arrow). (B) CT-guided RFA procedure showing deployed multiple arrays of LeVeen needle (arrow). (C) CT during arterial phase showing still contrast filling of the outer boundaries of the tumor (arrows) as a characteristic of insufficiently treated tumor with RFA. (D) Arteriography showing tumor blushes before selective embolization. (E) Arteriography after embolization of the tumor. (F) Control CT during venous phase after second RFA, showing adequately destroyed tumor (arrow) and ablated entrance route (arrow head).

can be controlled by creating several overlapping ablation zones, although this is time consuming. Also, RFA is less effective in tumors near large vessels, because the continuous blood flow dissipates the heat (heat sink effect). RFA of tumors close to larger bile ducts could result in injuries like biliary fistulae, strictures, or abscesses. Simultaneous cooling of bile ducts has been described as a preventive measure for these complications (36). For tumors close to organs such as the colon, stomach, or duodenum an open or laparoscopic approach should be chosen in order to create distance between the organs and the ablation site, thus decreasing the risk of heat destruction of the wall of these organs.

It is our policy to perform a post-RFA contrast-enhanced CT scan 1 week after the RFA. The CT scan should show a hypodensity at the site of the metastasis. If the CT scan still shows vascularization of the liver metastases (patient 3) a repeat RFA should be performed to fully destroy the tumor. In hypervascular lesions a selective embolization of the feeding artery will enhance the effectiveness of a second RFA. Because it is not possible to predict (even in hypervascular liver tumors like hepatocellular carcinoma) whether RFA will be successful, we advocate RFA first and, in case of insufficient ablation, perform embolization of only those tumors that are still hypervascular.

TABLE 1. CURRENT LITERATURE ABOUT TREATMENT OF LIVER METASTASES FROM THYROID CARCINOMA

Author	Year of publication	Total no. patients	No. of patients with thyroid liver metastases and diagnosis	Total no. of liver metastases ^a	Tumor diameter (cm) ^a	Therapy	Follow-up (months)
Brown <i>et al.</i> (13)	1984	42	1 FTC			¹³¹ I	
Siperstein <i>et al.</i> (14)	1997	6	1 MTC	1	1.5	RFA	2
Curley <i>et al.</i> (15)	1999	123	1 MTC			RFA	
Guglielmi <i>et al.</i> (16)	1999	1	1 FTC			Thionamides, laser photocoagulation, ¹³¹ I	
Machens <i>et al.</i> (17)	2000	1	1 MTC			TACE	Died < 24 hr ventricular failure, due to pheochromocytoma
Kondo <i>et al.</i> (18)	2000	1	1 FTC	1	2	Surgery	
Siperstein and Berber (19)	2001	88	6 MTC			RFA	
El Rassi <i>et al.</i> (20)	2002	34	1 MTC			Cytoreductive surgery, radiotherapy	22. died with recurrence of symptoms
Salvatori <i>et al.</i> (21)	2004	1	1 Hürthle	1	2.5	Hemihepatectomy	24, AFOD
Kelessis <i>et al.</i> (22)	2005	1	1 FTC	1	6	TSH-suppression, ¹³¹ I	14, died
Elvin <i>et al.</i> (23)	2005	42	2 MTC	2		RFA	38 (3–66)
Lorenz <i>et al.</i> (24)	2005	11	11 MTC			TACE	1–72, 3 patients died 6, 12, 24 after treatment
Kousou <i>et al.</i> (25)	2005	1	1 FTC	1.5		Surgery	24
Fromigüé <i>et al.</i> (26)	2006	12	12 MTC		3.8	TACE	Response duration 4–39

^aOnly thyroid liver metastasis patients.

FTC, follicular thyroid carcinoma; MTC, medullary thyroid carcinoma; TACE, transarterial chemoembolization; RFA, radiofrequency ablation; TSH, thyrotropin; AFOD, alive free of disease.

The precise role of RFA in the multimodality treatment of liver metastases from thyroid cancer needs to be further delineated, but the experience obtained with RFA in the treatment of other types of liver tumors will benefit the patient with liver metastases from thyroid carcinoma (37).

Disclosure Statement

No competing financial interests exist.

References

- Haq M, Harmer C 2005 Differentiated thyroid carcinoma with distant metastases at presentation: prognostic factors and outcome. *Clin Endocrinol (Oxf)* **63**:87–93.
- Hoie J, Stenwig AE, Kullmann G, Lindegaard M 1988 Distant metastases in papillary thyroid cancer. A review of 91 patients. *Cancer* **61**:1–6.
- Shaha AR, Shah JP, Loree TR 1997 Differentiated thyroid cancer presenting initially with distant metastasis. *Am J Surg* **174**:474–476.
- Kebebew E, Greenspan FS, Clark OH, Woeber KA, Grunwell J 2005 Extent of disease and practice patterns for medullary thyroid cancer. *J Am Coll Surg* **200**:890–896.
- Dupuy DE, Monchik JM, Decrea C, Pisharodi L 2001 Radiofrequency ablation of regional recurrence from well-differentiated thyroid malignancy. *Surgery* **130**:971–977.
- de Jong KP, 2007 Freeze or fry-cryoablation or radiofrequency ablation in liver surgery? *Nat Clin Pract Gastroenterol Hepatol* **4**:472–473.
- Ruers TJ, de Jong KP, Ijzermans JN 2005 Radiofrequency for the treatment of liver tumours. *Dig Surg* **22**:245–253.
- Berber E, Siperstein AE 2007 Perioperative outcome after laparoscopic radiofrequency ablation of liver tumors: an analysis of 521 cases. *Surg Endosc* **21**:613–618.
- Curley SA, Marra P, Beaty K, Ellis LM, Vauthey JN, Abdalla EK, Scaife C, Raut C, Wolff R, Choi H, Loyer E, Vallone P, Fiore F, Scordino F, De Rosa V, Orlando R, Pignata S, Daniele B, Izzo F 2004 Early and late complications after radiofrequency ablation of malignant liver tumors in 608 patients. *Ann Surg* **239**:450–458.
- Mulier S, Mulier P, Ni Y, Miao Y, Dupas B, Marchal G, De Wever I, Michel L 2002 Complications of radiofrequency coagulation of liver tumours. *Br J Surg* **89**:1206–1222.
- Hildebrand P, Leibecke T, Kleemann M, Mirow L, Birth M, Bruch HP, Burk C 2006 Influence of operator experience in

- radiofrequency ablation of malignant liver tumours on treatment outcome. *Eur J Surg Oncol* **32**:430–434.
12. Poon RT, Ng KK, Lam CM, Ai V, Yuen J, Fan ST, Wong J 2004 Learning curve for radiofrequency ablation of liver tumors: prospective analysis of initial 100 patients in a tertiary institution. *Ann Surg* **239**:441–449.
 13. Brown AP, Greening WP, McCready VR, Shaw HJ, Harmer CL 1984 Radioiodine treatment of metastatic thyroid carcinoma: the Royal Marsden Hospital experience. *Br J Radiol* **57**:323–327.
 14. Siperstein AE, Rogers SJ, Hansen PD, Gitomirsky A 1997 Laparoscopic thermal ablation of hepatic neuroendocrine tumor metastases. *Surgery* **122**:1147–1154.
 15. Curley SA, Izzo F, Delrio P, Ellis LM, Granchi J, Vallone P, Fiore F, Pignata S, Daniele B, Cremona F 1999 Radiofrequency ablation of unresectable primary and metastatic hepatic malignancies: results in 123 patients. *Ann Surg* **230**:1–8.
 16. Guglielmi R, Pacella CM, Dottorini ME, Bizzarri GC, Todino V, Crescenzi A, Rinaldi R, Panunzi C, Rossi Z, Colombo L, Papini E 1999 Severe thyrotoxicosis due to hyperfunctioning liver metastasis from follicular carcinoma: treatment with (131)I and interstitial laser ablation. *Thyroid* **9**:173–177.
 17. Machens A, Behrmann C, Dralle H 2000 Chemoembolization of liver metastases from medullary thyroid carcinoma. *Ann Intern Med* **132**:596–597.
 18. Kondo T, Katoh R, Omata K, Oyama T, Yagawa A, Kawaoi A 2000 Incidentally detected liver metastasis of well-differentiated follicular carcinoma of the thyroid, mimicking ectopic thyroid. *Pathol Int* **50**:509–513.
 19. Siperstein AE, Berber E 2001 Cryoablation, percutaneous alcohol injection, and radiofrequency ablation for treatment of neuroendocrine liver metastases. *World J Surg* **25**:693–696.
 20. El Rassi ZS, Ferdinand L, Mohsine RM, Berger F, Lombard-Bohas C, Boillot O, Partensky CC 2002 Primary and secondary liver endocrine tumors: clinical presentation, surgical approach and outcome. *Hepatogastroenterology* **49**:1340–1346.
 21. Salvatori M, Perotti G, Rufini V, Maussier ML, Summaria V, Fadda G, Troncone L 2004 Solitary liver metastasis from Hürthle cell thyroid cancer: a case report and review of the literature. *J Endocrinol Invest* **27**:52–56.
 22. Kelessis NG, Prassas EP, Dascalopoulou DV, Apostolikas NA, Tavernaraki AP, Vassilopoulos PP 2005 Unusual metastatic spread of follicular thyroid carcinoma: report of a case. *Surg Today* **35**:300–303.
 23. Elvin A, Skogseid B, Hellman P 2005 Radiofrequency ablation of neuroendocrine liver metastases. *Abdom Imaging* **30**:427–434.
 24. Lorenz K, Brauckhoff M, Behrmann C, Sekulla C, Ukkat J, Brauckhoff K, Gimm O, Dralle H 2005 Selective arterial chemoembolization for hepatic metastases from medullary thyroid carcinoma. *Surgery* **138**:986–993.
 25. Kouso H, Ikegami T, Ezaki T, Ishida T, Aimitsu S, Fujihara M, Mori M 2005 Liver metastasis from thyroid carcinoma 32 years after resection of the primary tumor: report of a case. *Surg Today* **35**:480–482.
 26. Fromigie J, de BT, Baudin E, Dromain C, Lebouilleux S, Schlumberger M 2006 Chemoembolization for liver metastases from medullary thyroid carcinoma. *J Clin Endocrinol Metab* **91**:2496–2499.
 27. van Tol KM, Hew JM, Jager PL, Vermey A, Dullaart RP, Links TP 2000 Embolization in combination with radioiodine therapy for bone metastases from differentiated thyroid carcinoma. *Clin Endocrinol (Oxf)* **52**:653–659.
 28. Durante C, Haddy N, Baudin E, Lebouilleux S, Hartl D, Travagli JP, Caillou B, Ricard M, Lumbroso JD, De VF, Schlumberger M 2006 Long-term outcome of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. *J Clin Endocrinol Metab* **91**:2892–2899.
 29. Joensuu H, Ahonen A 1987 Imaging of metastases of thyroid carcinoma with fluorine-18 fluorodeoxyglucose. *J Nucl Med* **28**:910–914.
 30. Grunwald F, Menzel C, Bender H, Palmedo H, Willkomm P, Ruhlmann J, Franckson T, Biersack HJ 1997 Comparison of 18FDG-PET with 131iodine and 99mTc-sestamibi scintigraphy in differentiated thyroid cancer. *Thyroid* **7**:327–335.
 31. Schluter B, Bohuslavizki KH, Beyer W, Plotkin M, Buchert R, Clausen M 2001 Impact of FDG PET on patients with differentiated thyroid cancer who present with elevated thyroglobulin and negative 131I scan. *J Nucl Med* **42**:71–76.
 32. Rubino C, De VF, Dottorini ME, Hall P, Schwartz C, Couette JE, Dondon MG, Abbas MT, Langlois C, Schlumberger M 2003 Second primary malignancies in thyroid cancer patients. *Br J Cancer* **89**:1638–1644.
 33. Subramanian S, Goldstein DP, Parlea L, Thabane L, Ezzat S, Ibrahim-Zada I, Straus S, Brierley JD, Tsang RW, Gafni A, Rotstein L, Sawka AM 2007 Second primary malignancy risk in thyroid cancer survivors: a systematic review and meta-analysis. *Thyroid* **17**:1277–1288.
 34. Liu DM, Salem R, Bui JT, Courtney A, Barakat O, Sergie Z, Atassi B, Barrett K, Gowland P, Oman B, Lewandowski RJ, Gates VL, Thurston KG, Wong CY 2005 Angiographic considerations in patients undergoing liver-directed therapy. *J Vasc Interv Radiol* **16**:911–935.
 35. Leung DA, Goin JE, Sickles C, Raskay BJ, Soulen MC 2001 Determinants of postembolization syndrome after hepatic chemoembolization. *J Vasc Interv Radiol* **12**:321–326.
 36. Elias D, Sideris L, Pocard M, Dromain C, De Baere T 2004 Intraductal cooling of the main bile ducts during radiofrequency ablation prevents biliary stenosis. *J Am Coll Surg* **198**:717–721.
 37. de Jong KP 2007 Review article: multimodality treatment of liver metastases increases suitability for surgical treatment. *Aliment Pharmacol Ther* **26**:161–169.

Address reprint requests to:

Koert P. de Jong, M.D., Ph.D.

Dept of HPB Surgery & Liver Transplantation

University Medical Center Groningen

University of Groningen

PO Box 30 001

9700 RB Groningen

The Netherlands

E-mail: k.p.de.jong@chir.umcg.nl