Microwave coagulation therapy of hepatocellular carcinoma

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ABSTRACT

Microwave coagulation therapy (MCT) is a relatively new method of tumor ablation compared to other minimally invasive local therapies for hepatocellular carcinoma (HCC). It is a thermal ablation modality based on the application of heat, potentially leading to larger ablation zones. In recent years, there is a steady increase in the application of this modality to the treatment of HCC because it offers several advantages in the management of tumors larger than 3 cm in diameter. This article reviews the advances in MCT for the treatment of HCC in recent years including its brief history, basic principles, main technical parameters, safety issues, current status in clinical application, limitations, and future perspectives.

Key words: Coagulation; hepatocellular carcinoma; microwave; treatment

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INTRODUCTION

Microwave is an ultra-short and high-frequency electromagnetic wave with a wavelength range between 1 and 1,000 mm, and a frequency range between 300 and 300,000 MHz.[1,2] The most common frequency of microwave used medically is 2,450, 915, and 433 MHz.[3,4] Hepatocellular carcinoma (HCC) is a common tumor with a dismal prognosis and development of novel therapies were needed for improving the treatment of this disease.[5] Microwave coagulation therapy (MCT) is a relatively novel method of tumor ablation compared with other minimally invasive local therapies for HCC such as high-intensity focused ultrasound, irreversible electroporation, laparoscopic liver resection, percutaneous ethanol injection, radiofrequency ablation (RFA), and stereotactic body radiation therapy.[6] This treatment method offers an easy-to-perform alternative option either in a percutaneous, laparoscopic or open surgical procedure.[7,8] In recent years, MCT has attracted increasing interests from clinicians for the treatment of HCC because this method provides the advantages of minimal invasiveness and safety in humans.[9]

This paper reviews the advances in using MCT for the treatment of HCC in recent years, with emphasis on the basic principles, and perspectives of this treatment modality for future research.

BRIEF HISTORY

In the late 1970s, some surgeons began to use microwave coagulation for the purpose of intra-operational hemostasis and tissue cutting when they found that as soon as the temperature in the target area exceeded 60 °C the heat will cause tissue solidification followed by cellular death.[10] In 1988, the first experiment of microwave coagulation

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for tumor inactivation was conducted successfully in the Second Department of Surgery, Kurume University Hospital in Fukuoka City, Japan.[11] Soon, successful use of microwave coagulation was reported throughout Japan, with large patient cohorts, multiple heating sessions, treating tumors with larger diameters, combination use with other ablation modalities, and review and management of side-effects.[12] A recent study reported the long-term efficacy results of surgical MCT for the treatment of 60 cases of unresectable HCC in the Kyushu Medical Center, National Hospital Organization, Fukuoka, Japan. The 1-, 3-, and 5-year survival rates were 93.9%, 53.8%, and 43.1%, respectively, almost the same as the results of palliative surgical resection.[13] In April 1996, MCT was included in the coverage list of Japanese Medical Insurance, which contributed to the advancement in the research on MCT for the treatment of HCC in Japan.[14]

In the 1990s, MCT was gradually accepted in other regions of the world for the treatment of HCC.[8]

BASIC PRINCIPLES

The fundamental principle of MCT is based on the facts that tumor tissues are more sensitive to heat than the adjacent normal tissues, and that microwave heat can be controllably delivered to the tumor tissues.[15] Compared with normal tissue, tumor tissues have low blood flow and extra-cellular pH value, as proven by experiments showing that the blood flow volume in murine HCC tissue is only 5% of that in normal liver tissue.[16] When a tumor is irradiated with microwave energy, the heat will make the blood flow stagnant at the local area.[17] When the temperature in tumor tissue goes up to 42-45 °C, the blood flow in the tumor stops, cancer cells become anoxic, mitochondria in cancer cells show vacuolation, resulting in the cessation of intra-cellular respiration, apoptosis, heat fixation, and death of cells.[12,18,19]

When the local temperature reaches 60 °C and above, tumor tissues will be immediately coagulated and damaged by the effects of thermal treatment.[20] A controllable temperature range of 60-120 °C can be presented rapidly to the target area by the treatment system.[21] During the procedure of MCT, a specially made needle is initially inserted into the center of tumor. The tip of the needle contains a point acting as an emission antenna.[22] The system includes an electric device that produces microwave energy forming a magnetic field around the point of the antenna.[23] The magnetic field makes nearby molecules spin and vibrate in very high velocity with resultant hyperthermia in the local area.[24,25] This is called the thermal effect of microwave antenna radiation.[26] Because energy density is very high in the area, protein will be coagulated by the heat swiftly in the contacted tissues leading to immediate degenerative necrosis of local tissue, which can be better evaluated using the histochemical method.[27] MCT is non-carbonizing, non-spattering, minimally invasive, and wound controllable.[28] With these advantages, this method is now widely used in coagulation therapies including dermatology, gynecology, stomatology, and otorhinolaryngology.[29,30]

Cool-tip microwave therapy apparatus incorporates a microcomputer, which automatically operates the system.[31] Electrical resistance, current, and power of the system are regulated automatically during the entire course of treatment.[32] The technique of cool recycling solved the problems of inappropriately high temperature in the rod antenna and a limited coagulation area that the conventional microwave systems had.[4] The new systems enhanced the operational safety, expanded therapeutic indications, improved the patients' quality-of-life, and post-operational survival.[17,33]

MCT for the treatment of tumors is now being investigated its potential to enhance host resistance to malignancies. This was resulted from reports of incidental observations showing spontaneous regression of remote metastasis after thermal ablation.[34] On one hand, microwave coagulation results in irreversible coagulation necrosis of tumor cells through the thermal effect;[35] on the other hand, the coagulated tumor tissue that retained in the body will stimulate the host to enhance its systemic immunity against cancer with consequent resistance to viable allogenic and heterogenic cancer cells.[36] Animal experiments demonstrated that in mice model of H22 implanted advanced HCC, intra-tumoral CD8+ cells increased remarkably in the MCT group compared to that in the surgery alone group. This provided supporting evidence for the immune enhancement by the coagulated tumor tissue that retained in the local area.[37,38] Studies showed that the local density of lymphocytes infiltration is closely related to the prognosis of patients with some cancer, that is, a higher density of intra-tumoral and peri-tumoral lymphocytes infiltration, like CD8+, is predictive of a better patient outcome.[39]

EQUIPMENT

Microwave ablation system

At present, the MCT systems with water-cool shaft or antenna are more commonly used in the clinic for the treatment of HCC.[4,25] All systems are equipped with flexible low-loss power cables and a surface coating microwave antenna of 15 gauges.[7,40] The tip of the needle-like antenna is not insulated and is exposed to the tissue to be ablated.[7] Electromagnetic microwaves are emitted by the microwave generator and will stimulate the water molecules in the neighboring tissue to induce heat and abrasion, resulting in coagulation necrosis of tissue.[12,19]

The technique of cool recycling makes the temperature in the antenna shaft below 37 °C to avoid pain at the puncture site of the patient undergoing MCT.[41] Coagulation temperature in the ablation area is precisely controlled by monitoring devices.[25] Two modes of thermometry are used simultaneously during the procedure. Thermometers are installed both in and outside the rod antenna. A warning temperature is set by the operator to ensure the safety of the patient.[42]

For ablation of larger tumors, two to three microwave antenna needles can be used at the same time to produce maximum coagulation area.[43] Simultaneous use of two antenna needles could not be simply regarded as a linear superposition of two solitary thermal fields, because the interaction between two thermal fields constitutes a spherical coagulation area that is significantly greater than the coagulation area when two needles are used separately with the same power and time period.[44] The mode of impulse transmission enhances the depth of microwave penetration and contributes to the increase in coagulation area and the decrease in tissue carbonization.[45]

Parameters

Most systems use 2,450 MHz as the working frequency for tumor destruction.[4,12] For MCT, the higher the frequency, the more powerful the instant energy, but the weaker the penetrating power.[46] Thus, the 2,450 MHz microwave is usually used for MCT because of the advantage of its powerful instant energy while the 915 and 433 MHz microwaves with strong penetration are used for thermotherapy of other diseases.[3,4] The novel dual-band systems have two working frequencies including 2,450 and 915 MHz.[47] The 915 MHz microwave creates a remarkably larger area of ablation and is suitable for one-time ablation of large tumors *in-situ* because this frequency produces double depth of penetration in tissues compared with that produced by the 2,450 MHz microwave.[48] The output power for ablation is usually set at 40-80 W.[4] Microwave with high power and high frequency (135 W, 2.45 GHz) has been used in the animal study for producing large ablation areas in short time periods.[28] Power and time period for coagulation are determined on the basis of tumor size.[9] With tumor sizes ranging from 3 to 5 cm in diameter, microwave power for ablation is set at 50-60 W for 5-15 min;[4] with tumors over 5 cm in diameter, two needles are used simultaneously.[25]

Image guidance modalities

MCT for the treatment of HCC can be used in an open surgery procedure or in a percutaneous approach.[7] The surgical use of MCT for HCC is performed under the monitor of direct visualization or image guidance modalities like ultrasound Type B.[13] After verification of the tumor dimensions, the rod antenna is inserted into the tumor for coagulation.[17]

When a percutaneous approach is taken, there are more choices regarding image guidance modalities including ultrasound, X-ray fluoroscopy, computed tomography, and magnetic resonance image (MRI).[48] Among them, ultrasound and MRI offer radiation-free alternatives to image guidance, and MRI provides high-resolution and multi-planar images.[49] However, MRI-compatible microwave electrode and accessories must be prepared.[50]

CURRENT STATUS IN CLINICS

Cool-tip MCT for the treatment of HCC has several beneficial characteristics in clinical application, as well as microwave systems, with an electrode with saline passing through and injected continuously into the target area.[51] Direct puncture of lesions makes the operational procedure relatively simple and easy.[17]

General anesthesia is necessary in a surgical MCT procedure while in a percutaneous approach local anesthesia is commonly used with venous analgesics such as pethidine and sedatives as additional pain-killers.[52] Under the guidance of a selected image modality, the tumor is localized, and the needle is directly inserted into the tumor with the needle tip placed at a calculated point.[11] The ablated area is assessed through real-time images to find tumor tissues that are still viable.[40] Repeated ablation procedures are performed to ensure no viable tumor tissue remained at the site.[53]

MCT is different from RFA, which has a longer history and has acquired a broad acceptance as a first-line treatment option for early HCC.[54] However, RFA has the limitations associated with treating large tumors and tumors at high-risk locations.[22] MCT has the advantage of treating larger tumors and is regarded as a valuable alternative to RFA. Compared with other available modalities and devices for thermal ablation, MCT offers the advantages of greater volume of tumor ablation, consistently greater temperatures in the ablation area, better analysis of heat transfer, and shorter ablation sessions.[7]

A recent single-center study reported the treatment outcome of MCT for the treatment of 719 consecutive HCC patients in more than 15 years. The 1-, 3-, 5-, 7-, and 10-year overall survival rates of all 719 patients were 97.7%, 79.8%, 62.1%, 45.3%, and 34.1%, respectively. One-third of the patients had Child-Pugh Class B cirrhosis, and a portion of them had multiple tumors. Compared with another group of 34 patients treated with hepatic resection during the same period, no significant difference was found in overall survival, disease-free survival or local recurrence rates between the two groups. Based on the results of this study, the researchers proposed that MCT should be considered as one of the first options for the treatment of HCC.[55]

ADVERSE EFFECTS

The adverse effects of MCT for the treatment of HCC are various and can be divided into mild, moderate, and severe categories.[9] Mild adverse effects include slight local pain at the puncture site, sensation of heat, bodily uneasiness felt during the coagulation process, and slightly abnormal results from a blood test such as mild elevation of blood urea nitrogen and creatine levels.[12] Post-ablation syndrome can be mild to moderate and is characterized by fever, chills, malaise, local pain, and nausea.[56] Moderate adverse effects comprise bacterial infection, diaphragmatic muscle injury, skin burns, tumor implantation in needle pass, pleuritis, hydrothorax, hemothorax, continuous discharge of necrotic tissue, local implantation of tumor cells, and hematoma under the hepatic capsule.[57,58]

However, severe adverse effects happen occasionally during and after the procedures of MCT such as anesthetic accident, colonic leakage, severe arrhythmia, damage to the biliary tract, abdominal bleeding, diaphragm injury, acute renal failure, generalized intra-peritoneal seeding of HCC, and serious infection.[59-63] Severe adverse effects can be fatal and need emergency treatment to save the patient.[63]

The rate of side-effects do not differ significantly from other interventions, but significantly more treatment sessions are needed with percutaneous microwave coagulation to achieve complete tumor ablation, which theoretically increases the risk of potential side-effects.[62] Most adverse effects can be controlled with timely and careful management. Safety precautions must be taken to avoid or reduce the occurrence of adverse effects including cautious indication selection, well-designed puncture route, the appropriate extent of coagulation, and sufficient peri-operational management.[59,61]

LIMITATIONS AND PERSPECTVES

It is now proven that MCT is a safe and effective method for the treatment of HCC and the condition of spontaneous rupture of HCC tumors.[64] With the advancement of techniques and equipment for clinical application of microwave, MCT will be promoted more widely and used more extensively than before, through the approaches of laparoscopy or image-guided percutaneous puncture.[20] Regrettably, intra-hepatic recurrence of HCC is common because MCT is indicated as a substitute for surgical resection for patients with advanced liver cirrhosis.[53] Nevertheless, MCT can be readily repeated when there is a recurrence of HCC.[53] Overall, MCT is great for cost-effectiveness compared with other treatment for HCC like sorafenib.[65]

The characteristic feature of MCT for the treatment of HCC is the conversion of energy by tumor tissue from the microwave into heat with resultant coagulation necrosis of the tissue.[25,26] MCT will be more promoted because it not only effectively kills HCC cells, but also preserves normal liver tissue to a great extent.[59]

Image artifacts must be recognized and carefully distinguished from anatomical structure to ensure the accuracy of the location of the needle tip.[66] Some issue will be further investigated like the impact of MCT on the systemic immunity of the HCC patient.[34] At present, there are very few reports on the association of MCT used in the treatment of HCC and its modification of patients' systemic immunity. Further investigations into this topic are warranted.

CONCLUSION

Microwaves can produce very high temperatures in very short time intervals. MCT is increasingly used in the treatment of HCC because it offers several advantages such as greater efficacy, minimal invasiveness, easy conduction, wider indications, and less adverse effects compared to other invasive methods. Overall, MCT for the treatment of HCC is a very promising technique to develop further. Sufficient pre-operative preparation, mastering the techniques of operation, and good collaboration between doctors, nurses, and patients are essential for enhancing therapeutic outcomes of HCC and reducing the incidence of side-effects. Investigations should be carried out to determine the modulation by MCT of both innate and adaptive immunity. Although MCT is still in its infancy, it has great promise for future use, especially with further improvements in the clinical implementation and technical developments.

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Conflict of interest
There is no conflict of interest.

REFERENCES

1. Inoue Y, Matsumura T, Hazumi M, Lee AT, Okamura T, Suzuki A, Tomaru T, Yamaguchi H. Cryogenic infrared filter made of alumina for use at millimeter wavelength. *Appl Opt* 2014;53:1727-33.
2. Lubner MG, Brace CL, Ziemlewicz TJ, Hinshaw JL, Lee FT Jr. Microwave ablation of hepatic malignancy. *Semin Intervent Radiol* 2013;30:56-66.
3. Huo X, Jow UM, Ghovanloo M. Radiation characterization of an intra-oral wireless device at multiple ISM bands: 433 MHz, 915 MHz, and 2.42 GHz. *Conf Proc IEEE Eng Med Biol Soc* 2010;2010:1425-8.
4. Zhou W, Liang M, Pan H, Liu X, Jiang Y, Wang Y, Ling L, Ding Q, Wang S. Comparison of ablation zones among different tissues using 2450-MHz cooled-shaft microwave antenna: results in *ex vivo* porcine models. *PLoS One* 2013;8:e71873.
5. Blechacz B, Mishra L. Hepatocellular carcinoma biology. *Recent Results Cancer Res* 2013;190:1-20.
6. Li D, Kang J, Golas BJ, Yeung VW, Madoff DC. Minimally invasive local therapies for liver cancer. *Cancer Biol Med* 2014;11:217-36.
7. Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: principles and applications. *Radiographics* 2005;25 Suppl 1:S69-83.
8. Yanaga K. Current status of hepatic resection for hepatocellular carcinoma. *J Gastroenterol* 2004;39:919-26.
9. Inokuchi R, Seki T, Ikeda K, Kawamura R, Asayama T, Yanagawa M, Umehara H, Okazaki K. Percutaneous microwave coagulation therapy for hepatocellular carcinoma: increased coagulation diameter using a new electrode and microwave generator. *Oncol Rep* 2010;24:621-7.
10. Segawa T, Tsuchiya R, Furui J, Izawa K, Tsunoda T, Kanematsu T. Operative results in 143 patients with hepatocellular carcinoma. *World J Surg* 1993;17:663-7; discussion 668.
11. Onizuka Y. Development of a microwave-induced hyperthermia system with multiple applicators. *Kurume Med J* 1989;36:189-97.
12. Matsuda T, Kikuchi M, Tanaka Y, Hiraoka M, Nishimura Y, Akuta K, Takahashi M, Abe M, Fuwa N, Morita K. Clinical research into hyperthermia treatment of cancer using a 430 MHz microwave heating system with a lens applicator. *Int J Hyperthermia* 1991;7:425-40.
13. Itoh S, Ikeda Y, Kawanaka H, Okuyama T, Kawasaki K, Eguchi D, Korenaga D, Takenaka K. Efficacy of surgical microwave therapy in patients with unresectable hepatocellular carcinoma. *Ann Surg Oncol* 2011;18:3650-6.
14. Matsuda T. The present status of hyperthermia in Japan. *Ann Acad Med Singapore* 1996;25:420-4.
15. Meyer JL. The clinical efficacy of localized hyperthermia. *Cancer Res* 1984;44:s4745-51.
16. Frérart F, Sonveaux P, Rath G, Smoos A, Meqor A, Charlier N, Jordan BF, Saliez J, Noël A, Dessy C, Gallez B, Feron O. The acidic tumor microenvironment promotes the reconversion of nitrite into nitric oxide: towards a new and safe radiosensitizing strategy. *Clin Cancer Res* 2008;14:2768-74.
17. Sommer CM, Sommer SA, Sommer WO, Zelzer S, Wolf MB, Bellemann N, Meinzer HP, Radeleff BA, Stampfl U, Kauczor HU, Pereira PL. Optimisation of the coagulation zone for thermal ablation procedures: a theoretical approach with considerations for practical use. *Int J Hyperthermia* 2013;29:620-8.
18. Nan Q, Zheng W, Fan Z, Liu Y, Zeng Y. Analysis to a critical state of thermal field in microwave ablation of liver cancer influenced by large vessels. *Int J Hyperthermia* 2010;26:34-8.
19. Matylevitch NP, Schuschereba ST, Mata JR, Gilligan GR, Lawlor DF, Goodwin CW, Bowman PD. Apoptosis and accidental cell death in cultured human keratinocytes after thermal injury. *Am J Pathol* 1998;153:567-77.
20. Spliethoff JW, Tanis E, Evers DJ, Hendriks BH, Prevoo W, Ruers TJ. Monitoring of tumor radio frequency ablation using derivative spectroscopy. *J Biomed Opt* 2014;19:97004.
21. Szmigielski S, Sobczynski J, Sokolska G, Stawarz B, Zielinski H, Petrovich Z. Effects of local prostatic hyperthermia on human NK and T cell function. *Int J Hyperthermia* 1991;7:869-80.
22. Liang P, Wang Y. Microwave ablation of hepatocellular carcinoma. *Oncology* 2007;72 Suppl 1:124-31.
23. Zastrow E, Hagness SC, Van Veen BD. 3D computational study of non-invasive patient-specific microwave hyperthermia treatment of breast cancer. *Phys Med Biol* 2010;55:3611-29.
24. Guan YS, Liu Y. Interventional treatments for hepatocellular carcinoma. *Hepatobiliary Pancreat Dis Int* 2006;5:495-500.
25. Lu Y, Nan Q, Li L, Liu Y. Numerical study on thermal field of microwave ablation with water-cooled antenna. *Int J Hyperthermia* 2009;25:108-15.
26. Lopresto V, Pinto R, Cavagnaro M. Experimental characterisation of the thermal lesion induced by microwave ablation. *Int J Hyperthermia* 2014;30:110-8.
27. Liu DQ, Lu MD, Tan JF, Wang Z, Zhou ZX. Microwave coagulation at different temperatures for hepatocellular carcinoma management: efficacy evaluation by enzyme histochemical staining. *Nan Fang Yi Ke Da Xue Xue Bao* 2006;26:1149-51. (in Chinese)
28. Lubner MG, Hinshaw JL, Andreano A, Sampson L, Lee FT Jr, Brace CL. High-powered microwave ablation with a small-gauge, gas-cooled antenna: initial *ex vivo* and *in vivo* results. *J Vasc Interv Radiol* 2012;23:405-11.
29. Jovanović-Ignjatić Z, Raković D. A review of current research in microwave resonance therapy: novel opportunities in medical treatment. *Acupunct Electrother Res* 1999;24:105-25.
30. Shi RJ, Tang JY, Wang QL. The application of microwave coagulating instrument in otolaryngology and stomatology (report of 157 cases). *Shanghai Kou Qiang Yi Xue* 2000;9:58-9. (in Chinese)
31. Jiao D, Qian L, Zhang Y, Zhang F, Li C, Huang Z, Zhang L, Zhang W, Wu P, Han X, Duan G, Han J. Microwave ablation treatment of liver cancer with 2,450-MHz cooled-shaft antenna: an experimental and clinical study. *J Cancer Res Clin Oncol* 2010;136:1507-16.
32. Sommer CM, Arnegger F, Koch V, Pap B, Holzschuh M, Bellemann N, Gehrig T, Senft J, Nickel F, Mogler C, Zelzer S, Meinzer HP, Stampfl U, Kauczor HU, Radeleff BA. Microwave ablation of porcine kidneys *in vivo*: effect of two different ablation modes ("temperature control" and "power control") on procedural outcome. *Cardiovasc Intervent Radiol* 2012;35:653-60.
33. Crocetti L, Bozzi E, Faviana P, Cioni D, Della Pina C, Sbrana A, Fontanini G, Lencioni R. Thermal ablation of lung tissue: *in vivo* experimental comparison of microwave and radiofrequency. *Cardiovasc Intervent Radiol* 2010;33:818-27.
34. Haen SP, Pereira PL, Salih HR, Rammensee HG, Gouttefangeas C. More than just tumor destruction: immunomodulation by thermal ablation of cancer. *Clin Dev Immunol* 2011;2011:160250.
35. Sofocleous CT, Sideras P, Petre EN. "How we do it" - a practical approach to hepatic metastases ablation techniques. *Tech Vasc Interv Radiol* 2013;16:219-29.
36. Han XJ, Dong BW, Liang P, Yu XL, Yu DJ. Local cellular immune response induced by ultrasound-guided tumor bed superantigen injection after percutaneous microwave coagulation therapy for liver cancer. *Zhonghua Zhong Liu Za Zhi* 2009;31:602-6. (in Chinese)
37. Nie Y, Chen Y, Mou Y, Weng L, Xu Z, Du Y, Wang W, Hou Y, Wang T. Low frequency magnetic fields enhance antitumor immune response against mouse H22 hepatocellular carcinoma. *PLoS One* 2013;8:e72411.
38. Gravante G, Sconocchia G, Ong SL, Dennison AR, Lloyd DM. Immunoregulatory effects of liver ablation therapies for the treatment of primary and metastatic liver malignancies. *Liver Int* 2009;29:18-24.
39. Paulson KG, Iyer JG, Simonson WT, Blom A, Thibodeau RM, Schmidt M, Pietromonaco S, Sokil M, Warton EM, Asgari MM, Nghiem P. CD8+lymphocyte intratumoral infiltration as a stage-independent predictor of Merkel cell carcinoma survival: a population-based study. *Am J Clin Pathol* 2014;142:452-8.
40. Wolf FJ, Aswad B, Ng T, Dupuy DE. Intraoperative microwave ablation

of pulmonary malignancies with tumor permittivity feedback control: ablation and resection study in 10 consecutive patients. *Radiology* 2012;262:353-60.

41. Di Vece F, Tombesi P, Ermili F, Maraldi C, Sartori S. Coagulation areas produced by cool-tip radiofrequency ablation and microwave ablation using a device to decrease back-heating effects: a prospective pilot study. *Cardiovasc Intervent Radiol* 2014;37:723-9.
42. Jacobsen S, Klemetsen Ø. Improved detectability in medical microwave radio-thermometers as obtained by active antennas. *IEEE Trans Biomed Eng* 2008;55:2778-85.
43. Phasukkit P, Tungjitkusolmun S, Sangworasil M. Finite-element analysis and *in vitro* experiments of placement configurations using triple antennas in microwavehepatic ablation. *IEEE Trans Biomed Eng* 2009;56:2564-72.
44. Chiang J, Hynes KA, Bedoya M, Brace CL. A dual-slot microwave antenna for more spherical ablation zones: *ex vivo* and *in vivo* validation. *Radiology* 2013;268:382-9.
45. Haines DE. Current and future modalities of catheter ablation for the treatment of cardiac arrhythmias. *J Invasive Cardiol* 1992;4:291-9.
46. Chou CK. Evaluation of microwave hyperthermia applicators. *Bioelectromagnetics* 1992;13:581-97.
47. Sneed PK, Matsumoto K, Stauffer PR, Fike JR, Smith V, Gutin PH. Interstitial microwave hyperthermia in a canine brain model. *Int J Radiat Oncol Biol Phys* 1986;12:1887-97.
48. Liu FY, Yu XL, Liang P, Wang Y, Zhou P, Yu J. Comparison of percutaneous 915 MHz microwave ablation and 2450 MHz microwave ablation in large hepatocellular carcinoma. *Int J Hyperthermia* 2010;26:448-55.
49. Keserci BM, Kokuryo D, Suzuki K, Kumamoto E, Okada A, Khankan AA, Kuroda K. Near-real-time feedback control system for liver thermal ablations based on self-referenced temperature imaging. *Eur J Radiol* 2006;59:175-82.
50. Kurumi Y, Tani T, Naka S, Shiomi H, Shimizu T, Abe H, Endo Y, Morikawa S. MR-guided microwave ablation for malignancies. *Int J Clin Oncol* 2007;12:85-93.
51. Umehara H, Seki T, Inokuchi R, Tamai T, Kawamura R, Asayama T, Ikeda K, Okazaki K. Microwave coagulation using a perfusion microwave electrode: preliminary experimental study using *ex vivo* and *in vivo* liver. *Exp Ther Med* 2012;3:214-20.
52. Gazzera C, Fonio P, Faletti R, Dotto MC, Gobbi F, Donadio P, Gandini G. Role of paravertebral block anaesthesia during percutaneous transhepatic thermoablation. *Radiol Med* 2014;119:549-57.
53. Shiina S. Image-guided percutaneous ablation therapies for hepatocellular carcinoma. *J Gastroenterol* 2009;44 Suppl 19:122-31.
54. Kim YS, Lim HK, Rhim H, Lee MW. Ablation of hepatocellular carcinoma. *Best Pract Res Clin Gastroenterol* 2014;28:897-908.
55. Takami Y, Ryu T, Wada Y, Saitsu H. Evaluation of intraoperative microwave coagulo-necrotic therapy (MCN) for hepatocellular carcinoma: a single center experience of 719 consecutive cases. *J Hepatobiliary Pancreat Sci* 2013;20:332-41.
56. Andreano A, Galimberti S, Franza E, Knavel EM, Sironi S, Lee FT, Meloni MF. Percutaneous microwave ablation of hepatic tumors: prospective evaluation of postablation syndrome and postprocedural pain. *J Vasc Interv Radiol* 2014;25:97-105.e1-2.
57. Kosugi C, Furuse J, Ishii H, Maru Y, Yoshino M, Kinoshita T, Konishi M, Nakagohri T, Inoue K, Oda T. Needle tract implantation of hepatocellular carcinoma and pancreatic carcinoma after ultrasound-guided percutaneous puncture: clinical and pathologic characteristics and the treatment of needle tract implantation. *World J Surg* 2004;28:29-32.
58. Yu F, Wang K, Yan ZL, Zhang XF, Li J, Dong H, Cong WM, Shi LH, Shen F, Wu MC. Clinical study of 169 patients with hepatic angiomyolipoma. *Zhonghua Wai Ke Za Zhi* 2010;48:1621-4. (in Chinese)
59. Sato M, Tokui K, Watanabe Y, Lee T, Kohtani T, Nezu K, Kawachi K, Kito K, Sugita A, Ueda N. Generalized intraperitoneal seeding of hepatocellular carcinoma after microwave coagulation therapy: a case report. *Hepatogastroenterology* 1999;46:2561-4.
60. Takahashi Y, Shibata T, Shimano T, Kitada M, Niinobu T, Ikeda K, Takami M, Inoue Y, Ishida T. A case report of intra-thoracic biliary fistula after percutaneous microwave coagulation therapy. *Gan To Kagaku Ryoho* 2000;27:1850-3. (in Japanese)
61. Ajisaka H, Miwa K. Acute respiratory distress syndrome is a serious complication of microwave coagulation therapy for liver tumors. *Am J Surg* 2005;189:730-3.
62. Ding J, Jing X, Liu J, Wang Y, Wang F, Wang Y, Du Z. Complications of thermal ablation of hepatic tumours: comparison of radiofrequency and microwave ablative techniques. *Clin Radiol* 2013;68:608-15.
63. Zhang H, Fan W, Huang Z, Zhang L, Song Z, Qi H. Computed tomography-guided percutaneous microwave ablation for diaphragm-abutting liver tumors: assessments of safety and short-term therapeutic efficacies. *Zhonghua Yi Xue Za Zhi* 2014;94:1313-7. (in Chinese)
64. Takao Y, Yoshida H, Mamada Y, Taniai N, Bando K, Tajiri T. Transcatheter hepatic arterial embolization followed by microwave ablation for hemobilia from hepatocellular carcinoma. *J Nippon Med Sch* 2008;75:284-8.
65. Cohen GS, Black M. Multidisciplinary management of hepatocellular carcinoma: a model for therapy. *J Multidiscip Healthc* 2013;6:189-95.
66. Pan WD, Zheng RQ, Nan L, Fang HP, Liu B, Tang ZF, Deng MH, Xu RY. Ultrasound-guided percutaneous microwave coagulation therapy with a "cooled-tip needle" for the treatment of hepatocellular carcinoma adjacent to the gallbladder. *Dig Dis Sci* 2010;55:2664-9.