



Capsule and Ablation Tract Related Features of Local Recurrence in Ultrasound Guided Microwave Ablation of Liver Metastases

Karaciğer Metastazlarında Ultrason Eşliğinde Yapılan Mikrodalga Ablasyon Tedavisi Sonrası Gelişen Lokal Nüksün Kapsül ve Ablasyon Traktı ile İlişkisi

Serkan Arıbal¹, Eyup Kaya¹

Abstract

Aim: We aimed to evaluate the capsule and ablation tract related features of local recurrence after ultrasound (US) guided percutaneous microwave ablation (MWA) of the liver metastases independently.

Methods: Between February 2016 and December 2019, 101 patients with US-guided percutaneous MWA of the liver metastases were analyzed. Nineteen patients having thirty-two ablated lesions with local recurrence (LR) were included in the study. Histopathologic type of tumor, pre-ablative features of the lesions and the ablation procedure data were noted. Tumor size, the closest distance between the lesion and the liver capsule was measured. The site of LR related to the liver capsule and related to ablation tract and the shape of the LR were noted.

Results: The median time of LR was 8.46±4.54 months (range, 3-20). The patient (n=19) and the ablated lesion (n=32) depended LR rates were 19% and 20% respectively. All LR of the parenchymal localized metastatic lesions originated from either tip or the side of the ablation tract and this relationship was found as statistically significant (p=0.035). No statistically significant relationship was found between vessel closeness and shape of LR (p=0.704) and between the site and the shape of LR (p=0.683).

Conclusion: We demonstrated that the LR arising from parenchymal localized metastatic lesions were from either the tip or the side of the ablation tract. We also defined some features of LR related to the ablation tract and liver capsule independently.

Keywords: Local recurrence, microwave ablation, ablation tract, liver metastasis, liver capsule

Öz

Amaç: Çalışmamızda karaciğer metastazlarında ultrason eşliğinde yapılan mikrodalga ablasyon tedavisi sonrası gelişen lokal nüksün karaciğer kapsülü ve ablasyon traktı ile ilgili özelliklerinin değerlendirilmesi amaçlanmıştır. **Yöntemler:** Şubat 2016 ile Aralık 2019 tarihleri arasında mevcut karaciğer metastazına US rehberliğinde perkutan mikrodalga abalasyon tedavisi yapılan 101 olgu retrospektif olarak değerlendirildi. Toplam 32 lokal nükse sahip ablate lezyonu bulunan 19 hasta çalışmaya dahil edildi. Metastazların histopatolojik tipleri, ablasyon öncesi özellikleri ve ablasyon işlemine ait bilgiler not edildi. Tümörün boyutları ve tümör ile karaciğer kapsülü arasındaki en kısa mesafe ölçüldü. Lokal nüksün karaciğer kapsülüne ve ablasyon traktına göre tarafı ve yerleşimi ile şekil özellikleri değerlendirildi.

Bulgular: Ortaça lokal nüksüresi 8.46±4.54 ay (3-20 aralığında) olarak bulundu. Hasta ve lezyon bağımlı lokal nüks oranları sırasıyla 19% ve 20% idi. Parankim içi yerleşimli lezyonlara ait lokal nükslerin tümü ablasyon traktının ucu ya da yanında yerleşimli olarak bulundu ve bu ilişki istatistiksel olarak anlamlıydı (p=0.035). Damar yakınlığı ile lokal nüksün şekli ve lokal nüksün tarafı ile şekli arasında istatistiksel olarak anlamlı ilişki saptanmadı (sırasıyla p=0.704 ve 0.683).

Sonuç: Çalışmamızda parankimal yerleşimli lezyonlardan gelişen lokal rekürrensins hepsinin ablasyon traktının uç ve yan kesimlerinden geliştiği ortaya konulmuştur. Ayrıca lokal rekürrensins karaciğer kapsülü ve ablasyon traktı ile ilişkili bir takım özellikleri ve bu bulguların birbiri ile ilgili ilişkileri ortaya konuldu.

Anahtar Kelimeler: Lokal rekürrens, mikrodalga ablasyon, ablasyon trakt, karaciğer metastazları, karaciğer kapsülü

¹ University of Health Science, Prof. Dr. Cemil Taşcıoğlu State Hospital, Department of Radiology, Istanbul, Turkey.



SA: 0000-0002-0338-2652

EK: 0000-0003-4927-5294

Ethics Committee Approval: The study was approved by Prof. Dr. Cemil Taşcıoğlu State Hospital ethical authority (02.06.2020/ No: 215).

Etik Kurul Onayı: Çalışma Prof. Dr. Cemil Taşcıoğlu Şehir Hastanesi etik komitesi tarafından onaylanmıştır (02.06.2020/ No: 215).

Conflict of Interest: No conflict of interest was declared by the authors.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support. **Finansal Destek:** Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Geliş Tarihi / Received: 07.08.2020

Kabul Tarihi / Accepted: 27.08.2020

Yayın Tarihi / Published: 31.08.2020

Sorumlu yazar / Corresponding author:

Serkan Arıbal

Adres/Address: Prof. Dr. Cemil TAŞCIOĞLU State Hospital, Department of Radiology, 34384 Şişli, Istanbul, Turkey.

e-posta: serkanaribal@gmail.com

Tel/Phone: +90 533 269 08 30

Fax: +90 212 314 55 55

Copyright © ACEM

Introduction

Because of being quite often site for the distant metastasis of the primary tumors, especially for colorectal metastasis (CRM), the liver takes an important place in the treatment strategies of cancer to have good long-term outcomes (1-3). Surgical resection is the first-line and the gold standard therapy for patients with liver metastasis (4,5). However, only one-fourth of the cases are deemed resectable at presentation (6). Apart from systemic therapies, local and regional treatment options have been a good alternative for these patients. When compared to surgery, locoregional procedures are minimally invasive treatment choices and the most prominent advantage over surgery is being a less adverse effect on liver functions by their hepatocyte sparing features. Nevertheless, the biggest disadvantage is their inferior local tumor control rates resulting recurrence (7).

There are many risk factors for local recurrence (LR) such as tumor size, histopathologic type, ablation zone, segmental distributions, presence of an adjacent vessel, ablation method used, described and analyzed in previous studies (8,9). As might be expected, subcapsular tumor localization is another significant and independent factor associated with LR (10,11). On the other hand, there are also a couple of studies suggesting that the subcapsular localization is not a significant factor for LR and poor survival rates (12,13). To the best of our knowledge, there is no study focused on the capsule and ablation tract features related to LR following the thermal ablation (TA) of liver metastasis.

The purpose of this study was to evaluate the capsule and ablation tract related features of local recurrence after ultrasound (US) guided percutaneous microwave ablation (MWA) of the liver metastases independently.

Material and methods

This retrospective study was approved by the local ethics committee. Informed consent has been obtained from all patients. It is confirmed by the author that the study is appropriate for the Declaration of Helsinki Standards.

Study Population: Between February 2016 and December 2019, 101 patients with US-guided percutaneous MWA of the liver metastases were analyzed with both their patient files including the whole follow-up information and all radiological images on local Picture Archiving and Communication System (PACS). All thermal ablation treatment decisions of the liver tumors are taken by the multidisciplinary local tumor board formed by the specialist in medical oncology, hepatopancreatobiliary surgery, nuclear medicine, radiation oncology, radiology and interventional radiology. The only inclusion criterion is to be having at least one lesion with MWA after a single session of TA. Among them, nineteen patients having thirty-two ablated lesions with LR were included in the study. Seventy-one patients having one hundred and five ablated lesions with no LR, seven patients having ten ablated lesions with residual tumor rather than LR after MWA and four patients having six ablated lesions with a short follow-up period (< 3 months after MWA) due to non-follow up or death are excluded from the study population. In addition, the patients in the study group had also four thermal ablated lesions with no evidence of LR (Figure 1).

Pre-procedural Assessments: Every single patient decided to perform percutaneous TA was referred to interventional radiology service for further evaluation. The

patients underwent ultrasound and doppler ultrasound evaluation to plan the ablation and the procedures accompanied by the

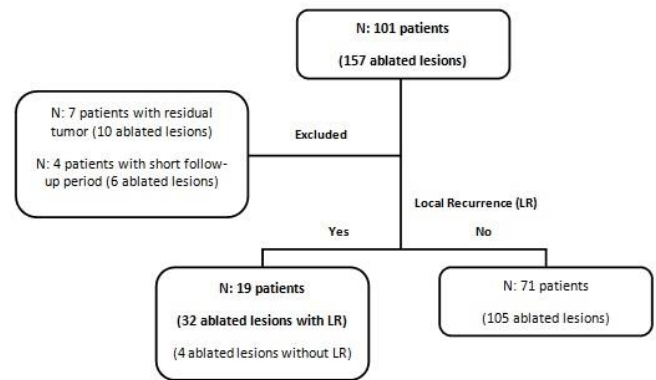


Figure 1: Study flow chart.

findings of contrast-enhanced (CE) triphasic liver computed tomography (CT) or dynamic CE liver magnetic resonance (MR) scans which were obtained within 1 month before the TA procedure. Identifications of metastases in the patients whose primary tumor was known were made according to imaging findings such as contrast wash-out throughout the dynamic series without any biopsy procedure. Depending on the localization of the tumor, the thermal ablation suitability criteria were accepted as follow: solitary tumors of up to 5 cm and up to 3 tumor measuring <3 cm. The general condition of the patients was evaluated according to Child-Pugh classification and Eastern Cooperative Oncology Group (ECOG) performance scale to make the final decision for the procedure. Additional findings such as ascites, adjacent structures (vascular, colon, gall bladder, etc.) were documented to plan all steps of procedures in detail. After exhaustive information about the TA procedure and taking some blood samples including whole blood count, bleeding and coagulation parameters, they were directed to anesthesia service for the convenience of anesthesia.

Thermal Ablation Procedure: All thermal ablation procedures were performed with percutaneous MWA using only US guidance under general anesthesia. 15-gauge electrodes with 2.45 GHz Solero and Acculis MWA generators (Angiodynamics, New York, USA) was the MWA systems used during the procedures. Aplio 500 ultrasound system (Toshiba Medical Systems Corporation, Tochigi, Japan) had been used with 3-6 Mhz convex or 4-9.2 Mhz linear array transducers for ablation guidance. In the presence of acid, percutaneous drainage was applied just before the procedure. Following the local and subcapsular anesthesia and a skin puncture, the ablation probe was advanced towards the center of the targeted lesion. Once the probe tip was positioned at the intended ablation zone, two interventional radiologists checked whether the lesion had been centralized or not from different plans by ultrasound probe maneuvers. After ensuring the probe centralization by consensus, the TA process was begun with general anesthesia. The ablation energy and duration were selected according to the targeted tumor ablation size and location using standard algorithms by aiming at least 5 mm of each margin around the tumor. Immediately after the ablation period was accomplished, the procedure was completed by performing tract ablation for the section up to the liver capsule.

Follow-up: All patients were followed by triphasic liver CT scans or dynamic CE MR imaging performed on the first day after ablation, quarterly in the first 2 years, and biannually thereafter for follow up. Besides, the US and Doppler US imaging were performed at the time of each follow-up admissions and patient files were examined in detail. LR was

defined as the pathologic contrast enhancement at any site of ablated lesion in the control CT or MR imaging after 3 months. Any lesion before this period was accepted as residual tumor rather than LR. We didn't perform biopsy procedure to make definitive diagnosis according to our hospital's tumor board decisions. In the case of suspicious imaging findings for LR, diffusion-weighted (DW) MR and Positron Emission Tomography (PET) scans were also applied.

Definitions and Data Obtaining: Age and gender of the patients were recorded. All ablated lesions were assessed prospectively in terms of the histopathologic type of primary tumor, pre-ablative tumor size and volume, post-ablative tumor size and volume at the first day after ablation and at the time of LR, presence of blood vessel proximity and the diameter of the vessel(s), liver segmental location, the closest distance to the liver capsule, type of LR, capsule and ablation tract related features of LR.

Histopathologic type of tumor, ablation procedure data, the segmental localization of the tumor according to Couinaud classification system and time of post-ablation LR were noted. Tumor size was measured in three dimensions; width (W), length (L) and height (H) using multiplanar reconstructed (MPR) CT or axial and coronal MR images and the volume (V) of the lesions was calculated using the following formula $V = W \times L \times H \times \pi/6$. The vessels closer than 10 mm to the lesions and their diameters were recorded. The closest distance in any image plan (axial, coronal or sagittal images) between the lesion and the liver capsule was measured. Subcapsular location was defined as a tumor lying within 10 mm of the liver capsule. Otherwise, it will be accepted as a parenchymal lesion. The site of LR related to the liver capsule was classified as capsular and noncapsular according to a straight line passing through the center of the lesion and parallel to the liver capsule (Figure 2A). The site of LR related to the ablation tract was classified as entry, tip and side (Figure 2B). Lastly, the shape of the LR was categorized into two patterns: nodular, crescentic (Figure 2C,D).

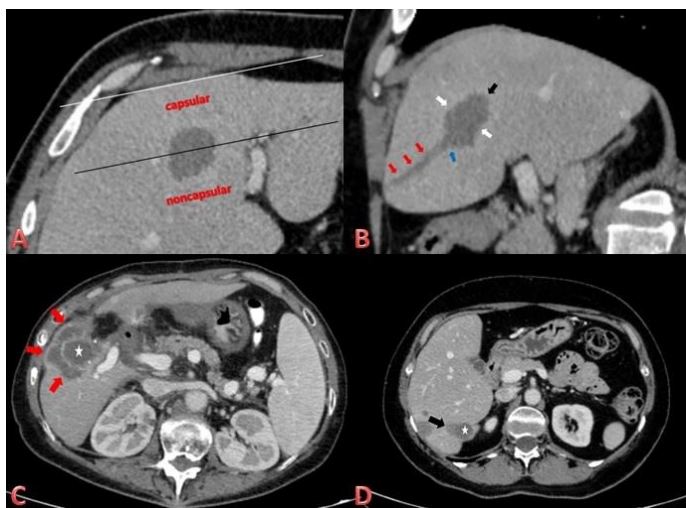


Figure 2: The classification of the local recurrence site as capsular and noncapsular according to liver capsule (A). The lesion was accepted as capsular side in case the large part of the LR was located within the capsular side of the straight line passing through the center of the lesion and parallel to the liver capsule. Otherwise it was accepted as noncapsular side. The classification of the local recurrence site (B) as entry (blue arrow), tip (black arrow) and side (white arrows) according to ablation tract (red arrows). Entry is accepted as the site which the ablation probe first enters to the lesion. Tip is accepted as the site which the ablation probe's last position immediately before the ablation and the side is defined as the both sides of the ovoid ablation zone. The shape of local recurrence (C,D) as nodular (black arrow) and crescentic (red arrows). White stars indicate the ablation zones of each lesions.

Statistical Analysis

The parametric data were presented as mean ± standard deviation values. Analysis of categorical variables was performed using the Chi-square test. Fisher Exact test was applied when more than 20% of the expected values were below 5. All the results were evaluated in the 95% confidence interval and the statistical significance level was defined as p-value < 0.05. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL) version 21.0 for International Business Machines (IBM) statistical package.

Results

The characteristics of the study population and the ablated metastatic lesions are presented in detail in table 1. About one third (35%) of the LR was located in segment 6 (n=11/32). Figure 3 represents the Couinaud's segmentation of the metastases with LR. Fourteen new liver metastases were detected in the follow-up imaging when the LR was detected in eight of nineteen patients. Of thirty-two ablated metastases with LR, sixteen lesions (50%) showed the presence of blood vessel proximity and the mean distance between the lesions and vessels was 1.04±1.90 mm. The median time of LR and follow-up were 8.46±4.54 months (range, 3-20) and 19.62±10.26 (range, 6-40) months respectively. The patient (n=19) and the ablated lesion (n=32) depended LR rates were 19% and 20% respectively. The capsule and ablation tract related features of the LR were detailed in table 2. The ratio for the LR arising from subcapsular localization was found as 69%. Also, 72% of the LR from the subcapsular located metastatic lesion was found in the capsular side (Figure 4). But we couldn't find the statistically significant relationship between the subcapsular LR occurrence and the subcapsular localization of the metastatic lesions (p=0.683, table 3). All LR of the parenchymal localized metastatic lesions originated from either tip or the side of the ablation tract and this relationship was found as statistically significant (p=0.035, table 4). No recurrence was detected from the ablation tract entry of these lesions. The LR was developed on the side of the vessel in eight of sixteen metastatic lesions (50%) with vascular closeness before MWA ablation (p=0.315) (Figure 5). In addition to these, no statistically significant relationship was found between vessel closeness and shape of LR (p=0.704) and between the site and the shape of LR (p=0.683) (table 5). None of the patients with LR had major complications after the procedure. Focal subcapsular hematoma in one patient, reactive perihepatic fluid in three patients and ipsilateral reactive minimal pleural effusion in two patients were noted. None of the minor complications described in these patients required any additional treatment and further evaluation.

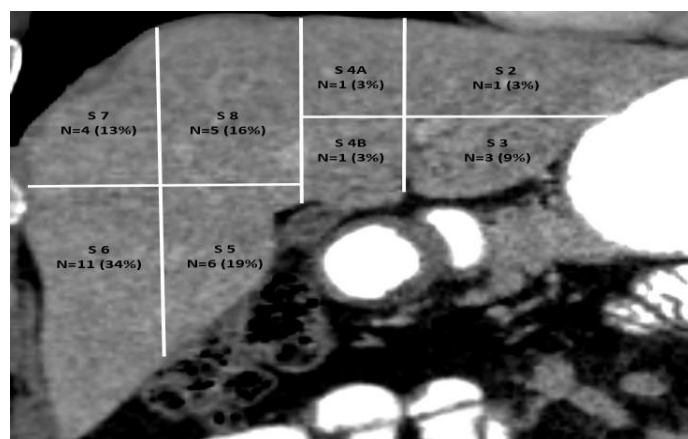


Figure 3: Couinaud's segmentation of the metastases with LR



Figure 4: 46-years-old female patient with liver metastases of breast cancer. There are two metastatic lesions located in segment 6 (A and B). Computed tomography (CT) image on the first day after microwave ablation showed the ablation zones with no evidence of residual tumor(C). But in 12th month control, axial (D) and coronal (E) CT images demonstrated the local recurrence. Nodular shaped LR at the entry zone of ablation tract with noncapsular site localisation (white arrow in D) and nodular shaped LR at the side zone of ablation tract with capsular site localisation (white arrows in E).

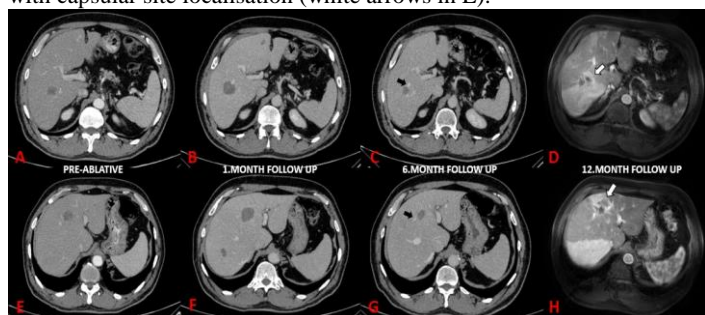


Figure 5: 53-years-old male patient with liver metastases of colon cancer. Pre and post-ablative computed tomography (CT) and magnetic resonance (MR) images of two metastatic lesions located in segment 6 (A-D) and segment 4A (E-H). There was no evidence of local recurrence (LR) for both lesions in 1st and 6th months follow-ups. In addition to this, the CT images showed the volume reduction of two lesions. But, control contrast-enhanced liver MR images at the time of 12th month follow-up showed the crescentic shaped LR on noncapsular site for the lesion in segment 6 (white arrow in D) and crescentic shaped LR on capsular site for the lesion in segment 4A (white arrow in H). Note that, while the LR in segment 6 developed from the site of vascular proximity (black arrow in C), the LR in segment 4A developed from the other site of the adjacent vascular structure (black arrow in G).

Table 1: The characteristics of the study population and ablated metastatic lesions.

Variables	Total / Mean±SD
Patient (total)	19
Male/Female	13/6
Lesion (total)	32
Male/Female	20/12
Age (years)	56.21±10.84
Female Age (years)	48.50±8.36
Male Age (years)	61.30±9.78
Primary malignancies	32
Colorectal	25 (79%)
Breast	2 (6%)
Lung	2 (6%)
Liver/Biliary	3 (9%)
Subcapsular localisation	17 (53%)
Parenchymal localisation	15 (47%)
Tumor volume (pre-ablative, mm ³)	5.14±5.09
Tumor volume (post-ablative 1st day, mm ³)	21.48±12.60
Tumor volume (at the time of LR, mm ³)	22.45±23.48
Time of LR (months)	8.46±4.54

SD : Standart Deviation, LR: Local Recurrence

Table 2. The capsule and ablation tract related features of the local recurrence.

Variables	Total N= 32 (%)
Shape	
Nodular	22 (69%)
Crescentic	10 (31%)
Tract Features	
Entry	8 (24%)
Side	12 (38%)
Tip	12 (38%)
Capsular Features	
Capsular site	22 (69%)
Non-capsular site	10 (31%)
Vessel Proximity	
No	16 (50%)
Portal Vein	7 (22%)
Hepatic Vein	9 (28%)

Table 3. Relationship between the lesion localization and the site of local recurrence.

Lesion Localization	Local Recurrence (site)		Total	P value
	Capsular	Noncapsular		
Subcapsular	16	6	22	0.683
Parenchymal	6	4	10	
Total	22	10	32	

Table 4. Relationship between the lesion and the ablation tract localizations of local recurrence.

Lesion Localization	Local Recurrence (Tract)		Total	P value
	Tip + Side	Entry		
Subcapsular	14	8	22	0.035
Parenchymal	10	0	10	
Total	24	8	32	

Table 5. Relationship of the shape of local recurrence between the lesion localization and the vascular closeness.

Lesion Localization	Local Recurrence (shape)		Total	P value
	Nodular	Crescentic		
Subcapsular	17	5	22	0.683
Parenchymal	5	5	10	
Total	22	10	32	
Vascular Closeness				0.704
No	12	4	16	
Yes	10	6	16	
Total	22	10	32	

Discussion

We have demonstrated in our study that there was not a specific shape and side features of LR related to both the liver capsule and the ablation tract. To the best of our knowledge, the present study was the first one which was evaluated the ablation tract and the liver capsule related features of LR after US-guided percutaneous MWA of the liver metastases independently.

When it is considered that the large part of the liver metastases is technically inappropriate for surgical resection, locoregional treatment strategies have been taken their place in the management of these patients as a minimally invasive choice (6,14). However, when compared to surgery, the prominent disadvantage of these locoregional procedures is their inferior

local tumor control rates resulting in recurrence (7). There are several studies reporting that the thermal ablation methods showed similar results to surgical treatment in patients with colorectal cancer liver metastases less than 1 cm and even superior to surgery in neuroendocrine tumor metastases (10,12,15). Apart from the patient status such as systemic treatments and the primary tumor depended features, it is important to understand the local environmental changes and features of the LR to improve the thermal ablative treatment procedures and to obtain some new treatment strategies related to approach and the ablation zone.

We found the patient-dependent LR rate as 19% and lesion-dependent LR rate as 20% in our study. Xu et al. reported that LR was discovered after ultrasound-guided MWA treatment in half of the patients in their study about ultrasound-guided percutaneous microwave ablation for intrahepatic cholangiocarcinoma (16). Although the reported LR rate was higher than our results, we think this was due to the prognostic feature of this specific tumor type in their study. In another study about the laparoscopic ultrasound-guided MWA for multifocal primary liver cancer, the LR ratio was reported as 12.5% which was lower than our result (17). In a very recent study which was about the comparison between the percutaneous and laparoscopic approaches in MWA, it is mentioned that the local tumor progression rates were 21.1% and 7.7% in percutaneous and laparoscopic approaches respectively (18). Therefore, it is clear that the laparoscopic thermal ablation methods are technically superior to percutaneous methods in terms of LR occurrence. On the other hand, Lorentzen et al. reported that the LR rates can be reduced up to 9.6% when contrast material usage is added to ultrasound guidance (19).

The basic mechanism of MWA is the transmission of electromagnetic energy produced by the generator to the active tip of the probe which is positioned within the lesion throughout the tract to produce intratumoral adequate heat which denatures the intracellular proteins and cell membranes. The heat is dissipated centrifugally around the probe tip resulting in the formation of ablation zones (20). Considering this basic principle of the thermal ablation procedure, the features of the ablation zone and the ablation tract could give some ideas about the local tumor progression. Although we couldn't find a statistically significant relationship between the data, most of the LR was occurred either in the tip (38%) or the side (38%) of the ablation tract rather than the entry zone (24%) of the ablation tract in the present study. When considered that the occurrence of the ablation zone (depending on the MWA system) first starts at the active tip of the probe and radiates towards both sides and posteriorly throughout the ablation probe settled in the ablation tract, the idea of positioning the ablation probe a little further by considering the safety limits and planning the ablation zone a little wider than the accepted standards can be discussed. We also found that almost all of the LR developed from the tip of the ablation tract were nodular in shape.

In thermal ablation practice, especially with US-guidance, both the subcapsular lesions and the sections of the lesion close to the liver capsule are sometimes disadvantageous places for the performer in terms of approaches and manipulations (21). The physicians usually prefer to use some assistive techniques such as hydrodissection to protect the liver capsule for an undesired and extrahepatic ablation (22). However, sometimes this discreet approach may cause the tip of the ablation probe not to be advanced and positioned well enough. Supportively, it is reported in some studies that the subcapsular tumors are associated with a higher rate of local tumor progression after thermal ablation because of the inability to achieve required tumor-free ablation margin (11,23).

However, it is also reported that there is no definitive evidence about the increase of local progression rate after thermal ablation in the capsular side of a peripheral tumor (24,25). We demonstrated in our study that about three out of four (69%) of the LR were seen at the capsular side of the ablation zone.

Another definition that could cause some technical problems directly effective on the ablation success is the "heat sink effect" due to the adjacent vessel (26). The blood flow with a relatively lower temperature within the lumen of the vascular structure near the ablation zone reduces the heat which is radiating through the ablation zone. In another word, it creates a cooling effect that will result in inadequate ablation. In this case, the development of a possible local recurrence will not be a surprise at all. This effect is more likely to be in radiofrequency ablation rather than the MWA (27). On the other hand, some authors did not report an association between the heat sink effect and MWA (28,29). Although we didn't determine any statistically significant relationship, the presence of blood vessel proximity was demonstrated in half of the ablated lesion with local recurrence in our study.

There are several limitations to our study that should be noted. First and the main limitation was the small sample size. Although we demonstrated some valuable results in percentages, it will be needed a larger sample size to have statistically significant data in future studies. Second, we only evaluated the patients who underwent the thermal ablation with only the MWA system and using only ultrasound guidance. No other imaging modalities and thermal ablation methods were analyzed. Third, no further evaluations were made related to histopathological types of lesions due to the small sample size. Forth, the performer dependent properties of the ablation procedure were not evaluated. Last, since we aimed to define the ablation tract and the liver capsule related features of LR which has been already occurred rather than evaluating the predisposing factors of LR occurrence, we didn't note the clinical parameters such as systemic chemotherapy treatment, presence of other distant metastases. In future studies, relationship between the features of LR and the clinical status of the patients could be evaluated.

In conclusion, we have discussed and defined some features of LR related to the ablation tract and liver capsule independently such as the relation between the recurrence and the blood vessel proximity, side of the LR throughout the ablation tract and its relation with the liver capsule. In future studies, defining these features detailly with large cohorts would offer an insight into the development of the thermal ablation methods and treatment strategies.

References

1. Chow FCL, Chok KSH. Colorectal liver metastases: An update on multidisciplinary approach. *World J Hepatol* 2019; 11(2): 150-172.
2. Silverberg E, Boring CC, Squires TS. Cancer statistics 1990. *Cancer Clin* 1990; 40:9-26.
3. Jessup JM, Mc Ginnis LS, Steele GD et al. National Cancer Data Base. Report on colon cancer. *Cancer* 1996; 78: 918-926.
4. Meijerink MR, Puijk RS, VanTilborg AAJM et al. Radiofrequency and microwave ablation compared to systemic chemotherapy and to partial hepatectomy in the treatment of colorectal liver metastases: a systematic review and meta-analysis. *Cardiovasc Intervent Radiol* 2018; 41: 1189-1204.
5. Minagawa M, Makuuchi M, Torzilli G et al. Extension of the frontiers of surgical indications in the treatment of liver metastases from colorectal cancer: long-term results. *Ann Surg* 2000; 231:487-499.

6. Geoghegan JG, Scheele J. Treatment of colorectal liver metastases. *Br J Surg.* 1999; 86:158–169.
7. Noori SS, Gonsalves CF, Shaw CM. Metastatic liver disease: Indications for locoregional therapy and supporting data. *Semin Intervent Radiol* 2017;34:145–166.
8. Mulier S, Ni Y, Jamart J et al. Local recurrence after hepatic radiofrequency coagulation: multivariate meta-analysis and review of contributing factors. *Ann Surg* 2005; 242:158–171.
9. Siperstein A, Garland A, Engle K et al. Local recurrence after laparoscopic radiofrequency thermal ablation of hepatic tumors. *Ann Surg Oncol* 2000; 7:106–113.
10. Leung U, Kuk D, D’Angelica MI et al. Long-term outcomes following microwave ablation for liver malignancies. *Br J Surg.* 2015; 102(1): 85–91.
11. Komorizono Y, Oketani M, Sako K et al. Risk factors for local recurrence of small hepatocellular carcinoma tumors after a single session, single application of percutaneous radiofrequency ablation. *Cancer* 2003;97: 1253– 62.
12. Shady W, Petre EN, Gonen M et al. Percutaneous Radiofrequency Ablation of Colorectal Cancer Liver Metastases: Factors Affecting Outcomes — A 10-year Experience at a Single Center. *Radiology* 2016; 278:601–611.
13. Sartori S, Tombesi P, Macario F et al. Subcapsular Liver Tumors Treated with Percutaneous Radiofrequency Ablation: A Prospective Comparison with Nonsubcapsular Liver Tumors for Safety and Effectiveness. *Radiology* 2008; 248:670 –679.
14. Curley SA, Izzo F, Delrio P et al. Radiofrequency ablation of unresectable primary and metastatic hepatic malignancies: results in 123 patients. *Ann Surg* 1999; 230:1–8.
15. Kose E, Kahramangil B, Aydın H et al. Outcomes of laparoscopic tumor ablation for neuroendocrine liver metastases: a 20-year experience. *Surg Endosc.* 2020;34(1):249-256.
16. Xu C, Li L, Xu W et al. Ultrasound-guided percutaneous microwave ablation versus surgical resection for recurrent intrahepatic cholangiocarcinoma: intermediate-term results, *International Journal of Hyperthermia* 2019, 36:1, 350-357.
17. Xu Z, Yang Z, Pan J, Hu Y. Individualized laparoscopic B-ultrasound-guided microwave ablation for multifocal primary liver cancer. *Videosurgery Miniinv* 2018; 13 (1): 9–16.
18. Corte AD, Ratti F, Monfardini L. Comparison between percutaneous and laparoscopic microwave ablation of hepatocellular carcinoma, *International Journal of Hyperthermia* 2020; 37:1:542-548.
19. Lorentzen T, Skjoldbye BO, Nolsoe CP. Microwave Ablation of Liver Metastases Guided by Contrast-Enhanced Ultrasound: Experience with 125 Metastases in 39 Patients. *Ultraschall in Med* 2011; 32: 492–496.
20. Vogl TJ, Nour-Eldin A, Hammerstingl RM et al. Microwave Ablation (MWA): Basics, Technique and Results in Primary and Metastatic Liver Neoplasms – Review Article. *Fortschr Röntgenstr* 2017; 189: 1055–1066.
21. An C, Cheng Z, Yu X et al. Ultrasound-guided percutaneous microwave ablation of hepatocellular carcinoma in challenging locations: oncologic outcomes and advanced assistive technology, *International Journal of Hyperthermia* 2020;37:1, 89-100.
22. Gilbert P, Arrington D, Yamada R, Hannegan C, Anderson MB, Selby Jr B, Guimaraes M. Protective techniques in image-guided percutaneous hepatic ablations. *Intervent Oncol* 360. 2016;4(5):75-85.
23. Hori T, Nagata K, Hasuike S, et al. Risk factors for the local recurrence of hepatocellular carcinoma after a single session of percutaneous radiofrequency ablation. *J Gastroenterol* 2003;38(10):977–981.
24. Choi D, Lim HK, Kim MJ, et al. Therapeutic efficacy and safety of percutaneous radiofrequency ablation of hepatocellular carcinoma abutting the gastrointestinal tract. *AJR Am J Roentgenol* 2004;183(5):1417–1424.
25. Poon RT, Ng KK, Lam CM et al. Radiofrequency ablation for subcapsular hepatocellular carcinoma. *Ann Surg Oncol* 2004;11(3):281–289.
26. Lu DS, Raman SS, Limanond P et al. Influence of large peritumoral vessels on outcome of radiofrequency ablation of liver tumors. *J Vasc Interv Radiol* 2003; 14:1267–74.
27. Wright AS, Sampson LA, Warner TF et al. Radiofrequency versus microwave ablation in a hepatic porcine model. *Radiology.* 2005;236(1): 132–139.
28. Brannan JD, Ladtkow CM. Modeling bimodal vessel effects on radio and microwave frequency ablation zones. *Conf Proc IEEE Eng Med Biol Soc.* 2009; 5989–5992
29. Dodd GD, Dodd NA, Lanctot AC et al. Effect of variation of portal venous blood flow on radiofrequency and microwave ablations in a blood-perfused bovine liver model. *Radiology.* 2013;267(1): 129–136.