Melanoma liver metastases with special imaging features on magnetic resonance imaging after microwave ablations: How to evaluate technical efficacy?

ABSTRACT

Purpose: To evaluate the technical feasibility of microwave ablation (MWA) for melanoma liver metastases with persistent high signal on magnetic resonance imaging (MRI).

Materials and Methods: Seven patients with 22 target melanoma liver metastases who underwent MWA treatment were included. All procedure-related complications were observed and recorded. One month after MWA, the imaging features of treated liver metastases and ablation zones with different MRI sequences were reviewed to evaluate technique efficacy. To verify the correctness of the evaluation, MRI scans during patient follow-up were reviewed and compared with images before MWA to analyze changes in treated liver metastases and ablation zones.

Results: All ablations were performed successfully, and there were no procedure-related major complications. After ablation, according to MRI, T1-weighted pre-contrast or contrast sequences, the persistence of high signals from the treated lesions was noted inside the ablation zones of 19 lesions. Among these 19 lesions, 17 were completely covered by the ablation zones and were considered successfully treated, whereas two lesions were not completely covered and were considered unsuccessfully treated. Three lesions could not be detected on any MRI sequence after ablation and were also considered successfully treated. Finally, MRI scans during patient follow-up care verified these evaluations.

Conclusion: MWA is a technically feasible option for melanoma liver metastases with special imaging features on MRI.

KEY WORDS: Liver metastases, melanoma, microwave ablation, technical efficacy

INTRODUCTION

Melanoma is uncommon in Asian countries; however, its incidence has been increasing worldwide. In Asian countries, acral and mucosal melanoma comprises more than 50% of melanoma cases, whereas in western countries, cutaneous melanoma is predominant. Approximately 1/3 of melanoma patients will develop distant metastases, and the liver is a common site of metastasis. Recent advances, such as immunotherapy and targeted therapy, have improved melanoma treatment. However, patients with melanoma liver metastases still have poor prognosis, and the reported median survival is typically < 1 year. Early detection of liver metastases is an important factor that enables patients achieve successful treatment. For melanoma liver metastases, magnetic resonance imaging (MRI) is more specific than other medical imaging modalities, especially for small lesions. On MRI, the typical melanoma liver metastases exhibit shortened T1 and T2 relaxation times, indicating a high signal on T1-weighted sequences and low signal on T2-weighted sequences. For treatment of melanoma liver metastases, hepatectomy remains the reference standard and improves survival time in eligible patients. However, only a few patients with melanoma liver metastases qualify for surgical treatment. Rose et al. reported that only 24 of

Cite this article as: Cao F, Xie L, Qi H, Ze S, Chen S, Shen L, et al. Melanoma liver metastases with special imaging features on magnetic resonance imaging after microwave ablations: How to evaluate technical efficacy? J Can Res Ther 2019:15:1501-7.
1750 patients with melanoma liver metastases ultimately accepted resection. For both primary hepatocellular carcinoma and metastatic hepatic carcinoma, thermal ablation therapy serves as a useful alternative to hepatectomy.[14,15]

Thermal ablation techniques are useful for unresectable liver metastases, resulting in uniform tumor killing and complete tumor treatment.[16] Current ablation techniques include radiofrequency ablation (RFA), microwave ablation (MWA), and cryoablation. Compared to RFA and cryoablation, MWA provides a larger ablation zone and faster treatment time. Therefore, MWA presents a promising new treatment for patients with unresectable liver metastases[17-19] and it is important to precisely evaluate treatment safety and patient responses after MWA. Notably, the imaging features after tumor ablation may vary according to tumor type, imaging modality, and ablation modality. Given these unique MRI features of melanoma liver metastases, MRI is the best tool to evaluate the treatment of liver metastases. However, ablation does not destroy melanin, making most melanoma liver metastases persistently bright on T1-weighted precontrast sequences after ablations. Thus it is difficult to determine whether metastases are enhanced on postcontrast sequences.[11] Subtraction imaging during enhancement could help to evaluate technical efficacy, but subtraction images have not been widely used in clinical medicine. Moreover, in some cases, movement artifacts have influenced the contribution of subtraction images.[20] Given that no previous research has been reported on this issue, this study aimed to describe the unique imaging features of melanoma liver metastases after MWA on MRI and discuss how to evaluate technique efficacy using MRI.

MATERIALS AND METHODS

Patients
This study was conducted as per the Declaration of Helsinki. Written informed consent was obtained from each patient before treatment. Institutional review board approval was not necessary because of the retrospective nature of this study. Between December 2008 and December 2018, 166 patients with melanoma at the Cancer Centre of Sun Yat-sen University were found with liver metastases. Fifteen consecutive patients with melanoma liver metastases received MWA. Five patients were excluded for a lack of radiographic follow-up, two patients were excluded for possessing a tumor size larger than 5 cm, and one patient was also excluded for technique failure without a second ablation. Thus, seven patients with a total of 22 liver metastases were included in our study [Figure 1]. All seven patients underwent local excision of the primary tumor. One patient underwent local resection of liver metastases, whereas the remaining patients received no prior local treatment. All 22 lesions were diagnosed by computed tomography (CT) (3 patients) or MRI (4 patients) scans, and 3 patients were also verified with a biopsy. Each case was discussed by the institutional interdisciplinary tumor board, which included surgeons, oncologists, pathologists, and radiologists. MWA was considered an appropriate treatment for liver metastases.

Diagnosis
A baseline examination was performed within 1 month before MWA, including both MRI and CT scans. Before the MWA procedure, all the lesions were diagnosed by typical imaging features. On CT scans, melanoma liver metastases appeared hypodense or hyperdense and enhanced with intense contrast. If a lesion was not confidently diagnosed using CT scans, MRI provided a definitive diagnosis. Most melanoma liver metastases exhibited a high signal on T1-weighted MRI, especially when the fat signal was suppressed. Regarding metastases that exhibited a low signal on T1-weighted images, these lesions were verified as metastases when enhancements were observed.[11,20]

Microwave ablation procedure
Before the procedure, patients were placed in the prone or supine position depending on the tumor location. CT scans were used to locate the liver metastases and design an appropriate puncture route. After routine disinfection and local anesthesia using 1% lidocaine, a 16-G microwave antenna (FORSEA; Qinghai Microwave Electronic Institute, Nanjing, China) was punctured into the lesion until the tip of the antenna exceeded the tumor edge by approximately 5 mm. For tumors >3 cm in size, two microwave antennas were used, or antenna paths were adjusted during the procedure. The MWA procedure was initiated using equipment. The MWA parameters varied based on the tumor size and the operator’s experience. Intravenous anesthesia (propofol [1.5–4.5 mg/kg continuous intravenous infusion/h]; AstraZeneca S.P.A., Italy) was used during the entire MWA procedure. After the procedure, CT scans were performed immediately to detect
whether the ablation zone was sufficient to cover the lesion and whether the procedure should be continued.\textsuperscript{[22]}

\textbf{Follow-up}

MRI scans were performed 1 month after MWA to evaluate technique efficacy and then every 3 months using contrast-enhanced MRI during patient follow-up. All imaging data were assessed by two experienced radiologists who were blind to the other’s findings. Any differences between the two radiologists were resolved by one experienced radiologist with more than 10 years of medical imaging diagnosis experience. Given that most treated lesions exhibited a high signal on T1-weighted images, it was difficult to use contrast-enhanced images to detect whether complete ablation was achieved. However, given the consistency in the high signal of treated lesions and non-enhanced ablation zones on contrast-enhanced images, especially during the portal venous phase or delayed phase, it was easy to detect whether the target lesions were completely covered by the ablation zones.\textsuperscript{[23]} Technique efficacy was defined as an ablation zone that completely covered the primary metastases. To further verify these evaluations, the tumor size on T1-weighted images was compared during follow-up. If the tumor size did not increase, the lesion was considered completely ablated. If the tumor size increased, then the lesion was considered incompletely ablated. When the ablation zone did not cover the lesion, then incomplete ablation was considered, and an increasing tumor size was also used to confirm residual tumor. All lesions covered in the ablation zone were evaluated on T1- and T2-weighted, diffusion-weighted (DW), and postcontrast images by the abovementioned two radiologists.

\textbf{RESULTS}

Of the 15 consecutive patients with melanoma liver metastases who underwent MWA treatment, 7 patients (4 males and 3 females) received MRI scans to evaluate technique efficacy and were included in this research. Regarding primary melanoma location, four patients had choroid melanomas, one had a rectal melanoma, and two had unclear original locations. Three patients were biopsied and diagnosed as melanoma liver metastases. The remaining patients were diagnosed by typical medical imaging, including CT and MRI scans. Four patients underwent MRI scans before the MWA procedures, and all 11 lesions exhibited a high signal on both T1- and T2-weighted images and DW images. The other 3 patients underwent CT scans before the MWA procedure. On unenhanced images, 6 of 11 lesions exhibited a high density and inhomogeneous enhancement with contrast. The other 5 lesions appeared with low density and inhomogeneous enhancement with contrast. A median number of 3 lesions (range: 2–6) per patient with a median size of 16.37 mm (range: 6.66–43.72 mm) were treated. Eight lesions were <10 mm, 12 lesions were >10 mm and <30 mm, and 2 lesions were >30 mm. Five patients underwent curative therapy, and 2 patients underwent palliative therapy to reduce tumor burden. The mean follow-up was 7 months (range: 3–25 months). There were no procedure-related major complications [Table 1].

After MWA, on MRI scans the persistence of high signals inside the ablation zones of treated lesions were observed in 19 lesions on T1-weighted sequence MRI, resulting in a very strong contrast with non-enhanced ablation zones on contrast-weighted sequences. Among these lesions, 17 were completely covered by the ablation zones and were considered completely ablated, whereas 2 lesions were not completely covered and were considered incompletely ablated. Three lesions of one patient with rectal melanoma could not be detected on any MRI sequence after ablation, and no peripheral enhancement was observed [Table 2]. These lesions were also considered completely ablated. On T2-weighted and DW images, nonviable tumors covered by the ablation zone exhibited a low signal, whereas viable tumors not covered by the ablation zone exhibited a high signal [Figure 2a-f]. For the 19 treated lesions that were still detected after MWA, the tumor sizes of the 16 treated lesions that achieved complete ablation did not increase during follow-up, whereas the tumor sizes of the 3 lesions without complete ablation increased. A biopsy was performed for one lesion, and pathology also confirmed the tumor [Figure 3a-f]. For the other 3 lesions not detectable after MWA, no peripheral enhancement was observed during follow-up. Finally, according to MRI and follow-up for these 22 treated lesions, 20 lesions achieved complete ablation and 2 did not. For these 2 lesions from 2 patients, 1 patient received chemotherapy and immunotherapy and 1 accepted TACE.

\textbf{DISCUSSION}

In melanoma, the liver is a common site of metastases, and the treatment of liver metastases influences the prognosis of most patients. For these patients, locoregional therapy significantly

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\textbf{Table 1: The basic characteristics of patients}

| Patient n/sex/age (years) | Primary location | Tumor diagnosis | Treated number | Largest tumor size (mm) | Imaging modality before MWA | Imaging modality of follow up | Follow up time (months) |
|---------------------------|------------------|----------------|----------------|-------------------------|-----------------------------|---------------------------|------------------------|
| 1/male/45                 | Chorioid         | Imaging        | 4              | 13.98                   | MRI                         | MRI                       | 25                     |
| 2/male/28                 | Unknown          | Biopsy         | 2              | 25.49                   | CT                          | MRI                       | 3                      |
| 3/male/43                 | Chorioid         | Biopsy         | 6              | 43.72                   | CT                          | MRI                       | 7                      |
| 4/female/60               | Rectum           | Imaging        | 3              | 25.9                    | CT                          | MRI                       | 12                     |
| 5/male/65                 | Unknown          | Biopsy         | 3              | 20.94                   | MRI                         | MRI                       | 4                      |
| 6/female/31               | Chorioid         | Imaging        | 2              | 8.07                    | MRI                         | MRI                       | 8                      |
| 7/female/52               | Chorioid         | Imaging        | 2              | 7.90                    | CT                          | MRI                       | 4                      |

MWA=Microwave ablation, MRI=Magnetic resonance imaging, CT=Computed tomography
improves the median overall survival time. Faries et al.\(^6\) summarized their 20-year experience of hepatic resection for melanoma. Of 1078 patients with melanoma liver metastases, only 58 (5.4%) finally underwent resection ± ablation; however, the median overall survival was 8 months for non-surgical patients and 24.8 months for surgical patients. Pawlik et al.\(^7\) reported 40 patients who accepted hepatic resection for melanoma. The median time to recurrence was 8.3 months, and the median overall survival time was 28.2 months. Only a low percentage of patients with metastases from melanoma are considered suitable for surgical therapy. However, with the development of numerous ablation technologies, ablation treatments have made it possible to treat patients with melanoma liver metastases who are not candidates for hepatectomies. To our knowledge, only a few studies examining the ablation of melanoma liver metastases have been reported. Faries et al.\(^6\) compared 40 patients who underwent resection only for melanoma liver metastases with 18 patients who underwent ablation only (10 patients) or who had resection (8 patients) and reported 5-year OS rates of 28.6% and 33.3%, respectively. Bale et al.\(^8\) performed RFA in 20 patients with melanoma liver metastases and reported a median overall survival of 19.3 months and OS rates at 1, 3, and 5 years of 64%, 41% and 14%, respectively. Melanoma liver metastases frequently contain melanin, and this paramagnetic agent leads to special imaging features on MRI.\(^{24}\) However, these studies did not clearly describe how to evaluate technique efficacy after ablation. Numerous imaging methods, such as ultrasound, CT, and MRI, have been widely used to evaluate melanoma liver metastases. In the clinic, CT is the most commonly used modality to detect melanoma liver metastases and evaluate technique efficacy. Any increase, enhancement,

Table 2: Imaging features of targeted lesions before and after microwave ablation in different sequences on magnetic resonance imaging

| Image sequences       | Detected on MRI before MWA\(^{(n=11)}\) | Detected on MRI after MWA\(^{(n=22)}\) |
|-----------------------|------------------------------------------|---------------------------------------|
| T1-weighted imaging   |                                          |                                       |
| Hypointense           | 0                                        | 0                                     |
| Hyperintense          | 11                                       | 19                                    |
| Not seen              | 0                                        | 3                                     |
| T2-weighted imaging   |                                          |                                       |
| Hypointense           | 0                                        | 17                                    |
| Hyperintense          | 11                                       | 2                                     |
| Not seen              | 0                                        | 3                                     |
| DW imaging            |                                          |                                       |
| Hypointense           | 0                                        | 17                                    |
| Hyperintense          | 11                                       | 2                                     |
| Not seen              | 0                                        | 3                                     |
| Enhanced imaging      |                                          |                                       |
| Enhancement in any phase |                                        | 0                                     |
| No enhancement in any phase |                                    | 0                                     |
| No available enhancement |                                    | 11                                    |

MWA=Microwave ablation, MRI=Magnetic resonance imaging, DW=Diffusion-weighted

Figure 2: (a-f) Magnetic resonance images of a 44-year-old woman with liver metastases from choroidal melanoma. The lesion exhibits a high signal on T1-weighted contrast (a, arrow), T2-weighted (b, arrow), and diffusion-weighted images (c, arrow). 1 month after microwave ablation, the lesion was still detected inside the ablation zone and exhibited a high signal on T1-weighted contrast images (d, arrow) and a low signal on T2-weighted images (e, arrow) and diffusion-weighted images (f, arrow)
or new nodule suggests disease progression; however, CT is insensitive for melanoma liver metastases, especially small lesions.\textsuperscript{26} Once a liver metastasis is large enough to be detected on CT scans, more lesions are likely to be present in the liver.\textsuperscript{26}

Given the special imaging features of melanoma liver metastases, MRI is more specific than other modalities. Typical melanoma liver metastases exhibit shortened T1 and T2 relaxation times, indicating high signals on T1-weighted images and low signals on T2-weighted images.\textsuperscript{11} Sofue et al.\textsuperscript{21} reported 38 patients who were suspected of possessing melanoma liver metastases that appeared as intermediate imaging findings on CT. MRI verified that 23 patients had metastases. Among these 23 patients, 18 exhibited typical shortened T1 and T2 relaxation times. On T1-weighted images, the high signal may be caused by hemorrhage, fat, or high levels of protein. However, for melanoma, the presence of shortened T1 relaxation times is related to melanin inside the lesion. Typical liver melanotic lesions exhibit a shortened T1 and T2 pattern, and other atypical patterns are also noted. Maeda et al.\textsuperscript{27} reported 15 patients with melanoma liver metastases, and 4 of these patients exhibited a short T1 and long T2 pattern. In our study, before the MWA procedure, 4 patients underwent MRI. All of these patients exhibited an atypical high signal on T1-and T2-weighted and DW images. Regarding the other two patients who experienced recurrence during follow-up, the new lesions exhibited a high signal on T1-and T2-weighted and DW images. All the lesions in our study exhibited a high signal on T2-weighted images, which differed from previous reports.\textsuperscript{11,21}

For most of the melanoma liver metastases that exhibited high signals on T1-weighted images, the high signal did not disappear after MWA. Given the high signal on T1-weighted pre-contrast sequences, it could be difficult to detect whether the treated lesions were enhanced and assess the possible residual viable tumor after contrast enhancement. Lee et al.\textsuperscript{28} reported that high precontrast T1 signal intensity of melanoma liver metastases on MRI made it impossible to determine whether enhancement occurred in most lesions, and positive enhancement was identified in only 14.6% of patients. However, when the subtraction technique was used, the rate increased to 68.3%. Positive enhancement and intermediate high T2 signal intense were significantly associated with progression. Mariani et al.\textsuperscript{29} also used the subtraction technique to evaluate the technical success of RFA in 15 patients with melanoma metastases. They found the majority of ablation zones were spontaneously hyperintense on T1 images, but they explained it via coagulation necrosis and hemorrhagic alterations, which usually present a spontaneous hyperintense signal on T1 weighted images. In our study, instead of the ablation zones, we found that the majority of ablated lesions presented spontaneously hyperintense on T1 images, which made the evaluation of technique efficacy difficult. The subtraction imaging technique had not been widely used in clinical medicine, and consequently other

\begin{figure}[h]
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\caption{(a-f) Magnetic resonance images during follow-up of a 43-year-old man with liver metastases from a choroidal melanoma. One month after microwave ablation, the lesion exhibited a high signal was completely covered by the ablation zone on post-contrast images (a, arrow). During follow-up, the lesion inside the ablation zone did not increase in size after 7 months (b, arrow). One month after microwave ablation, the lesion that exhibited a high signal was not covered by the ablation zone (c, arrow) on post-contrast images. Four months later, the tumor size increased (d, arrow). 7 months later, the tumor size continued increasing (e, arrow). A biopsy was performed for this lesion, and pathology confirmed the tumor (f)\textsuperscript{11,21}}
\end{figure}
approaches should be applied to help evaluate the lesions. In our studies, without the subtraction technique, we could also accurately evaluate the efficacy.

The high signal resulted in a very strong contrast with a non-enhanced ablation zone on the contrast-weighted sequence; therefore, it was straightforward to evaluate the ablative margin and technique efficiency. Given the lack of previous research about MRI imaging features for treated melanoma liver metastases after MWA, we also had doubts that the tumor was still viable after ablation, given the persistence of the high signal on T1-weighted images. We first performed a biopsy of the treated tumor inside the ablation zone. In addition to necrotic tissue, copious melanin was observed, which could explain why the high signal on the T1-weighted images did not disappear on MRI scans. However, this finding does not unequivocally mean that the liver metastases remain viable. To further confirm our view, we compared the tumor size of treated lesions that were detected on MRI during the follow-up. For the treated lesions covered by ablation, the size did not increase, whereas the lesions without complete ablation continued increasing in size. In this study, 19 treated lesions were still detectable on MRI after MWA. Tumor sizes of the 17 treated lesions that were completely covered by ablation zones did not increase during follow-up, whereas the tumor sizes of the 2 lesions that were not completely covered by ablation zones increased. In addition, we also reviewed the imaging features of treated lesions on T2-weighted and DW images. In our research, 11 lesions from 4 patients were subjected to MRI before MWA, and all the lesions exhibited a high signal on both T2-weighted and DW images. After MWA and excluding 3 lesions that could not be detected on MRI, all 17 completely ablated lesions exhibited a low signal on both T2-weighted and DW images, and some portion of the other 2 incompletely ablated lesions still exhibited a high signal on these sequences. Therefore, T2 and DWI sequences may help evaluate technique efficacy after MWA. After MWA, not all melanoma liver metastases were detected on MRI. In our study, 3 lesions under treatment could not be detected inside the ablation zone in one patient with liver metastases from rectal melanoma. For these lesions, the use of contrast enhancement helped detect any increase, enhancement, or new nodules and also assess the residual tumor. In total, 2 lesions from 2 patients were not completely ablated based on MRI scans and follow-up. The reasons were as follows; one lesion adhered to large vessels and the other lesion was so small its exact location could not be identified before the MWA procedure.

The study has some limitations. First, the number of patients included in our research is relatively small, and a larger sample size is necessary to confirm our conclusion. Second, 3 patients did not receive MRI scans before the MWA procedure. Finally, the patients in our study exclusively underwent MWA, and the imaging features after RFA or cryoablation will be evaluated in future studies.

CONCLUSION

MWA is an effective treatment for melanoma liver metastases, and the persistence of high signals from ablated lesions on T1-weighted contrast sequences does not necessarily indicate treatment failure. It is easy to evaluate whether a treated lesion that exhibits a high signal is completely covered by the ablation zone using the T1 contrast sequence MRI. A sufficient ablative margin beyond the tumor border is necessary to achieve technical efficacy and T2-weighted and DWI sequences may be used to help determine whether ablation succeeds or fails. MRI is the best modality for follow-up after MWA of melanoma liver metastases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgments

This study was supported by the National Natural Science Foundation of China (81771954) and Science and Technology Planning Project of Guangdong Province, China (2015A020214011 & 2017A010105028).

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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