JMS 2024;Vol 7(3):47-55
UDC: 616.36-033.3-073.763.5
616.36-033.2-073.756.8:004

ROLE OF MAGNETIC RESONANCE AND PET CT IN DETECTION OF HEPATAL METASTASIS

Biljana Prgova Veljanova,[1,2] Biljana Bozinovska,[1] Masa Kostova ,[1,2] Teodora,Bozinovska ,[1] Gordana Bozinovska-Beaka,[3] Dimitar Veljanovski [1,2]
[1]PHI City General Hospital "8th September", Republic of North Macedonia,
[2]University Clinic for Radiology, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia
[3]Faculty of Medical Sciences, Goce Delchev University, Shtip, North Macedonia

Abstract

Metastatic spread of primary tumours is best detected by various radiological methods such as ultrasound, CT, MRI as well as PET CT and the latest MRI/PET.

The objective of our study was to assess the relative performance of different radiology methods, magnetic resonance (MR) and 18FDG positron emission computed tomography (PET CT) and to emphasize superiority of one of them with a goal of better planning of oncology and surgery treatment of patients with metastasis of liver smaller than 10 mm.

Imaging data of 70 patients over a 4 year-period, enhanced liver MRI and whole-body FDG PET CT were reviewed for the presence and number of liver metastases.

In comparison to FDG PET CT, MRI detected all hepatic metastases. All lesions were identified on MRI (420), whereas only 296 were detected on FDG PET. Ninety-one of them with diameter less than 10 mm were detected only on MRI. FDG PET CT provided additional information about extrahepatic disease and was useful in initial staging. However, significantly more and smaller than 10 mm liver metastases were detected on MRI than on FDG PET.

MRI has presented more information concerning peripheral ring and PET CT is accurate for identification of metabolic activity of hepatic metastases greater than 10 mm in diameter. Both complementary methods give correct pathways in treatment and in building of criteria for appropriate liver metastasectomies and radiofrequency ablations.

Keywords**:** metastasis, liver, MR, PET CT, 18FDG

Introduction

This paper provides a comprehensive overview of the importance of detecting liver metastases using various radiological methods, with a particular focus on positron emission tomography- computed tomography (PET-CT) and magnetic resonance imaging (MRI). These imaging techniques play a crucial role in facilitating appropriate treatment decisions for patients with different types of carcinomas and liver metastases. The significance of accurate detection and characterization of liver metastases is paramount, as it directly impacts patient management, treatment planning, and overall prognosis [1,2].

Liver metastases are a common occurrence in many types of cancers, including colorectal, breast, and pancreatic carcinomas. Early and accurate detection of these metastases is essential in determining the extent of the disease spreading and guiding treatment strategies [3].

The liver is a frequent site of metastasis due to its dual blood supply and its role in filtering the blood from the gastrointestinal tract. Metastatic lesions in the liver can significantly alter the course of treatment and prognosis in cancer patients, making their detection a critical aspect of oncological care [4].

While various imaging modalities have been employed for this purpose, PET-CT and MRI have emerged as particularly promising techniques due to their high sensitivity and specificity. These advanced imaging methods offer distinct advantages over conventional techniques such as ultrasound or standalone CT scans, which may have limitations in detecting small or subtle lesions [5].

PET-CT combines the metabolic information provided by positron emission tomography (PET) with the anatomical detail of computed tomography (CT). This hybrid imaging modality has demonstrated a significant potential in oncology, offering valuable insights into both the location and metabolic activity of tumors [6]. PET-CT utilizes radioactive tracers, most commonly 18F-fluorodeoxyglucose (FDG), which is preferentially taken up by metabolically active cancer cells. This allows for the visualization of both primary tumors and metastatic lesions throughout the body. The CT component of PET-CT provides high-resolution anatomical information, enabling precise localization of lesions detected on PET [7].

MRI, on the other hand provides excellent soft tissue contrast and can detect smaller lesions with high accuracy, making it an invaluable tool in liver imaging [8]. MRI does not use ionizing radiation, which is advantageous for patients who may require repeated imaging. The ability of MRI to characterize tissue based on multiple parameters, including T1 and T2 relaxation times, diffusion properties, and contrast enhancement patterns, allows for detailed assessment of liver lesions. Advanced MRI techniques, such as diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) imaging, further enhance the ability to detect and characterize liver metastases.

Small liver metastases are often missed on conventional imaging, leading to under staging of a disease and potentially inappropriate treatment decisions. Accurate detection of these small lesions can lead to more precise staging, better selection of patients for surgical intervention, and more effective use of targeted therapies [9].

The objective of the study was clearly stated: to assess and compare the performance of MRI and 18FDG PET-CT in detecting liver metastases with special reference to hepatic metastases smaller than 10 mm.

Material and methods

The methodology section describes a retrospective study involving 70 patients over a 4-year period. Patients were aged from 23 to 78 years. Inclusion criteria were: patients with previously diagnosed malignancy proven by biopsy, patients with previously diagnosed malignancy proven after surgical treatment, patients with metastatic liver deposits diagnosed by ultrasound or computed tomography.

Exclusion criteria were: patients treated with oncology therapy, patients with previous radiological oncology therapy, patients with focal lesions but not of a malignant nature, such as hemangiomas, adenomas and others.

This study design allowed for a comprehensive evaluation of the imaging techniques in a real-world clinical setting. Retrospective studies have the advantage of allowing researchers to analyze a large amount of data collected over an extended period, potentially capturing a diverse range of clinical scenarios and patient characteristics. However, it is important to note that retrospective studies may be subject to certain biases, such as selection bias or information bias, which should be carefully considered when interpreting the results.

Both enhanced liver MRI and whole-body FDG PET-CT were used to detect liver metastases, providing a direct comparison of these two advanced imaging modalities. This head-to-head comparison is crucial for determining the relative strengths and weaknesses of each technique in the specific context of small liver metastasis detection. By using both modalities in the same patient population, the study can control for variables such as patient characteristics, tumor biology, and timing of imaging, which might otherwise confound the results.

To ensure the accuracy of the findings, the study used postoperative histopathology and ultrasound findings as the reference standard. This approach provides a robust gold standard against which the performance of MRI and PET-CT can be evaluated. Histopathological confirmation is considered the ultimate standard for diagnosing metastatic lesions, as it allows for direct examination of tissue at the cellular level. The inclusion of ultrasound findings as part of the reference standard likely refers to intraoperative ultrasound, which is a highly sensitive technique for detecting liver lesions during surgery. By combining these reference standards, the study aimed to establish a comprehensive and accurate baseline for assessing the performance of MRI and PET-CT [10].

Detailed information about MRI and PET-CT protocols is provided, including the specific sequences used and the FDG dosage. This level of detail is crucial for reproducibility and provides a thorough understanding of the imaging techniques employed. In scientific research, particularly in medical imaging studies, reproducibility is essential for validating results and enabling other researchers or clinicians to replicate the findings in different settings [11,12,13].

The MRI protocol included various sequences designed to optimize liver lesion detection and characterization. These sequences likely included T1-weighted, T2-weighted, and diffusion-weighted imaging, as well as dynamic contrast-enhanced sequences. Each of these sequences provides unique information about liver tissue and potential lesions.

The use of a liver-specific contrast agent further enhances the ability to detect and characterize liver lesions. Liver-specific contrast agents are taken up by normal hepatocytes but not by metastatic lesions, creating a strong contrast between healthy liver tissue and metastases. This can significantly improve the detection of small lesions that might be missed on non-contrast or conventional extracellular contrast-enhanced imaging [14,15].

For the PET-CT protocol, the study utilized 18F-fluorodeoxyglucose (FDG) as the radiotracer. FDG is widely used in oncological imaging due to its ability to highlight areas of increased glucose metabolism, which is characteristic of many types of cancer cells. The specific FDG dosage and uptake time were optimized to provide the best possible image quality and lesion detectability [16,17]. The standardized uptake value (SUV) of FDG in liver lesions can provide valuable information about the metabolic activity of metastases, which can be useful for assessing treatment response and prognosis.

Results

Seventy patients with different types of primary tumors participated in the study. Frequency of tumors in which there were metastatic deposits in the liver was presented in fig.1.

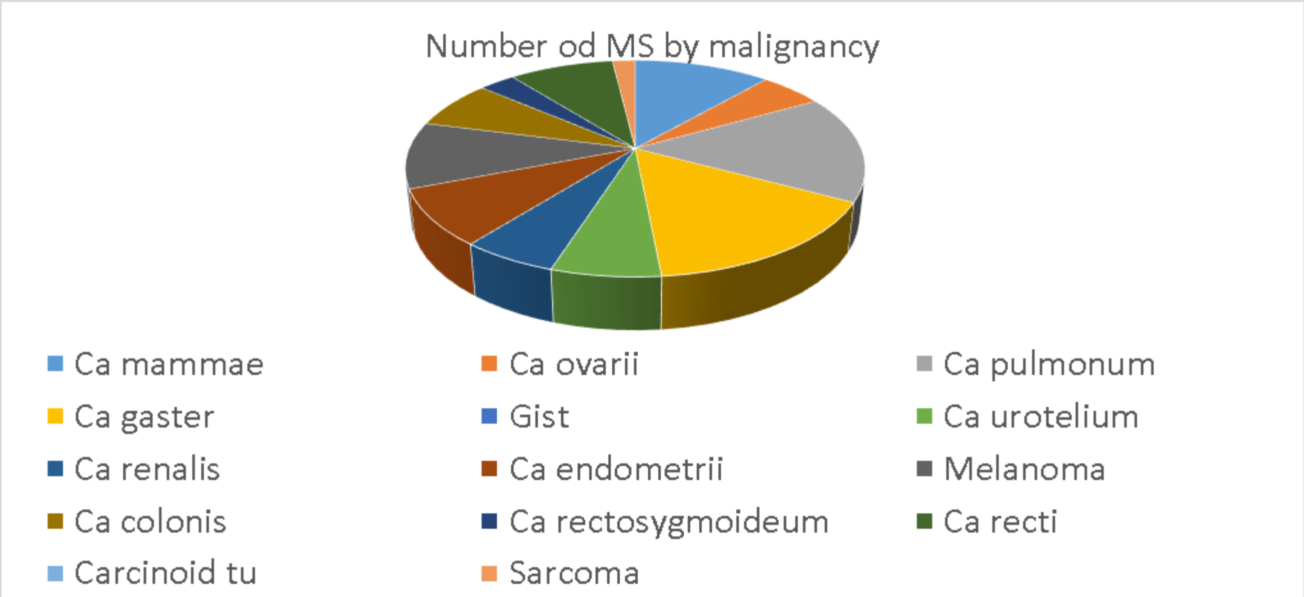

Figure 1. Frequency of tumors with metastatic deposits in the liver.

The gender structure of patients consisted of 26 (37.14%) men and 44 (62.86%) women. The analysis of the initial results showed that in our group of patients there was a larger number of female patients and a higher representation of metastatic liver changes in females.

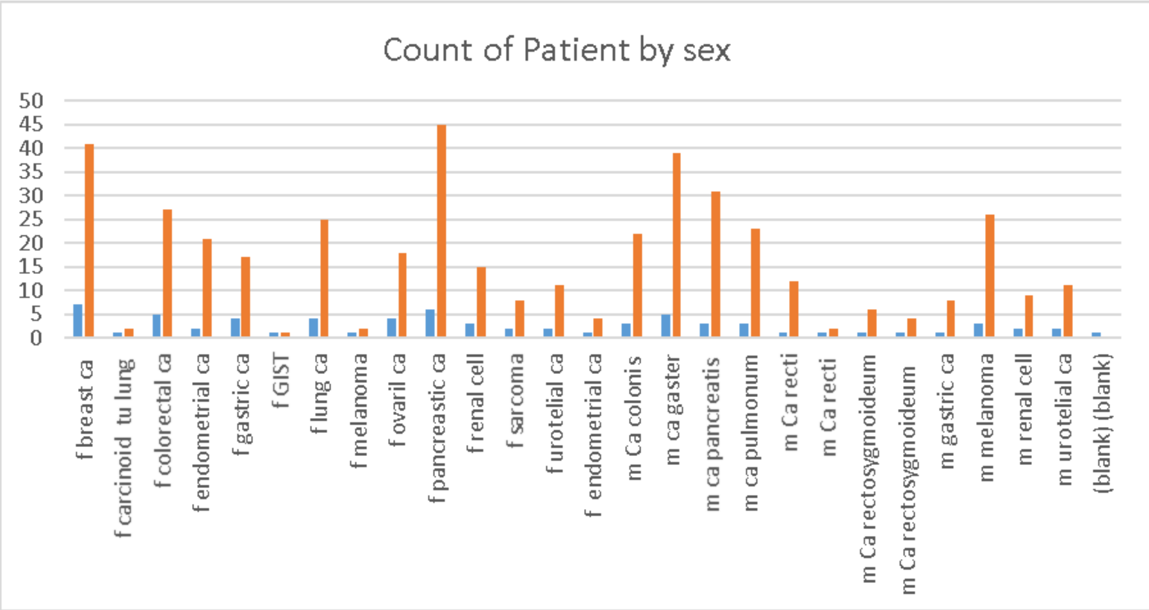

Figure 2. The gender structure of patients

Metastatic liver deposits were more common in women with primary breast and pancreatic tumors. In other primary tumors, gender had no influence.

MRI demonstrated superior performance in detecting hepatic metastases, identifying all 420 lesions present in the study population. This underscores the high sensitivity of MRI for liver lesion detection, particularly when using optimized protocols and liver-specific contrast agents.

FDG PET-CT, while still effective, detected only 296 lesions.

A critical finding was that 91 lesions with a diameter less than 10 mm were detected only on MRI.

Table 1. Distribution of number of hepatic metastases smaller and larger than 10 mm on MR

Total number of liver metastases on MR	**n (%)**
1	1 (1.43)
2	6 (8.57)
3	13 (18.57)
4	8 (11.43)
5	6 (8.57)
6	10 (14.28)
7	9 (12.86)
8	2 (2.86)
9	6 (8.57)
11	1 (1.43)
12	4 (5.71)
13	3 (4.28)
15	1 (1.43)
Total 420	**70**

Table 2. Distribution of number of hepatic metastases larger than 10 mm on FDG PET-CT

Total number of liver metastases on FDG PET-CT	**n (%)**
0	7 (10)
1	5 (7.14)
2	11 (15.71)
3	9 (12.86)
4	8 (11.43)
5	10 (14.28)
6	7 (10)
7	1 (1.43)
8	4 (5.71)
9	3 (4.28)
10	4 (5.71)
12	1 (1.43)
Total 296	**70**

No statistically significant difference was found in the number of lesions larger than 10 mm detected by PET CT and MR (p=0.37).

The number of lesions smaller than 10 mm detected by MR was significantly higher compared to PET CT (p=0.043).

The conclusion emphasizes the higher sensitivity of MRI in detecting liver metastases, particularly those smaller than 10 mm. This finding has significant implications in clinical practice, suggesting that MRI should be the preferred modality for detailed evaluation of the liver in patients with known or suspected liver metastases.

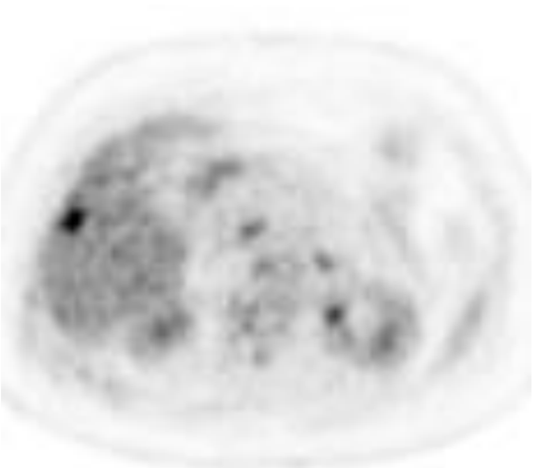

Figure 3. Morphological presentation of smaller metastatic deposits on the liver on MRI in a patient operated on for breast cancer with suspected metastasis in the V segment of the liver with a diameter of 8 mm, hyposignal compared to the rest of the hepatic parenchyma, without emphasized vascularization and without biliary invasion roads

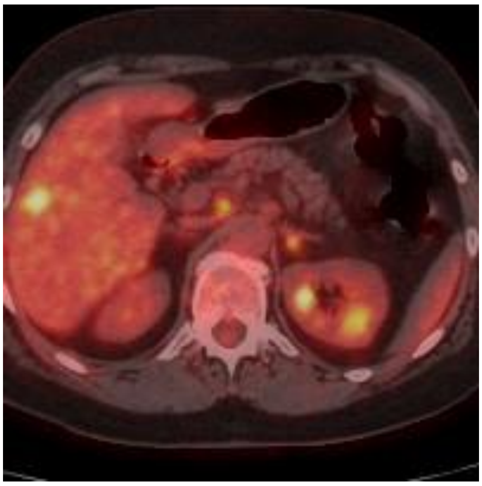

Figure 4. On the PET CT performed 1 month after MR, the same metastasis is shown with a high retention of the intravenously applied radioisotope FDG 18, with an SUV max of 6.7

Discussion

The largest number of metastases are multiple, to be precise, only 10% of cases have solitary metastases and usually involve different lobes.

The complexity of the hepatic vascularization and the microenvironment provide an opportunity for the development and invasion of malignant cells due to their slowed movement or rather stagnation in the sinusoids of the liver. The portal vein primarily delivers tumor emboli from malignant changes in various organs.

Prompt detection of hepatic metastases has a very important role in evaluation, prognosis and definition of the most appropriate therapeutic strategy in these patients, which is based on the descriptions and radiological findings from the preoperative radiological examinations.

Since 2016, extreme progress has been made in the diagnosis of liver metastases with the improvement of DWI techniques and Gd-EOB-DTPA MRI, which have been investigated in different institutions and different studies published in the last 5 years. The results have confirmed that a combination of different types of "imaging" techniques provide a very accurate diagnosis and presentation of liver metastases. Asato *et al*. confirmed a significantly higher sensitivity of the combination of DWI sequence with Gd-EOB-DTPA MRI (91.4%) compared to CT (80.9%), especially in metastases with a diameter of less than 10 mm (73.3% *vs*. 56.0% lesions ≤1 cm; 91.9% *vs*. >1 cm; 99.2% *vs*. >2 cm [23].

Our study included analysis of metastases and their presentation on MRI in DWI and post-contrast portovenous phase, PET CT analysis with number determination and anatomical localization.

It was shown that MRI was a more sensitive method for metastatic deposits smaller than 10 mm 91% compared to PET CT, 80.7%.

In a retrospective study by Tahtabasi *et al*. 42 patients with gastric and colorectal cancer origin were included and examined by MRI and PET CT [24].

In this study, MRI detected up to 25% more metastases compared to PET CT, but only in metastases smaller than 10 mm, while in metastases larger than 10 mm, both studies did not show a significant difference in sensitivity and specificity. This also correlates with our study, where MRI showed greater sensitivity in relation to metastases smaller than 10 mm by sorting their exact number and localization.

In the study by Souza *et al*. [25], which included an analysis of 15 patients with suspected liver metastases of various malignant origin, an analysis of PET CT and MRI 3 Tesla magnetic field strength was made. Conclusion was based on a per-patient analysis and it was shown that for the detection of metastases smaller than 10 mm, MRI with intravenous contrast application was a superior method, up to 96% over PET CT, which was also shown in our study. But, the specificity of MR compared to PET CT is somewhat lower considering the limiting character of our device which is 1.5 Tesla magnetic field strength.

The hepatobiliary phase, complementary to the sequence in DWI where the restriction of movement of water molecules in the tissue is detected, shows metastases that are smaller than 10 mm with a higher degree of demarcation of their borders compared to other modalities such as 18 FDG PET CT and CT [26].

The study by Matteo Renzulli *et al.* [27] included an analysis of different results in the last 10 years, where with the development of new magnetic resonance techniques such as DWI, techniques with intravenous contrast application and specific hepatobiliary contrast have led to a remarkable progression in the detection and analysis of metastatic liver deposits of various malignant origins.

What is the impact of these findings on international oncological guidelines and protocols? The latest edition of oncology protocols revised in 2017 by the European Society of Medical Oncology unfortunately puts magnetic resonance in the detection of liver metastases as the second modality after CT of the thorax and abdomen, and if there is suspicion of liver metastases, then liver MR is recommended.

On the other hand, other authors in their individual papers propose and prove that in fact magnetic resonance imaging should be performed immediately after an ultrasound examination of the liver, and if there is any suspicion of ultrasound, it should be performed immediately with combined techniques such as DWI and post-contrast series [28,29].

The latest version of the National Comprehensive Cancer Network (NCCN) guidelines for colorectal cancer is in the direction of CT being the first-line modality for the detection of liver metastases [30,31].

Conclusion

According to the results of the study, it can be seen that with the advancement and introduction of new techniques with magnetic resonance, it is much superior in showing the smaller metastatic deposits of the liver, and that in those with a diameter of less than 10 mm. MR provides opportunities for multiple sequences and models with and without contrast enhancement, during which an accurate assessment of the type of invasion of the metastases, whether it is biliary or vascular, is carried out.

Despite its lower sensitivity for small liver lesions, FDG PET-CT provided valuable additional information about extrahepatic disease. This capability makes PET-CT particularly useful in initial staging, as it can identify metastases in other organs or lymph nodes that might not be visible on liver-specific MRI. The whole-body imaging capability of PET-CT is a significant advantage in oncological staging, allowing for a comprehensive assessment of disease extent in a single examination.

References

1. Gotra A, Sivakumaran L, Chartrand G, et al. Liver segmentation: indications, techniques and future directions. Insights Imaging. 2017;8(4):377-392.
2. Al-Ibraheem A, Ruzzeh S, Badarneh M, Al-Adhami D, Telfah A. Beyond CT: A Case Analysis of Serial [18F]FDG PET/CT for Assessment of Necrosis and Early Recurrence in Colorectal Liver Metastases. Cureus. 2023;15(12):51393.
3. Birrer DL, Tschuor C, Reiner C, et al. Multimodal treatment strategies for colorectal liver metastases. Swiss Med Wkly. 2021;151:20-390.
4. Fernandez FG, Drebin JA, Linehan DC, Dehdashti F, Siegel BA, Strasberg SM: Five-year survival after resection of hepatic metastases from colorectal cancer in patients screened by positron emission tomography with F-18 fluorodeoxyglucose (FDG-PET). Ann Surg 2004;240:438–447.450
5. Yang M, Martin DR, Karabulut N, Frick MP (2003) Comparison of MR and PET imaging for the evaluation of liver metastases. J Magn Reson Imaging 17:343–349
6. Böhm B, Voth M, Geoghegan J, Hellfritzsch H, Petrovich A, Scheele J, Gottschild D (2004) Impact of positron emission tomography on strategy in liver resection for primary and secondary liver tumors. J Cancer Res Clin Oncol 130:266–272
7. Kinkel K, Lu Y, Both M, Warren RS, Thoeni RF. Detection of hepatic metastases from cancers of the gastrointestinal tract by using noninvasive imaging methods (US, CT, MR imaging, PET): a meta-analysis. Radiology. 2002;224(3):748-756.
8. Marom EM, McAdams HP, Erasmus JJ, et al. Staging non-small cell lung cancer with whole-body PET. Radiology. 1999;212(3):803-809.

9. Grassetto G, Fornasiero A, Bonciarelli G, et al. Additional value of FDG-PET/CT in management of "solitary" liver metastases: preliminary results of a prospective multicenter study. Mol Imaging Biol. 2010;12(2):139-144.
10. Kim MJ, Lee KH, Lee KT, et al. The value of positron emission tomography/computed tomography for evaluating metastatic disease in patients with pancreatic cancer. Pancreas. 2012 Aug;41(6):897-903.
11. Semelka RC, Cance WG, Marcos HB, Mauro MA. Liver metastases: comparison of current MR techniques and spiral CT during arterial portography for detection in 20 surgically staged cases. Radiology. 1999;213:86–91.
12. Yu JS, Rofsky NM. Hepatic metastases: perilesional enhancement on dynamic MRI. AJR Am J Roentgenol. 2006;186:1051–1058.
13. Semelka RC, Hussain SM, Marcos HB, Woosley JT. Perilesional enhancement of hepatic metastases: correlation between MR imaging and histopathologic findings-initial observations. Radiology. 2000;215:89–94.
14. Baron RL, Peterson MS. Liver tumor detection: comparison of Gd-BOPTA-enhanced MR, contrast-enhanced CT, and CT arterial portography (abstract) Radiology. 1995;197:415.
15. Caudana R, Morana G, Pirovano GP, et al. Focal malignant hepatic lesions: MR imaging enhanced with gadolinium benzyloxypropionictetra-acetate (BOPTA) – preliminary results of phase II clinical application. Radiology. 1996;199:513–520.
16. Reimer P, Rummeny EJ, Daldrup HE, et al. Enhancement characteristics of liver metastases, hepatocellular carcinomas, and hemangiomas with Gd-EOB-DTPA: preliminary results with dynamic MR imaging. Eur Radiol. 1997;7:275–280.
17. Paulatto L, Dioguardi Burgio M, Sartoris R, et al. Colorectal liver metastases: radiopathological correlation. Insights Imaging. 2020;11(1):99.
18. Hardie AD, Naik M, Hecht EM, et al. Diagnosis of liver metastases: value of diffusion-weighted MRI compared with gadolinium-enhanced MRI. Eur Radiol. 2010;20(6):1431-1441.
19. Seneterre E, Taourel P, Bouvier Y, et al. Detection of hepatic metastases: ferumoxides-enhanced MR imaging versus unenhanced MR imaging and CT during arterial portography. Radiology. 1996;200:785–792.
20. Oudkerk M, van den Heuvel AG, Wielopolski PA, Schmitz PI, Borel Rinkes IH, Wiggers T. Hepatic lesions: detection with ferumoxide-enhanced T1-weighted MR imaging. Radiology. 1997;203:449–456
21. Blokhuis TJ, van der Schaaf MC, van den Tol MP, Comans EF, Manoliu RA, van der Sijp JR: Results of radio frequency ablation of primary and secondary liver tumors: long-term follow-up with computed tomography and positron emission tomography-18F-deoxyfluoroglucose scanning. Scand J Gastroenterol Suppl 2004;241:93–97.
22. Hagspiel KD, Neidl KF, Eichenberger AC, Weder W, Marincek B. Detection of liver metastases: comparison of superparamagnetic iron oxide-enhanced and unenhanced MR imaging at 1.5 T with dynamic CT, intraoperative US, and percutaneous US. Radiology. 1995;196:471–478.
23. Tirumani SH, Jagannathan JP, Braschi-Amirfarzan M, et al. Value of hepatocellular phase imaging after intravenous gadoxetate disodium for assessing hepatic metastases from gastroenteropancreatic neuroendocrine tumors: comparison with other MRI pulse sequences and with extracellular agent. Abdom Radiol (NY). 2018;43(9):2329-2339.
24. Tahtabasi M, Erturk SM, Basak M. Comparison of MRI and 18F-FDG PET/CT in the Liver Metastases of Gastrointestinal and Pancreaticobiliary Tumors. Sisli Etfal Hastan Tip Bul. 2021;55(1):12-17.
25. D'souza MM, Sharma R, Jaimini A, Saw SK, Pandey S, et al. (2017) Detection of hepatic metastases by 18F-FDG PET/ CT and MRI. J Nucl Med Radiol Imaging 2017: JNMRI-101.
26. Karaosmanoglu AD, Onur MR, Ozmen MN, Akata D, Karcaaltincaba M. Magnetic Resonance Imaging of Liver Metastasis. Semin Ultrasound CT MR. 2016;37(6):533-548.
27. Renzulli M, Clemente A, Ierardi AM, et al. Imaging of Colorectal Liver Metastases: New Developments and Pending Issues. Cancers (Basel). 2020;12(1):151.
28. Coates GG, Borrello JA, McFarland EG, Mirowitz SA, Brown JJ. Hepatic T2-weighted MRI: a prospective comparison of sequences, including breath-hold, half-Fourier turbo spin echo (HASTE). J Magn Reson Imaging *1998*; 8:642-649

29. Dromain C, de Baere T, Baudin E, et al. MR imaging of hepatic metastases caused by neuroendocrine tumors: comparing four techniques. AJR Am J Roentgenol. 2003;180(1):121-128.
30. d'Assignies G, Fina P, Bruno O, et al. High sensitivity of diffusion-weighted MR imaging for the detection of liver metastases from neuroendocrine tumors: comparison with T2-weighted and dynamic gadolinium-enhanced MR imaging. Radiology. 2013;268(2):390-399.
31. Carlbom L, Caballero-Corbalán J, Granberg D, Sörensen J, Eriksson B, Ahlström H. Whole-body MRI including diffusion-weighted MRI compared with 5-HTP PET/CT in the detection of neuroendocrine tumors. Ups J Med Sci. 2017;122(1):43-50.