Imaging of metastatic melanoma

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Learning objectives

1. To demonstrate the merit of each imaging technique in the evaluation of metastatic spread of melanoma.
2. To discuss the potential patterns and location of distant dissemination of melanoma.

Background

Primary melanoma

Definition:

-Aggressive tumor originating from melanocytes.

Epidemiology:

-2,2-19,2/100 000 in Europe

-1,5/100 000 mortality rate

Risk factors:

- White race
- Sun sensitivity
- Severe sunburns
- Many moles
- Freckles
- Family history of skin cancer

Primary Melanoma workout:

-Breslow and Clark for staging primary lesion

-TNM classification:

- Breslow thickness

- Clark level
- Locoregional metastasis
- Distant metastasis
- Serum LDH is an independent prognostic factor aside from the location of metastasis

-Poor prognosis for advanced disease

Disease staging is performed using the TNM classification on a clinical or pathological base (Table 1 on page 4).
Imaging plays a pivotal role in the staging, follow-up and monitoring of treatment response of malignant melanoma.
The purpose of this poster is to evaluate the potential patterns and location of distant dissemination and the merit of each imaging technique in the evaluation of metastatic spread.

Metastatic melanoma

Definition:

Metastatic melanoma is tumor spread beyond the primary lesion. Tumor dissemination occurs through lymphatic or hematogenous spread Fig. 1 on page 4. Metastasis is subdivided in locoregional metastasis Fig. 2 on page 5 or distant metastasis. Locoregional metastasis mainly occurs through lymphatic spread.

Locoregional metastasis:

- Local recurrences
- Satellite metastasis Fig. 3 on page 6
- In-transit metastasis Fig. 4 on page 7
- Nodal basin

Distant metastasis are classified in 3 groups, according to the side of metastasis and serum LDH:

- M1a: Metastasis to distant skin, subcutaneous tissue or distant lymph nodes with a normal serum LDH
- M1b: Metastasis to the lung with a normal serum LDH
- M1c: Metastasis to any other viceral organ with a normal serum LDH or with any metastasis with an elevated serum LDH

Images for this section:

	Clinical Staging				Pathologic staging		
					T	N	M
0	Tis	N0	M0	0	Tis	N0	M0
IA	T1a	N0	M0	IA	T1a	N0	M0
IB	T1b	N0	M0	IB	T1b	N0	M0
	T2a	N0	M0		T2a	N0	M0
IIA	T2b	N0	M0	IIA	T2b	N0	M0
	T3a	N0	M0		T3a	N0	M0
IIB	T3b	N0	M0	IIB	T3b	N0	M0
	T4a	N0	M0		T4a	N0	M0
IIC	T4b	N0	M0	IIC	T4b	N0	M0
III	Any T	N>N0	M0	IIIA	T1-4a	N1a	M0
					T1-4a	N2a	M0
				IIIB	T1-4b	N1a	M0
					T1-4b	N2a	M0
					T1-4a	N1b	M0
					T1-4a	N2b	M0
					T1-4a	N2c	M0
				IIIC	T1-4b	N1b	M0
					T1-4b	N2b	M0
					T1-4b	N2c	M0
					Any T	N3	M0
IV	Any T	Any N	M1	IV	Any T	Any N	M1

Table 1: Table of the clinical and pathologic TNM classification. Further discussion is beyond the scope of this poster. Further down this poster, we will point out when imaging for metastatic melanoma is indicated in asymptomatic patients.

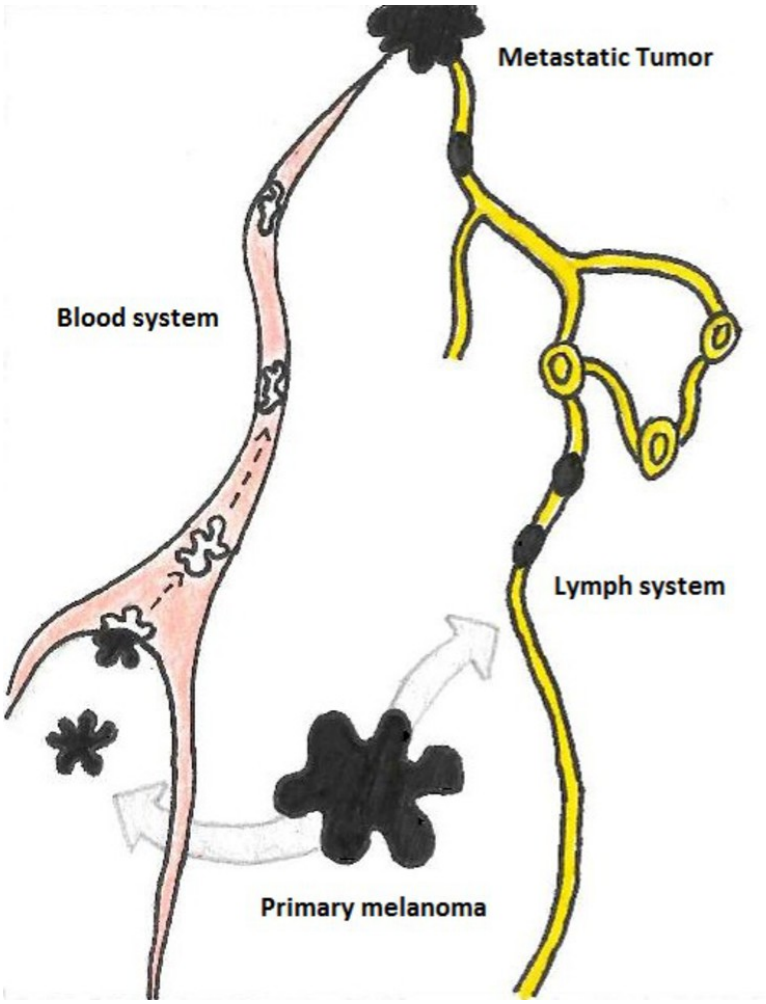

Fig. 1: Schematic drawing of hematogenous and lymphatic dissemination.

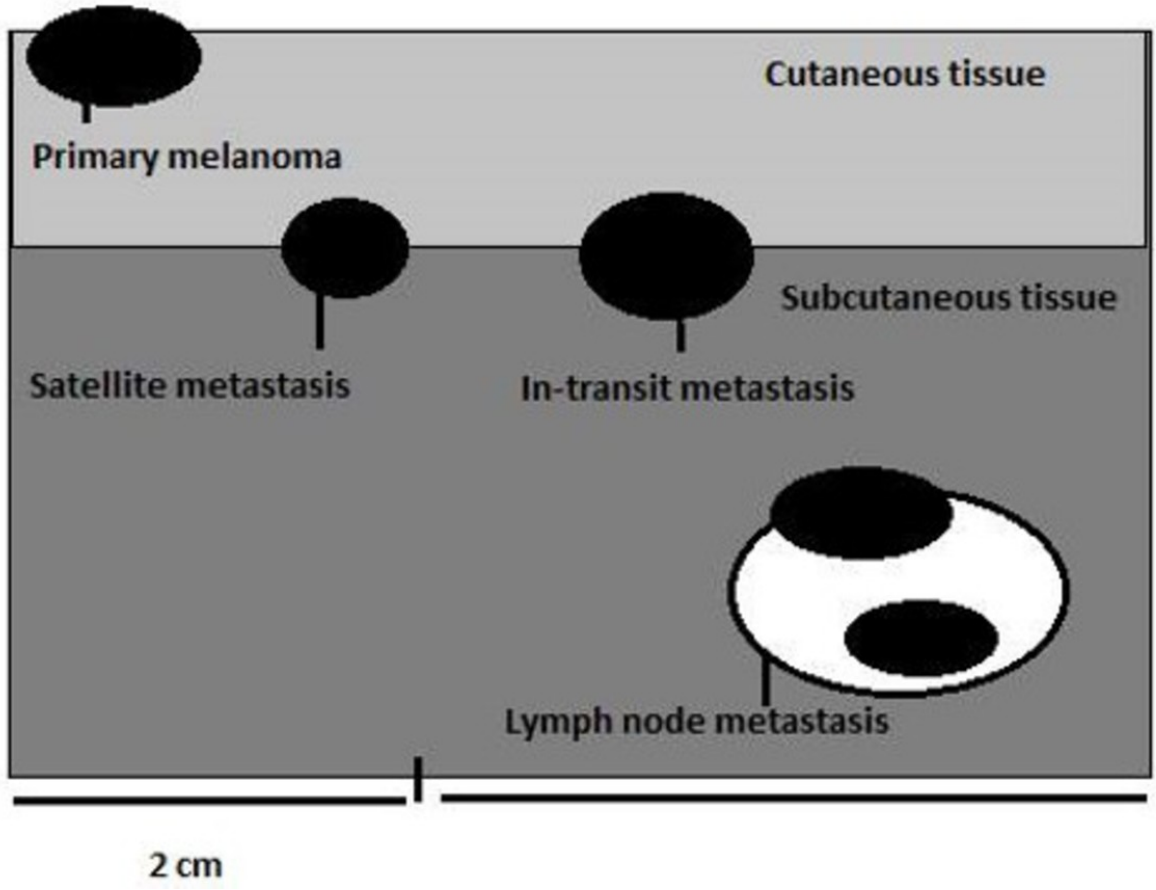

Fig. 2: Schematic drawing of locoregional metastasis.

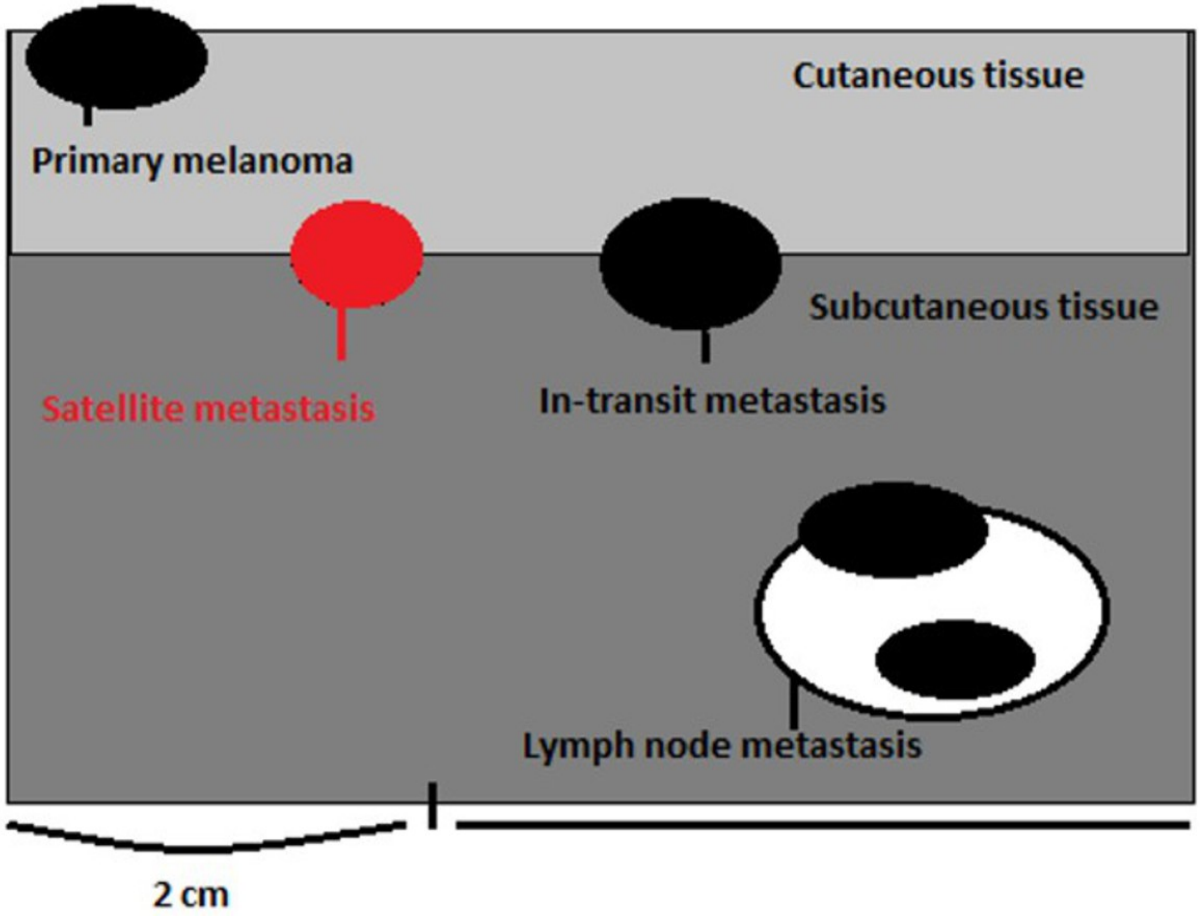

Fig. 3: Schematic drawing of locoregional metastasis. Satellite metastasis (red) are cutaneneous or subcutaneous metastasis located between the primary lesion or scar tissue and the draining lymph node basin. They are located within 2 cm from the primary tumor or scar tissue. Satellite metastasis are considered a nodal metastasis in the TNM classification.

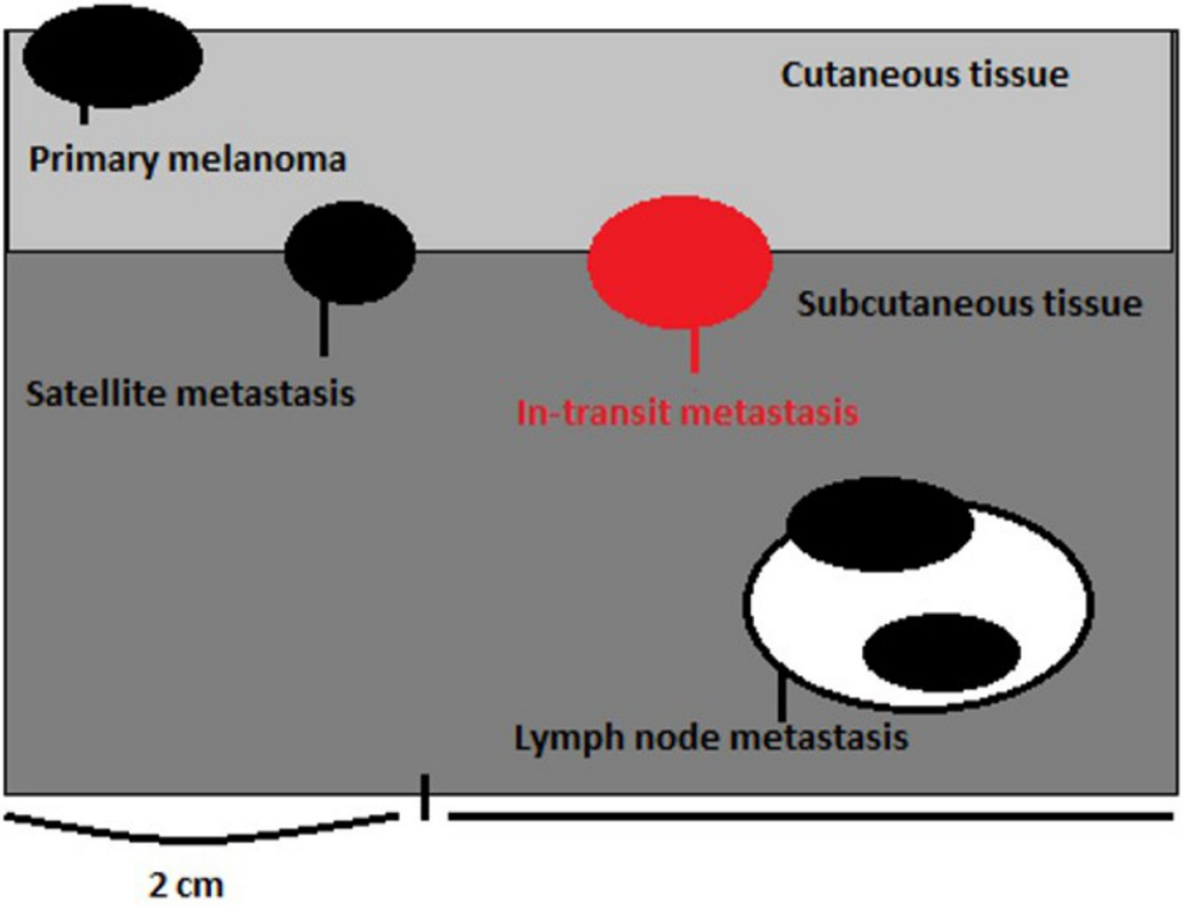

Fig. 4: Schematic drawing of in-transit metastasis. In-transit metastasis (red) are cutaneous or subcutaneous metastasis located between the primary lesion or scar tissue and the draining lymph node basin. They are 2 cm away from the primary tumor or scar and before reaching the regional lymph node basin. In-transit metastasis are considered a nodal metastasis in the TNM classification.

Findings and procedure details

I. MERIT OF EACH IMAGING TECHNIQUE IN THE EVALUATION OF METASTATIC SPREAD OF MELANOMA

1. General need for imaging
2. Ultrasound
3. Radiography
4. Computed tomography
5. Magnetic resonance imaging
6. Lymphoscintigraphy
7. Positron emission tomography - computed tomography

II. POTENTIAL PATTERNS AND LOCATION OF DISTANT DISSEMINATION OF MELANOMA

1. Locoregional metastasis
2. Chest
3. Central nervous system
4. Abdomen
5. Musculoskeletal system
6. Miscellaneous

I. MERIT OF EACH IMAGING TECHNIQUE IN THE EVALUATION OF METASTATIC SPREAD OF MELANOMA

1. General need for imaging

	Clinical Staging				Pathologic staging			Imaging recommandations asymptomatic patients
					T	N	M	
	0 Tis	N0	M0		0 Tis	N0	M0	
IA	T1a	N0	M0	IA	T1a	N0	M0	
IB	T1b	N0	M0	IB	T1b	N0	M0	
	T2a	N0	M0		T2a	N0	M0	No imaging for asymptomatic patients
IIA	T2b	N0	M0	IIA	T2b	N0	M0	
	T3a	N0	M0		T3a	N0	M0	
IIB	T3b	N0	M0	IIB	T3b	N0	M0	
	T4a	N0	M0		T4a	N0	M0	
IIC	T4b	N0	M0	IIC	T4b	N0	M0	
III	Any T	N>N0	M0	IIIA	T1-4a	N1a	M0	
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				IIIB	T1-4b	N1a	M0	
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					T1-4a	N1b	M0	Consider screening with Chest X-ray, CT, brain MRI and/or PET-CT
					T1-4a	N2b	M0	
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					T1-4b	N2b	M0	
					T1-4b	N2c	M0	
					Any T	N3	M0	
IV	Any T	Any N	M1	IV	Any T	Any N	M1	

Table 2: The red line indicates in which patients screening with imaging should be considered. Asymptomatic patients with IA-IIA disease do not need screening with imaging. Patients with at least stage IIB disease, imaging should be considered. These are patients with a primary tumor of 2,1-4 mm thickness with ulcerations (T3b) or patients with primary tumor of >4 mm thickness (T4a). It is recommended to screen with Chest-XR, CT and/or PET/CT every 3-12 months and annual MRI of the brain during 2-5 years. After 5 year of follow-up, asymptomatic patients do not need any screening with imaging.

Table 2

References: Department of Radiology, University Hospital Antwerp - Antwerp/BE

2. Ultrasound

-Advantages:

- Cheap
- Primary melanoma
- Evaluation of local recurrence, in-transit or regional lymph nodes metastases Fig. 5 on page 17
- Fine needle aspiration cytology (FNAC) Fig. 6 on page 18 :
  -In-transit and satellite: 95% sensitivity and 100% specificity
  -Nodal basins: 79% sensitivity and 100% specificity

-Disadvantages:

- Limited use for distant metastasis

-Imaging characterization:

- Hypo-echoic Fig. 7 on page 19
- Hypervascularisation on power doppler Fig. 8 on page 20

3. Radiography

-Advantages:

- Cheap
- Low radiation dose
- Chest x-ray for baseline comparison Fig. 9 on page 21

-Disadvantages:

- Low sensitivity and specificity
  -Bone metastasis only visible when cortical destruction or #30% trabecular bone loss occurs Fig. 10 on page 22
- Limited role in staging/evaluation of metastatic melanoma

-Imaging characterization:

- Hilar enlargement Fig. 11 on page 22
- Lung nodules or masses Fig. 9 on page 21
- Bone metastasis are generally osteolytic Fig. 10 on page 22

4. Computed tomography

-Advantages:

- Quick examination of large body parts
- Widespread availability
- Different windowing settings for the evaluation of bone and different organ systems on one examination Fig. 12 on page 23
- Best technique detecting lung metastasis
- Monitoring treatment outcome: CT + serum LDH à predicting survival

-Disadvantages:

- Radiation dose
- Not the highest sensitivity and specificity in most organ systems

-Imaging characterization:

- Hypervascular metastasis
  -Enhancing on peak hepatic arterial phase Fig. 13 on page 24
  -Heterogeneous, rim or nodular enhancement
- Hepatic metastasis
  -Multiphase CE CT with at least 2 different phases Fig. 14 on page 25
- Intratumoral haemorrhage Fig. 15 on page 25
  -Non CE CT and CE CT in acute setting
  -MRI when available

5. Magnetic resonance imaging

-**Advantages:**

- Detailed tumor size and preoperative assessment
- Highest sensitivity and specificity in most organ systems, except for lung metastasis
- Characterization questionable lesions
- Whole-body MRI promising technique

-Disadvantages:

- Limited availability
- Limited field of view
- Patient-related contraindications

-MRI characterization:

- Paramagnetic effect of melanin with typical signal on T1- and T2-WI Fig. 16 on page 26
  -Hyperintense on T1-WI
  -Hypointense on T2-WI
- Melanotic metastasis comprise 25 % of lesions: >10% melanin cells
- Amelanotic metastasis with non specific signal intensity Fig. 17 on page 27
- Hypervascular metastasis with contrast behavior similar to CT Fig. 18 on page 28 Fig. 19 on page 28
- Intratumoral haemorrhage in 19% of brain metastasis Fig. 29 on page 36 Fig. 30 on page 37
  -Acute, subacute and chronic bleeding

6. Lymphoscintigraphy

- Sentinel node is the first lymph node or group of lymph nodes, draining the tumor
- Radioactive tracer

- Primary staging
- Considered in stage IA
- Should be performed in stage IB and II

7. Positron emission tomography - computed tomography

-Advantages:

- Metabolic function and high anatomic resolution Fig. 20 on page 30
- High specificity and sensitivity
- Characterization of indeterminate lesions Fig. 21 on page 30
- Exact staging for patients with resectable distant metastasis

-Disadvantages:

- Expensive
- High radiation dose
- Limited availability

-PET alone has a poor anatomic resolution and low specificity and is not routinely used in metastatic melanoma

II. POTENTIAL PATTERNS AND LOCATION OF DISTANT DISSEMINATION OF MELANOMA

Metastatic pattern of malignant melanoma

Table 3

Metastatic pattern	Literature	Our data
Skin, subcutaneous tissue and regional lymph nodes	59%	83%
Lung	36%	20%
Brain	20%	14%
Liver	20%	8%
Bone	17%	8%

Table 2: This table shows a comparison between literature data and our data of the most common sites of metastasis in melanoma.

References: **Department of Radiology, University Hospital Antwerp - Antwerp/BE**

1. Locoregional metastasis

-Clinical examination

-US and subsequent FNAC if indicated

-CT and MRI not routinely used

-Locations:

- Local recurrences
- Satellite metastasis Fig. 23 on page 32
- In-transit metastasis Fig. 23 on page 32
- Nodal basin

2. Chest

-CT modality of choice

-Lung is most affected visceral organ (36%)

-Most lesions measure 1-2 cm

-Feeding vessel as sign of hematogenous spread

-Location:

- Lung parenchyma
- Pleura
- Mediastinal and hilar lymph nodes
  Fig. 24 on page 32

3. Central nervous system

-MRI modality of choice

-Acute haemorrhagic brain metastasis: CT and CE CT Fig. 29 on page 36 Fig. 30 on page 37

-Locations:

- Brain: 20%
  -Intra-axial Fig. 25 on page 33 Fig. 26 on page 34
  -Leptomeningeal Fig. 27 on page 35 Fig. 28 on page 36
- Spinal:
  -Intramedullary
  -Leptomeningeal Fig. 31 on page 38
  -Epidural Fig. 17 on page 27

4. Abdomen

-Multiphasic CE CT Fig. 14 on page 25

-MRI for questionable lesions
-Locations:

- Liver: 20%
  -Variable in size, up to 15 cm.
  -Intralesional hemorrhage, calcifications and necrotic areas Fig. 32 on page 38

- Adrenal glands, usually unilateral Fig. 33 on page 39
- Gastrointenstinal tract: small bowel > colon > stomach Fig. 34 on page 39
- Duodenum, rectum, esophagus and anus infrequent Fig. 35 on page 40
- Spleen unfrequent Fig. 36 on page 40
- Kidney, pancreas Fig. 37 on page 41 and gallbladder Fig. 38 on page 42 rare
- Lymph nodes Fig. 39 on page 43

5. Musculoskeletal system

-CT for bone
-PET/CT or MRI for questionable lesions Fig. 21 on page 30
-MRI for muscle
-Osteolytic, slightly expansile lesions Fig. 10 on page 22
-Rarely isolated muscle involvement

-Location:

- Bone: 17%
  -Axial skeleton
  -Ribs
  -Others Fig. 40 on page 43
- Muscles:
  -Lower extremities > trunk > upper extremities Fig. 23 on page 32

6. Miscellaneous

- Although cardiac Fig. 12 on page 23 and breast metastasis is rare, the prevalence is higher in melanoma compared to other tumors Fig. 41 on page 43
- Salivary glands is extremely rare Fig. 41 on page 43
- Primary melanoma of the eye and paranasal sinuses is known. Metastasis should be considered in disseminated disease, but metachronous tumor should always be considered

Images for this section:

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Table 2

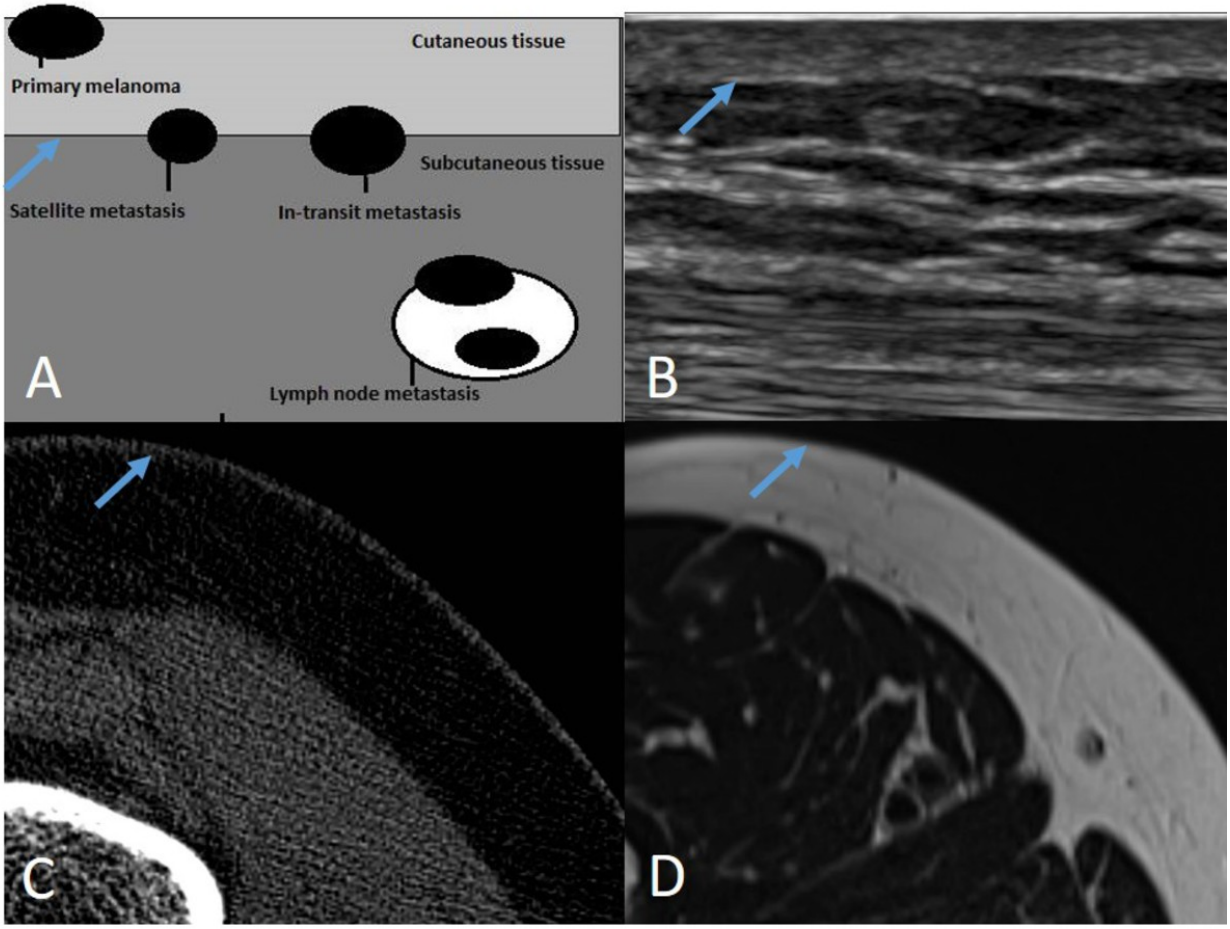

Fig. 5: Schematic drawing (A) of locoregional metastasis indicating the primary lesion, satellite metastasis, in-transit metastasis and metastasis to the nodal basin. An anatomical correlation with US (B), CT (C) and MRI (D) of the upper leg. The blue arrow indicates the transition between cutis and subcutis. US has a higher anatomical resolution of the cutis and subcutis than CT and MRI. Unfortunately, US is limited by its poor deep penetration.

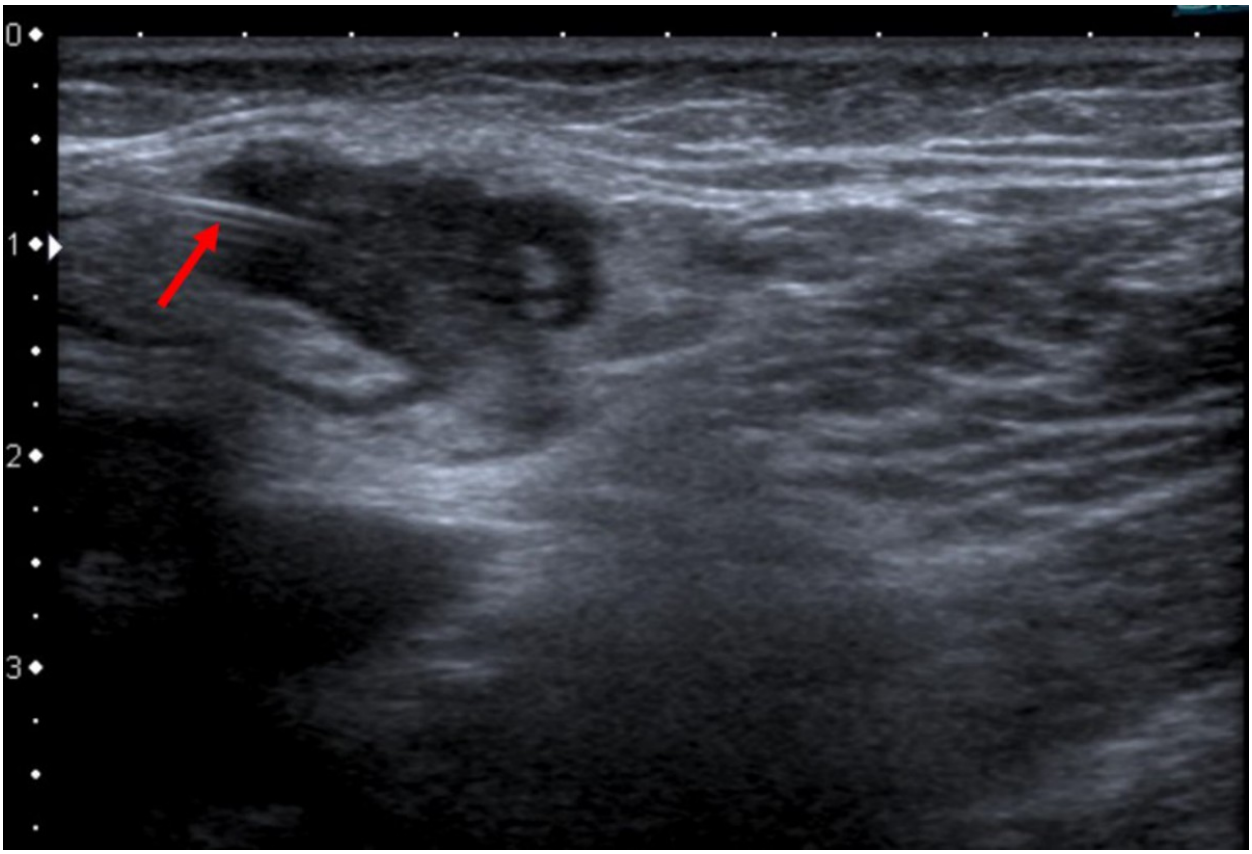

Fig. 6: US guided FNAC shows the needle (red arrow) in a hypo-echoic lesions. Histopathology confirmed metastatic melanoma.

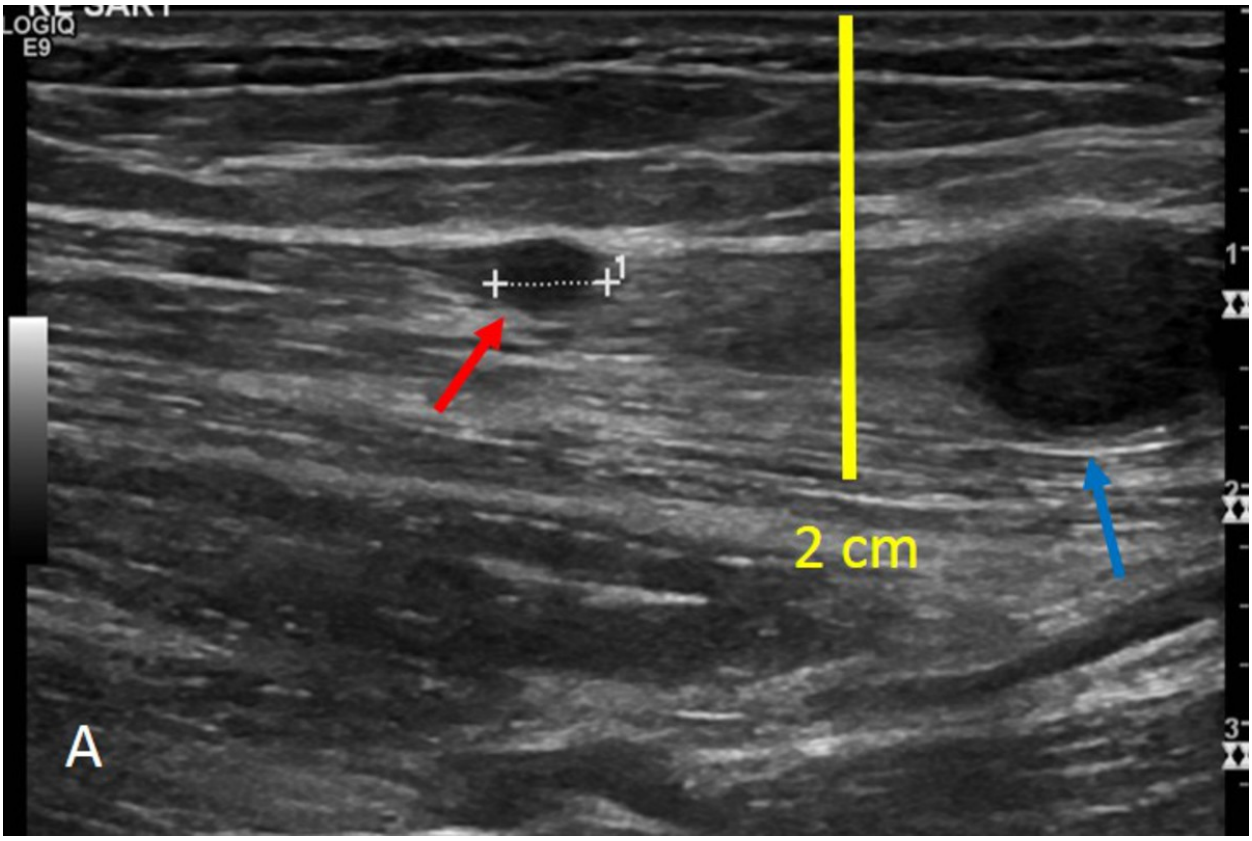

Fig. 7: Grey-scale US (A) of the left upper leg shows multiple hypoechoic lesions located in the sartorius muscle. The lesion indicated by the blue arrow is a satellite metastasis and the red arrow indicates an in-transit metastasis. The yellow line demarcates the difference between satellite and in-transit metastasis. The lesions have a cable-like appearance, initially interpreted as a neurogenic tumor. The lesions show increased vascularity on power doppler US (B).

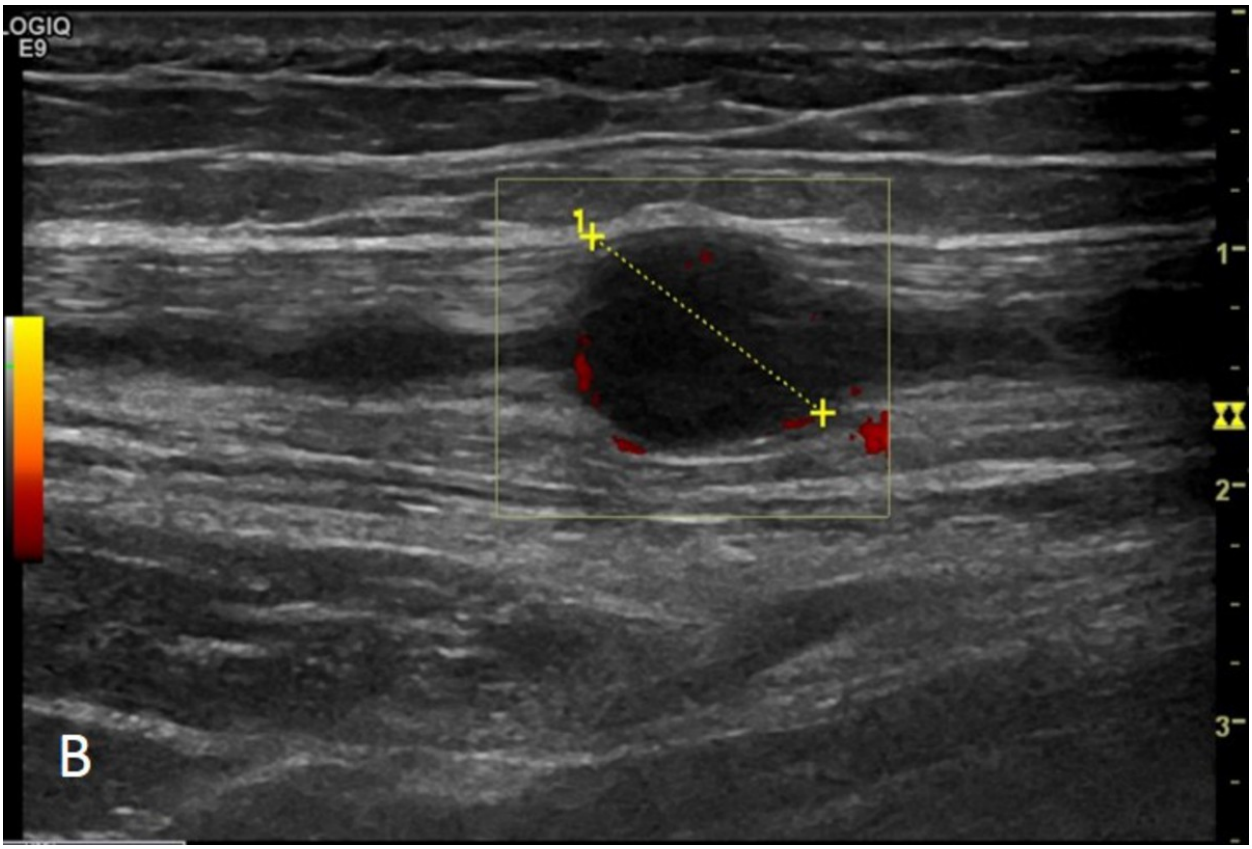

Fig. 8: Grey-scale US (A) of the left upper leg shows multiple hypoechoic lesions located in the sartorius muscle. The lesion indicated by the blue arrow is a satellite metastasis and the red arrow indicates an in-transit metastasis. The yellow line demarcates the difference between satellite and in-transit metastasis. The lesions have a cable-like appearance, initially interpreted as a neurogenic tumor. The lesions show increased vascularity on power doppler US (B).

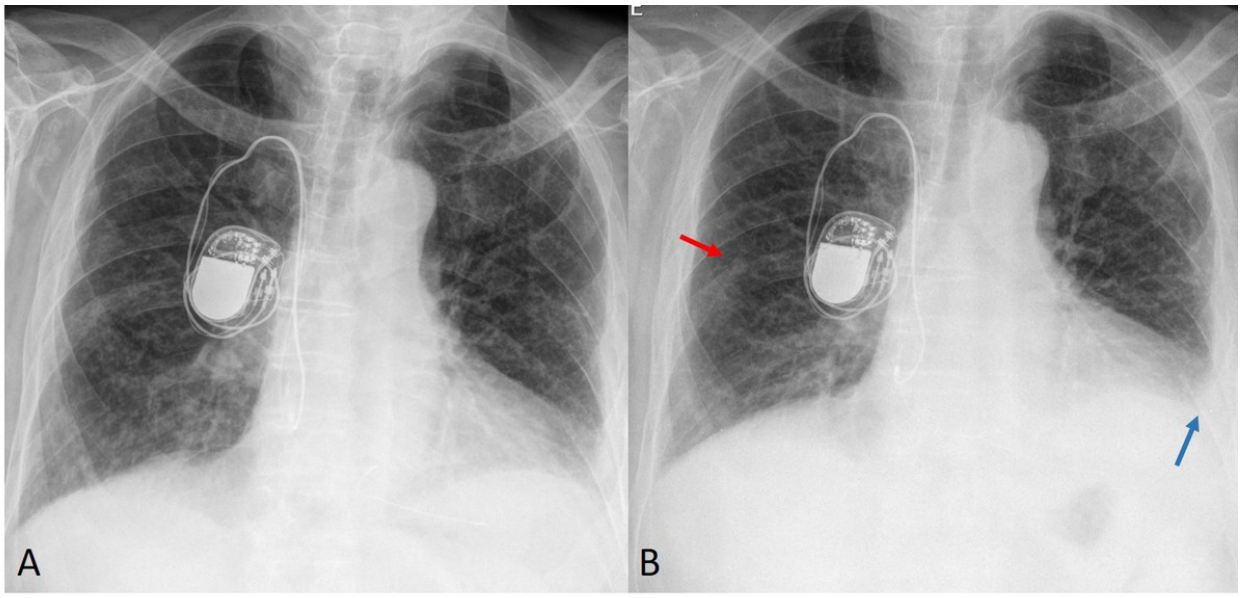

Fig. 9: A baseline X-ray of the chest (A), helps to detect small lung metastasis (red arrow) in the right lung and the pleural effusion in the left lung (blue arrow).

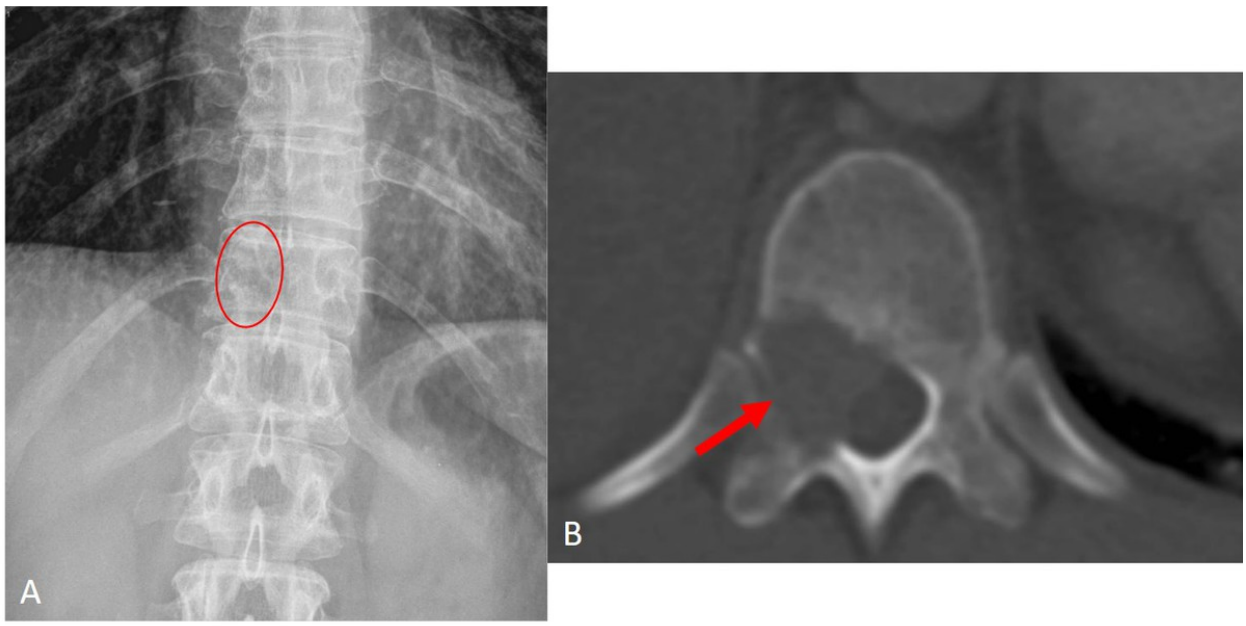

Fig. 10: Plain radiograph (A) shows destruction of the cortical outline of the pedicle of Th11 (red circle). CT (B) confirms a osteolytic metastasis with soft tissue component expanding in the spinal cord (red arrow).

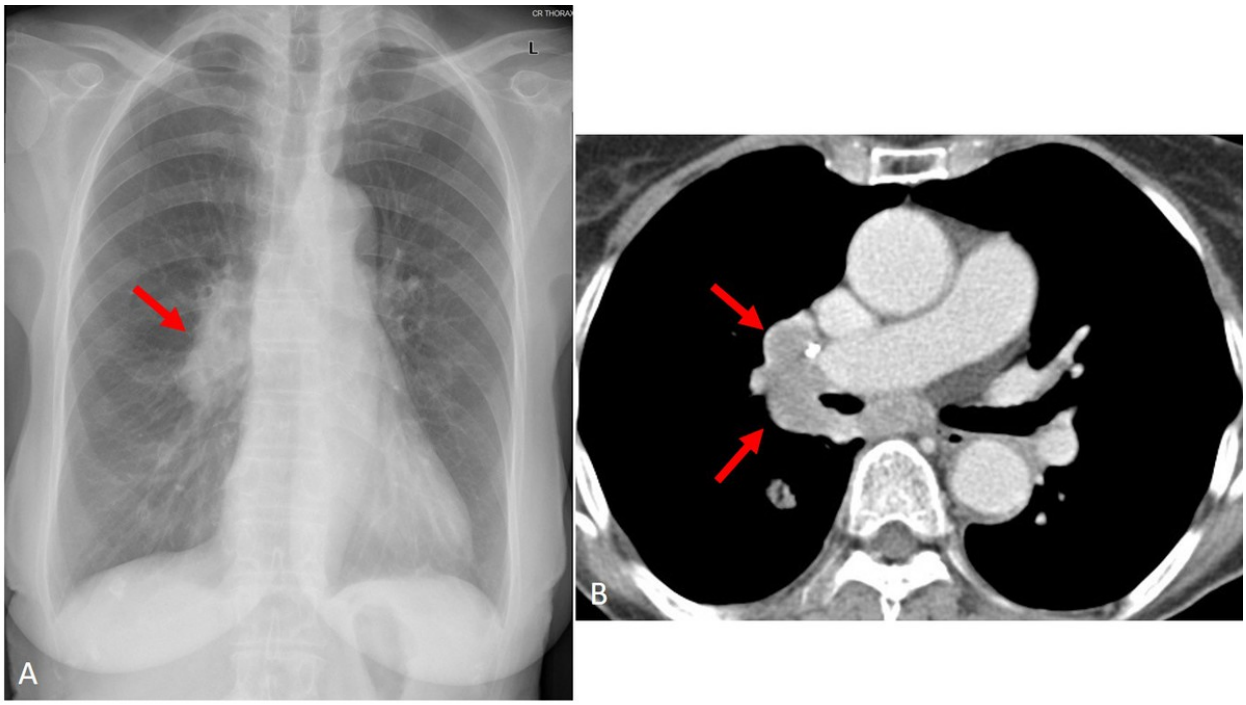

Fig. 11: PA chest X-ray (A) shows an enlarged right hilum (red arrow), suspicious for adenopathy which was confirmed on CE CT (B) (red arrows).

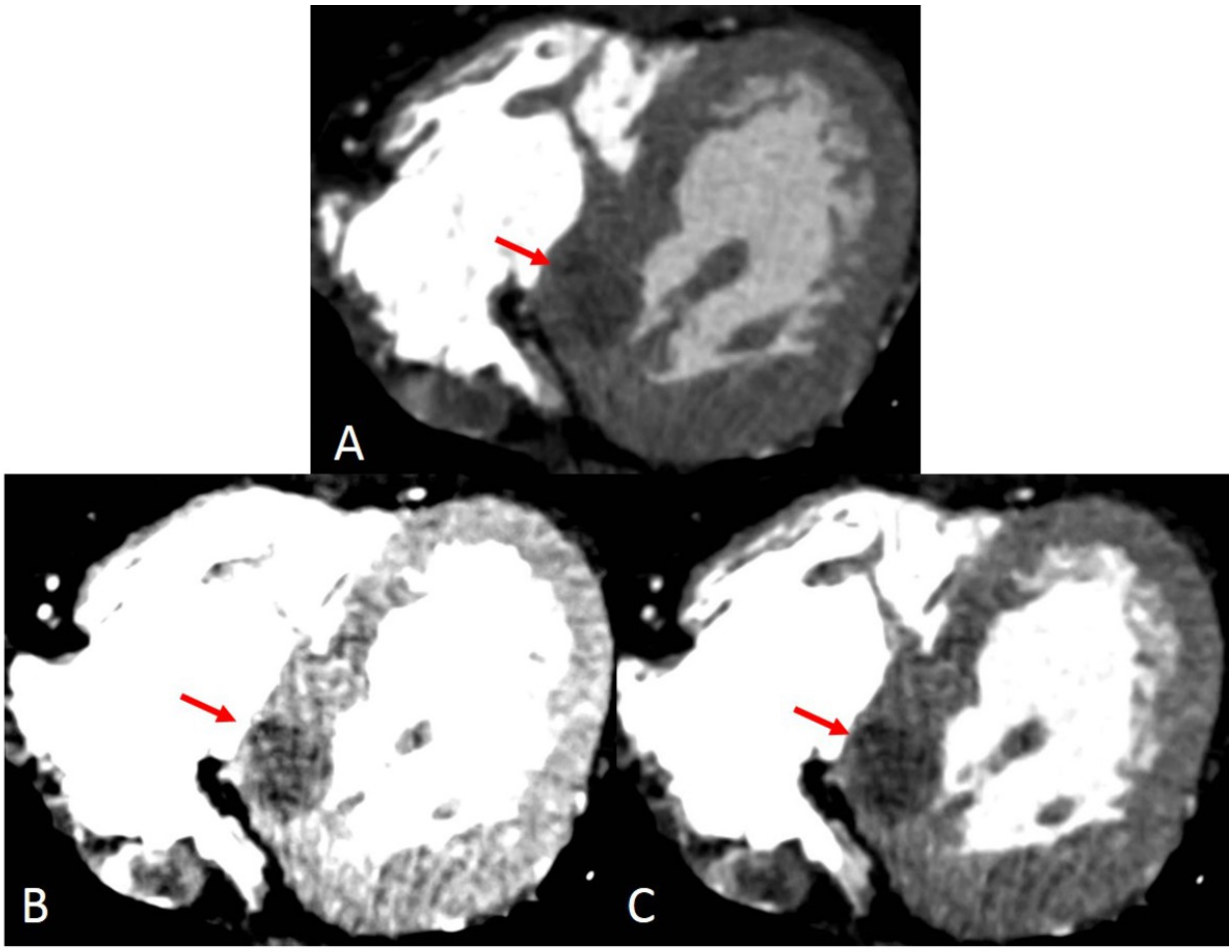

Fig. 12: Axial CE CT Chest. A, mediastinal window settings, shows a mass in the interventricular septum. Adjusting the window settings (B and C), allows a better visualisation of the mass.

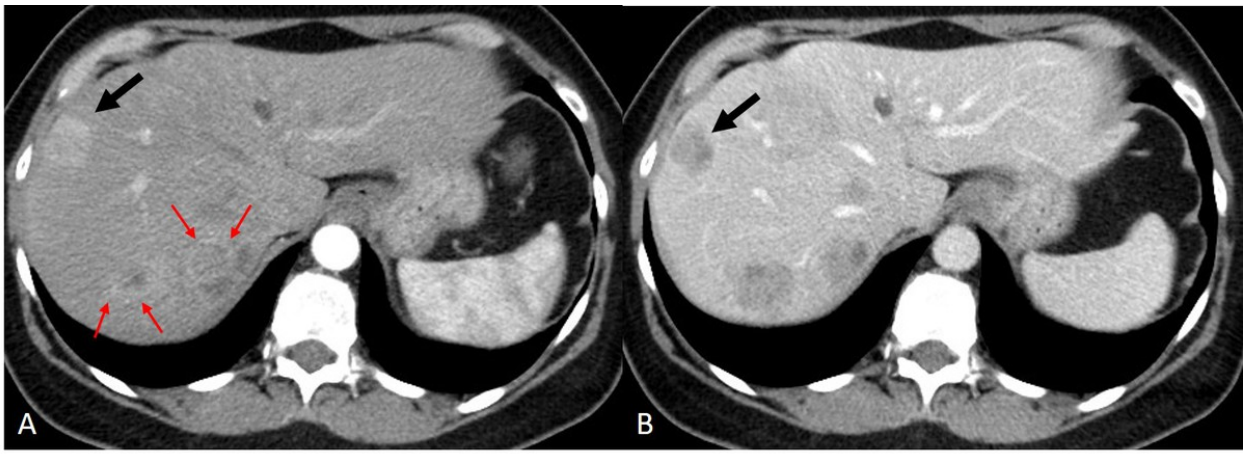

Fig. 13: CE CT arterial phase (A) and portovenous phase (B): A shows a lesion with enhancement in the arterial phase (black arrow) and washout in the portovenous phase. Two other lesions (red arrows) show peripheral rim enhancement in the arterial phase.

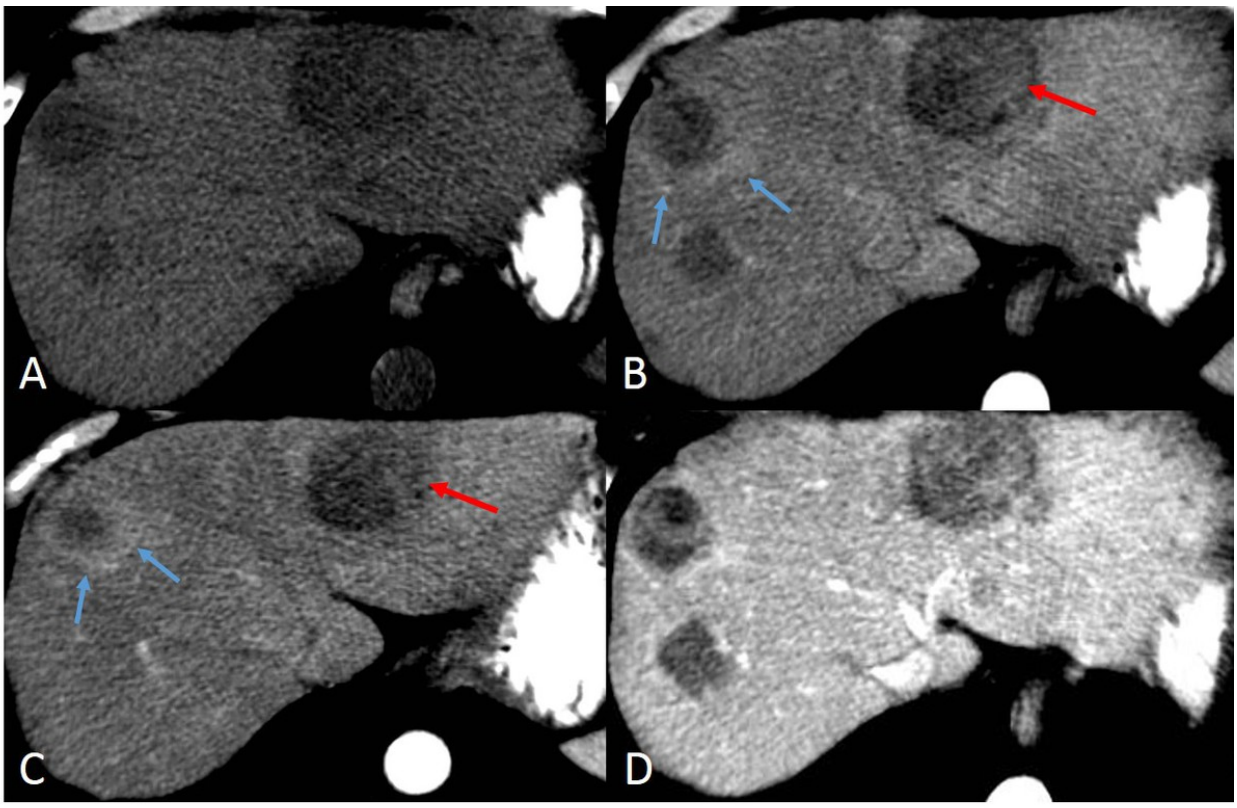

Fig. 14: Axial CT of the abdomen. Non-CE CT (A) shows multiple low attenuating liver masses. CE CT in the arterial phase (B and C), shows heterogeneous enhancement of a lesion (red arrow) as well as rim enhancement (blue arrow). CE CT in the portovenous phase (D), shows no washout.

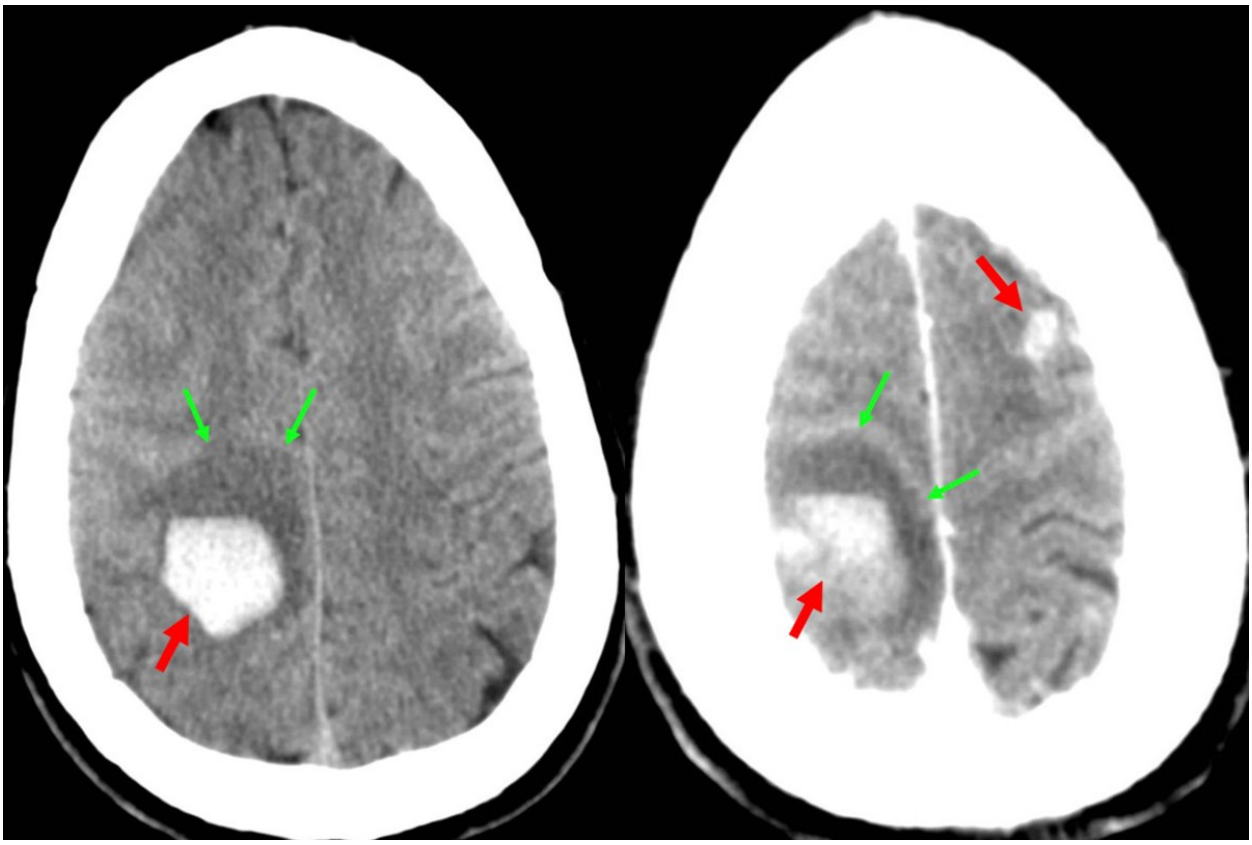

Fig. 15: Non CE CT shows a haemorrhagic lesion (red arrow) with peripheral edema (green arrows).

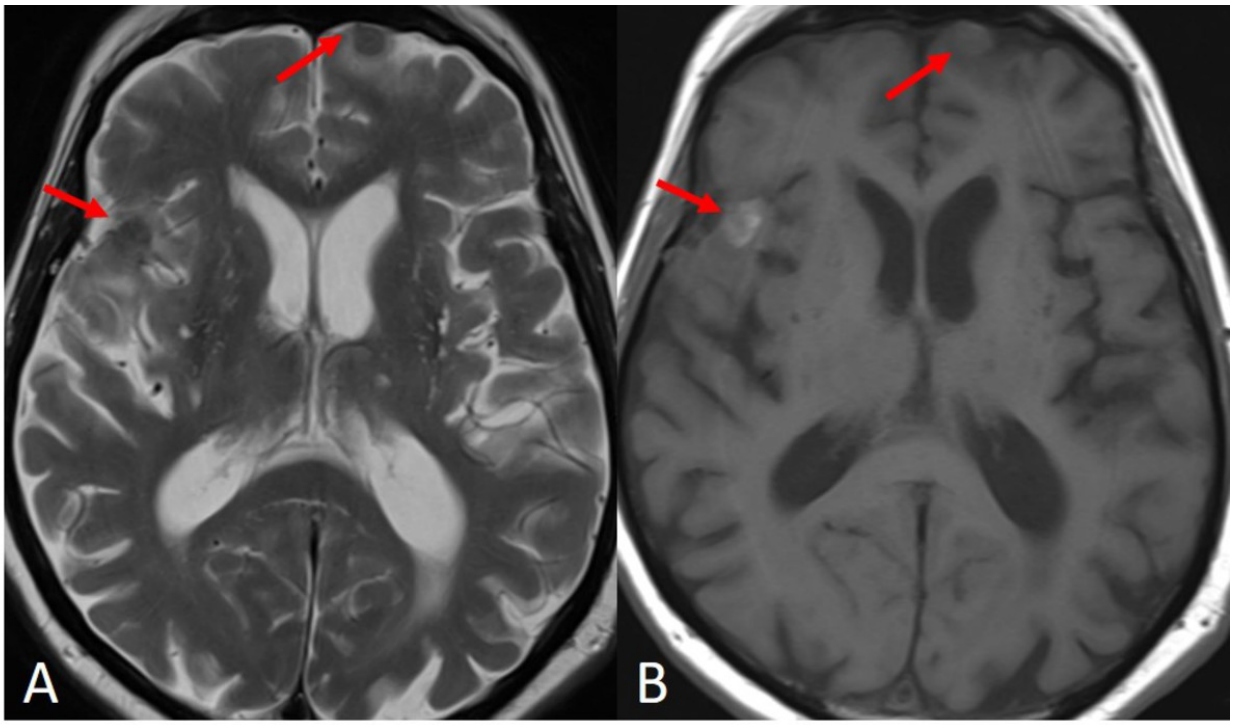

Fig. 16: An illustration of the specific behavior of metastatic melanoma within the brain on T1- and T2-WI. T2-WI (A) shows hypointense cortical nodules in the left frontal lobe and in the right temporal lobe (red arrows). The same lesions are hyperintense on T1-WI (B).

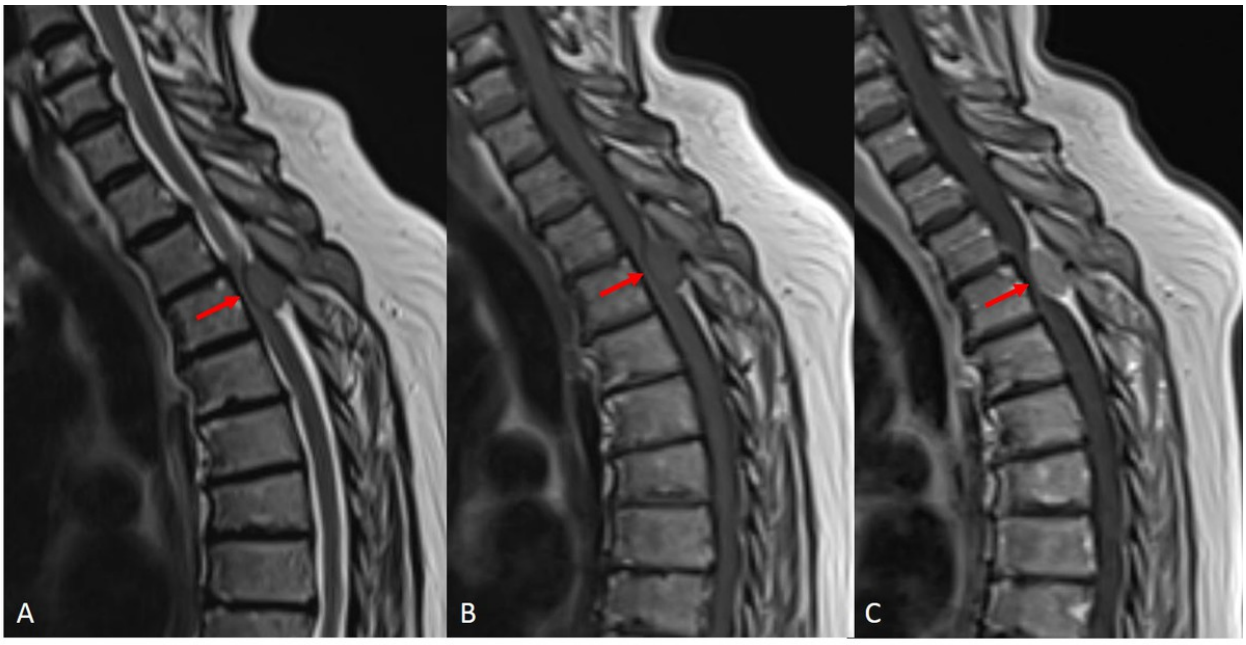

Fig. 17: T2-WI (A) and T1-WI (B) shows a lesion isointense to muscle posterior in the spinal canal , located in the epidural space (red arrow). T1-WI after gadolinium administration (C) shows marked enhancement. This is an example of metastatic melanoma with nonspecific signal characterization.

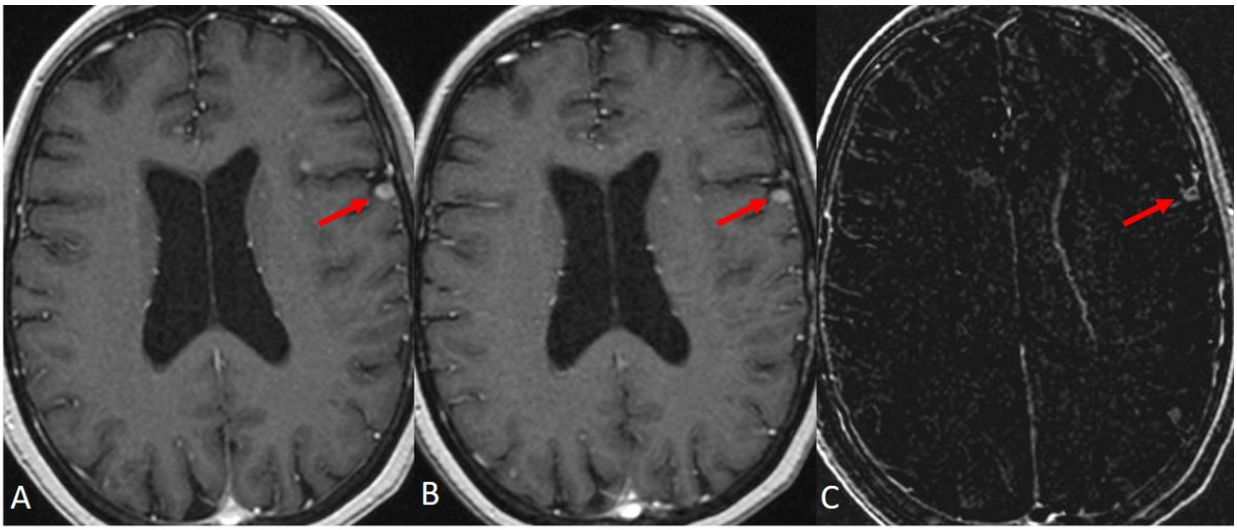

Fig. 18: T1 WI shows a spontaneous hyperintense leptomeningeal metastasis at the left Sylvian fissure. After gadolinium administration, there is a marked enhancement on T1 WI + Gd (B) and subtraction images (C).

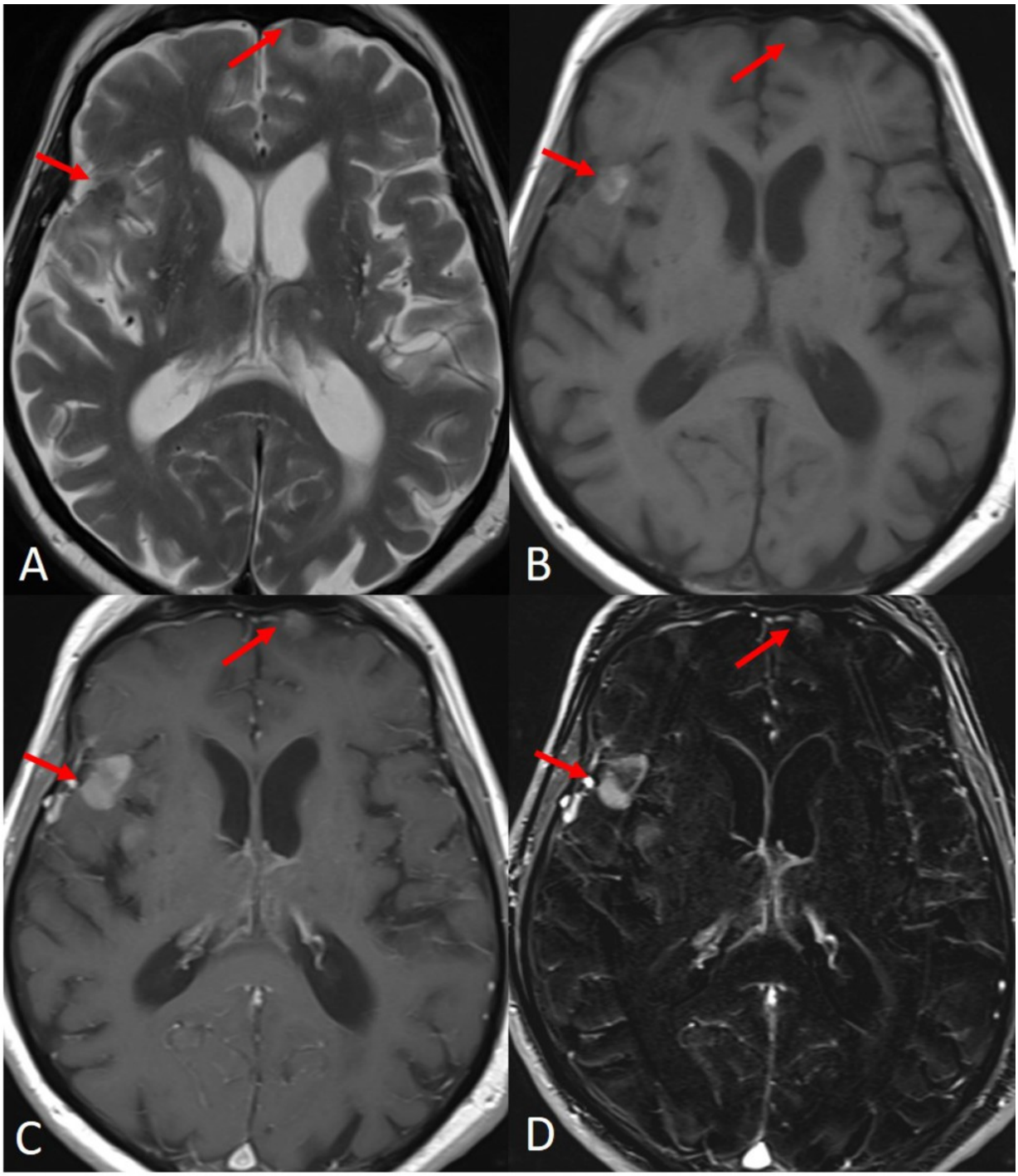

Fig. 19: An illustration of the specific behavior of metastatic melanoma within the brain on T1- and T2-WI. T2-WI (A) shows hypointense cortical nodules in the left frontal lobe and in the right temporal lobe (red arrows). The lesions are hyperintense on T1-WI (B). After administration of Gd contrast (C), there is marked enhancement seen on T1-WI and on the T1-WI subtraction images(D).

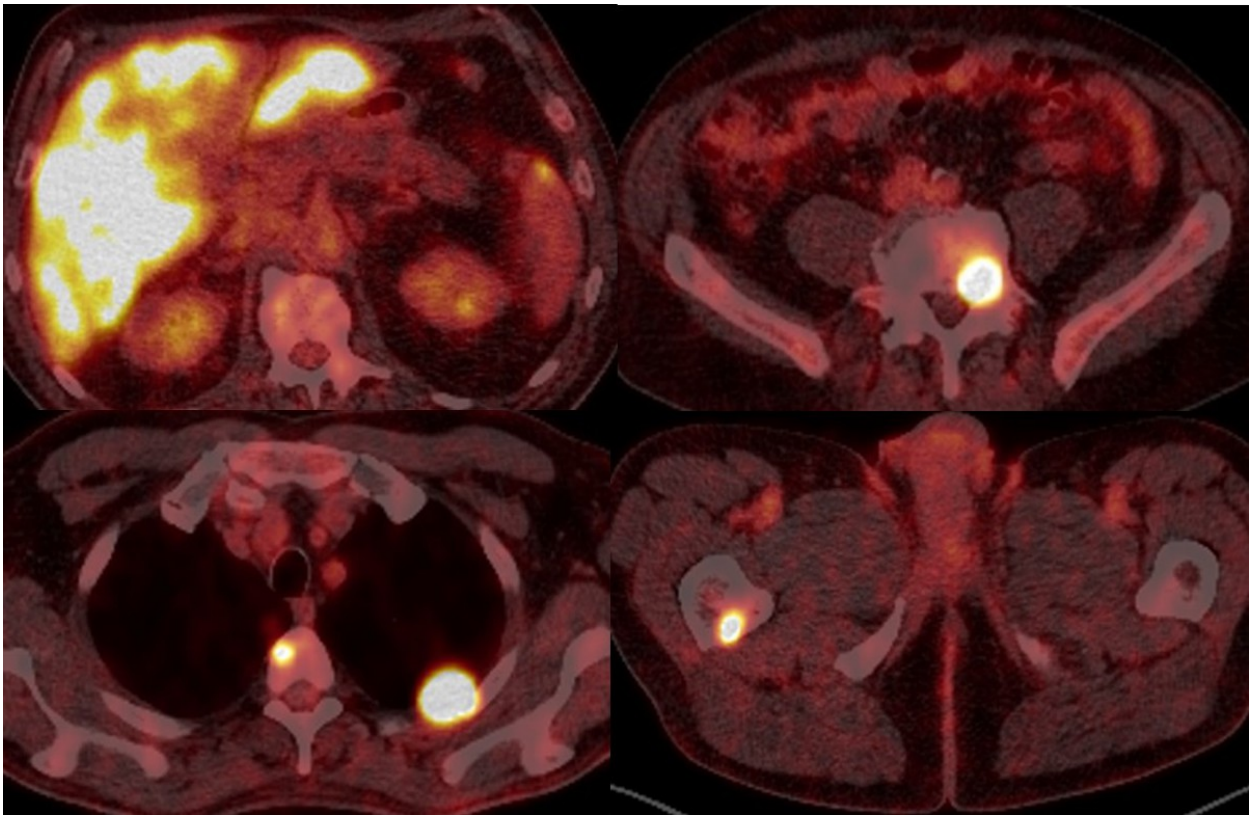

Fig. 20: Fusion PET/CT shows marked tracer hypercaptation in various locations in keeping with metastasis.

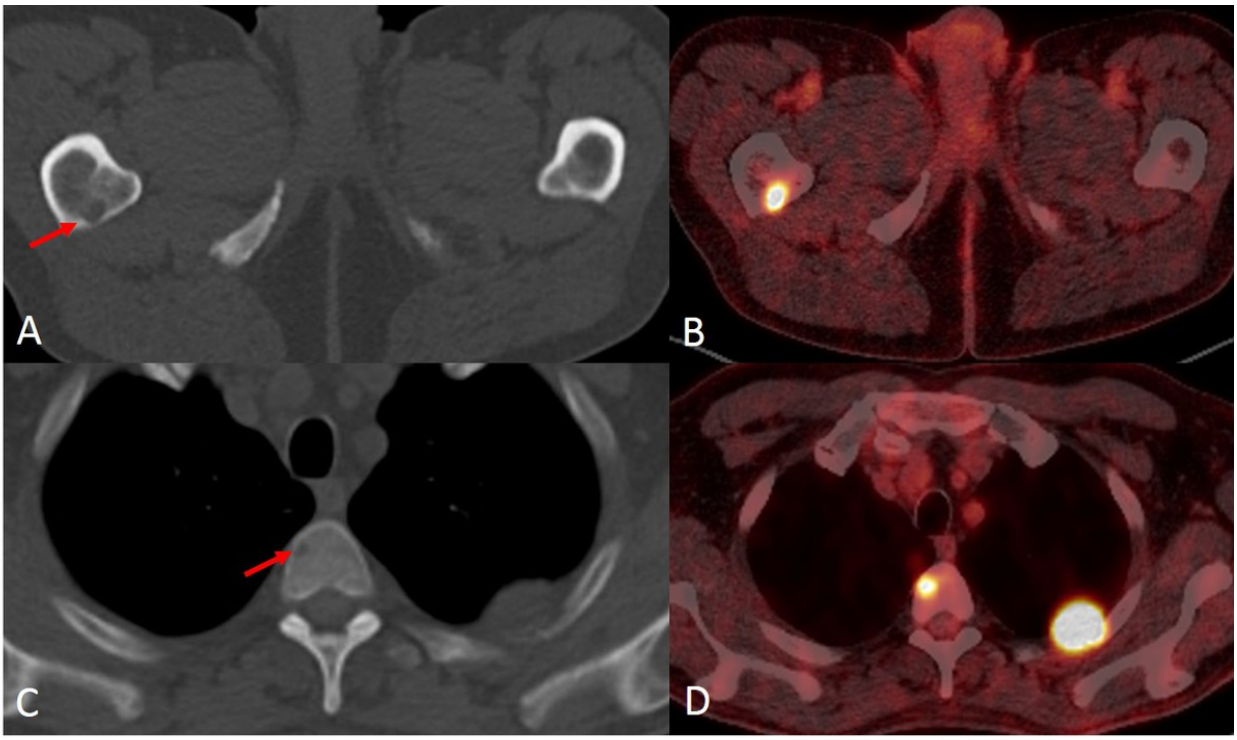

Fig. 21: Axial CT shows questionable lytic lesions in the right femoral neck (A) and in the thoracic spine (C). Fusion PET/CT (B and D) confirms metabolic activation, in this patient, in keeping with metastatic melanoma.

Fig. 22: CE CT of the abdomen (A) shows an enhancing subcutaneous metastasis located in the right gluteal region (white arrow). Follow-up CE CT (B) shows a marked enlargement of the lesions (white arrow).

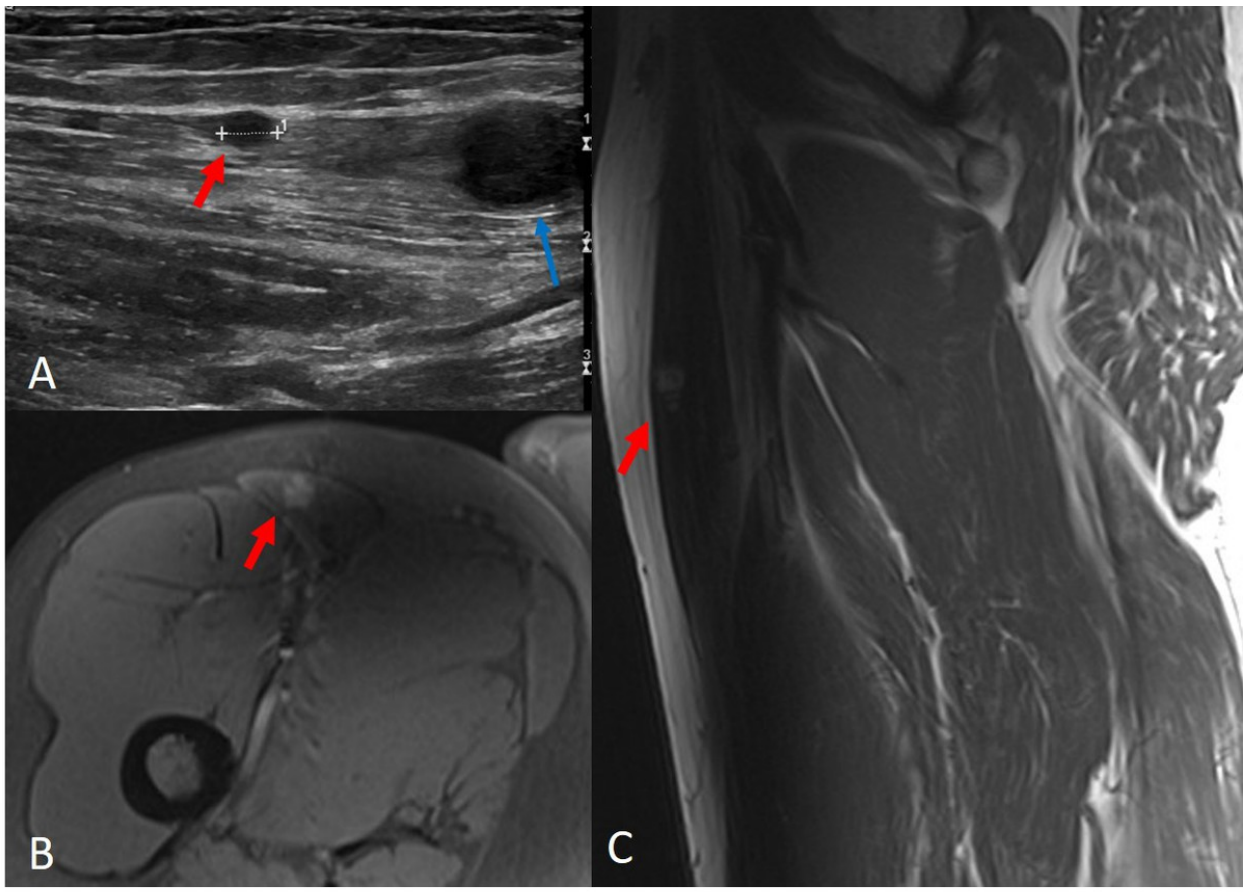

Fig. 23: Grey-scale US of the right upper leg (A) shows one satellite (blue arrow) and multiple in-transit metastases (red arrow) located in the sartorius muscle. Axial T1-WI with fs (B) and sagittal T1 WI (C) shows a spontaneous hyperintense nodular lesion in the sartorius muscle.

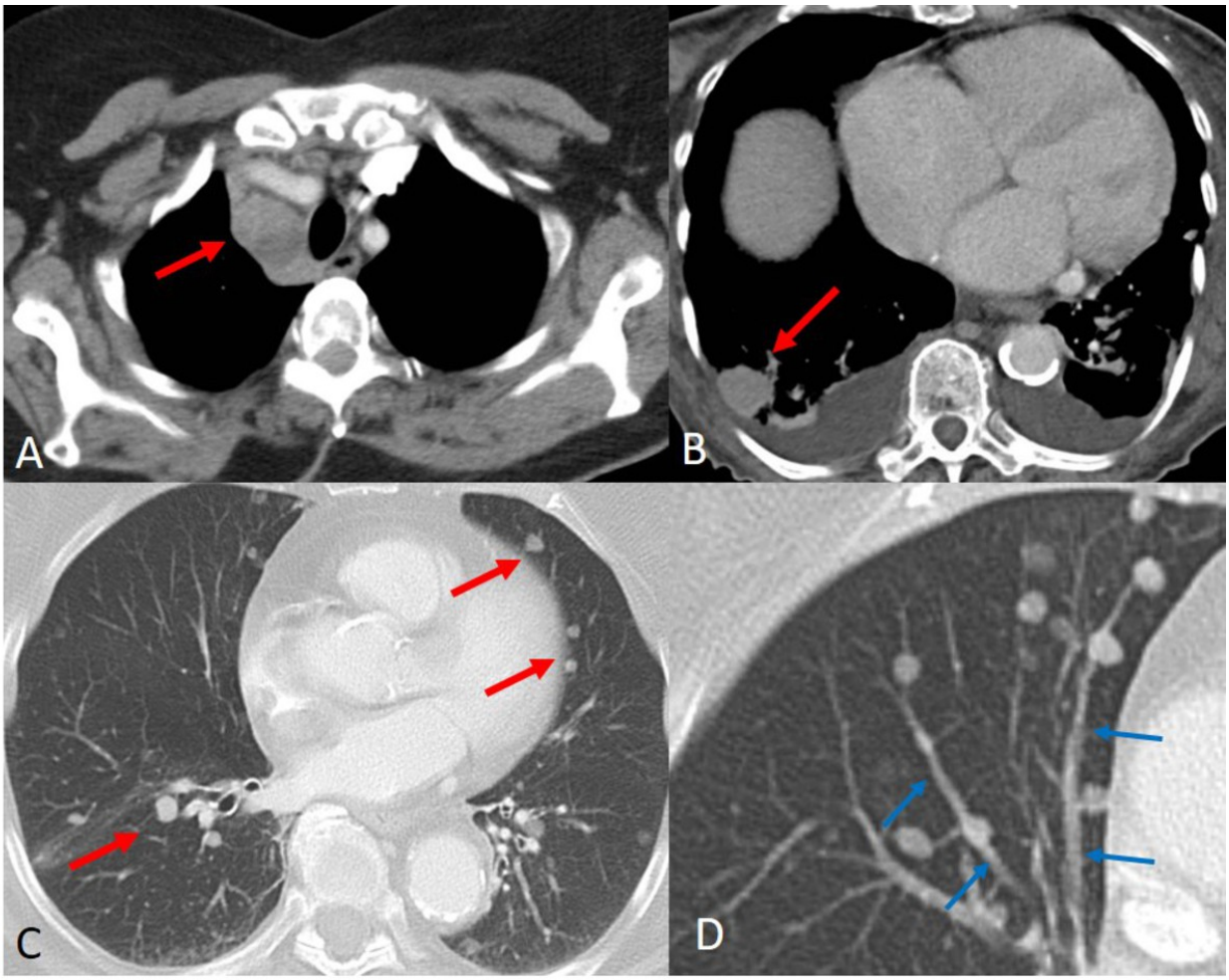

Fig. 24: CE CT of the chest of different patients shows mediastinal lymph node (A), pleural (B), multiple pulmonary (C) metastases. Illustration of feeding vessels (blue arrows), in keeping with hematogenous spread (D).

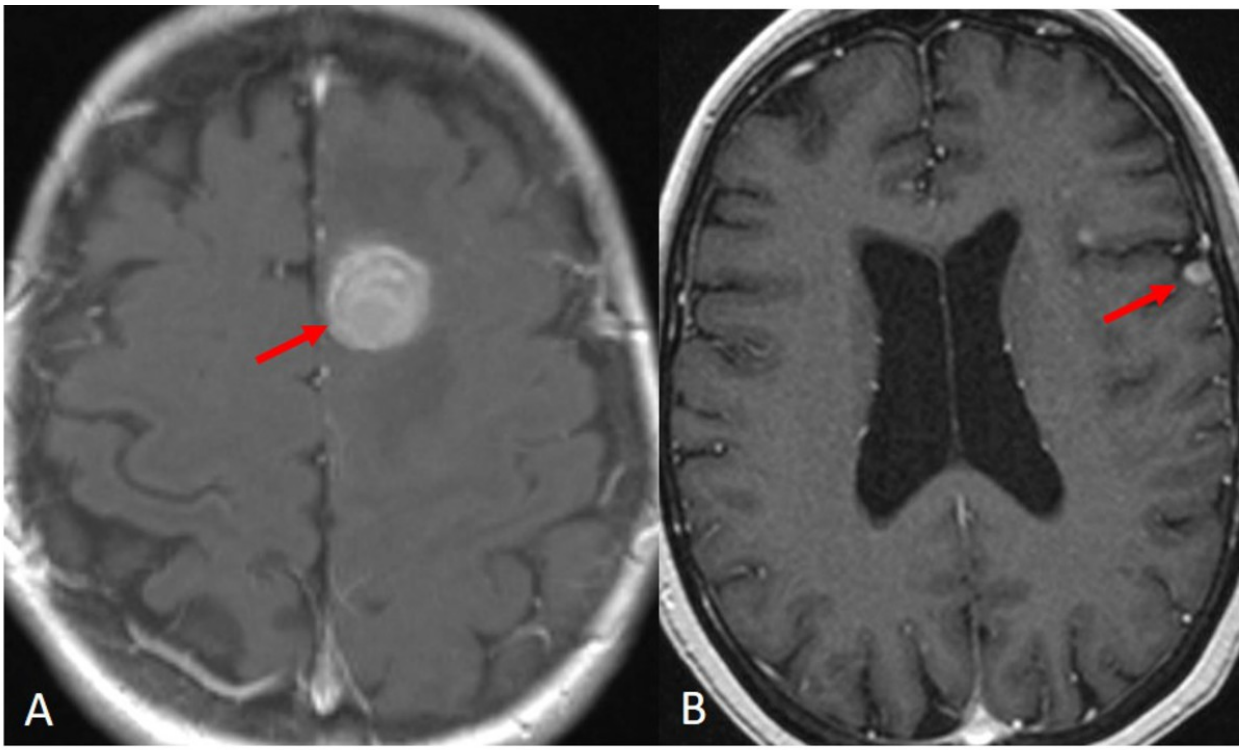

Fig. 25: Axial T1-WI after gd shows a cortical lesion in the frontal lobe (A) and a nodular leptomeningeal lesion posterior of the sylvian fissure (B).

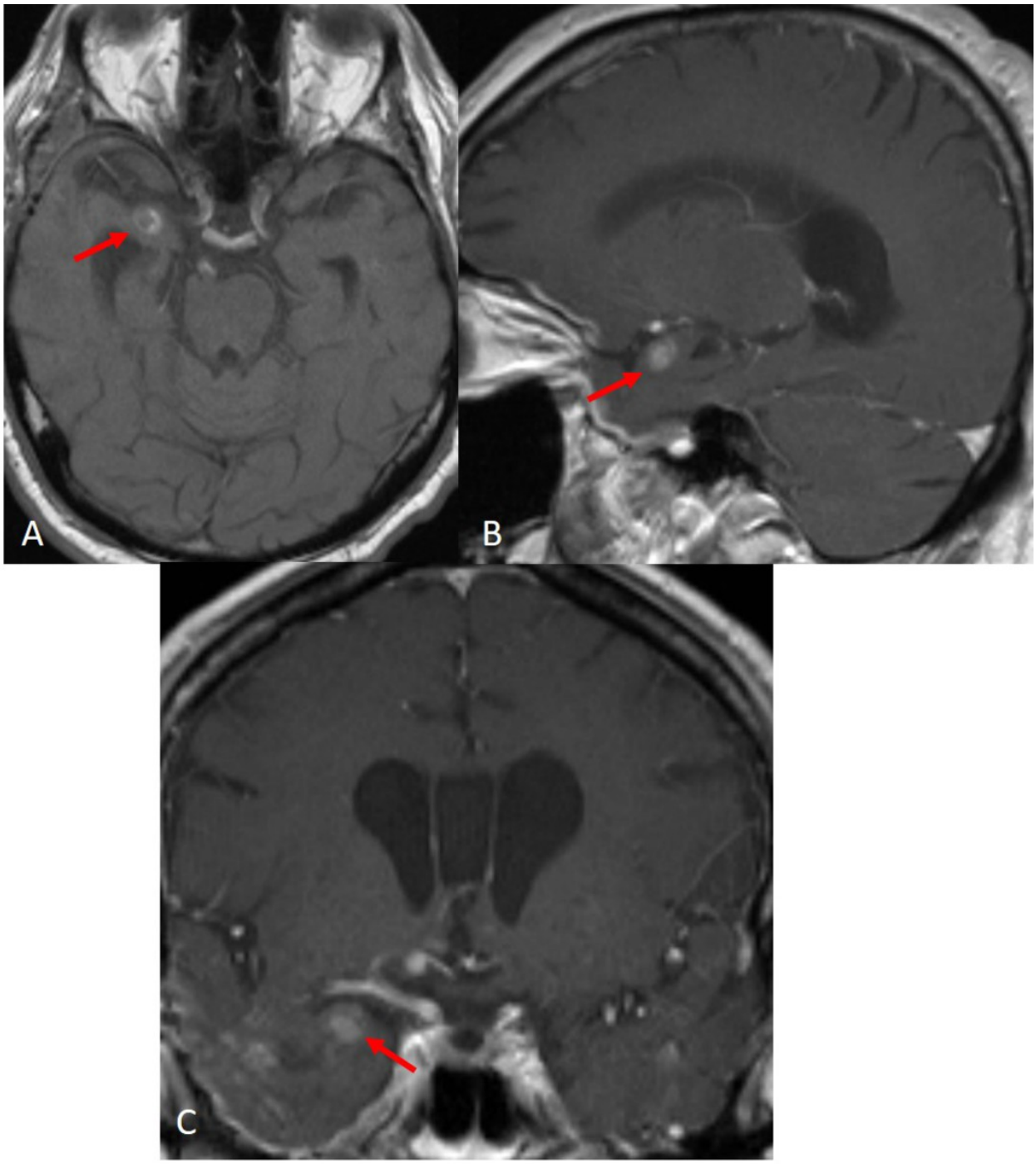

Fig. 26: Axial T1-WI (A) shows a spontaneous hyperintense lesion in the right hypocampus. Saggital (B) and coronal (C) T1-WI + gd clearly demonstrates the hippocampal localization.

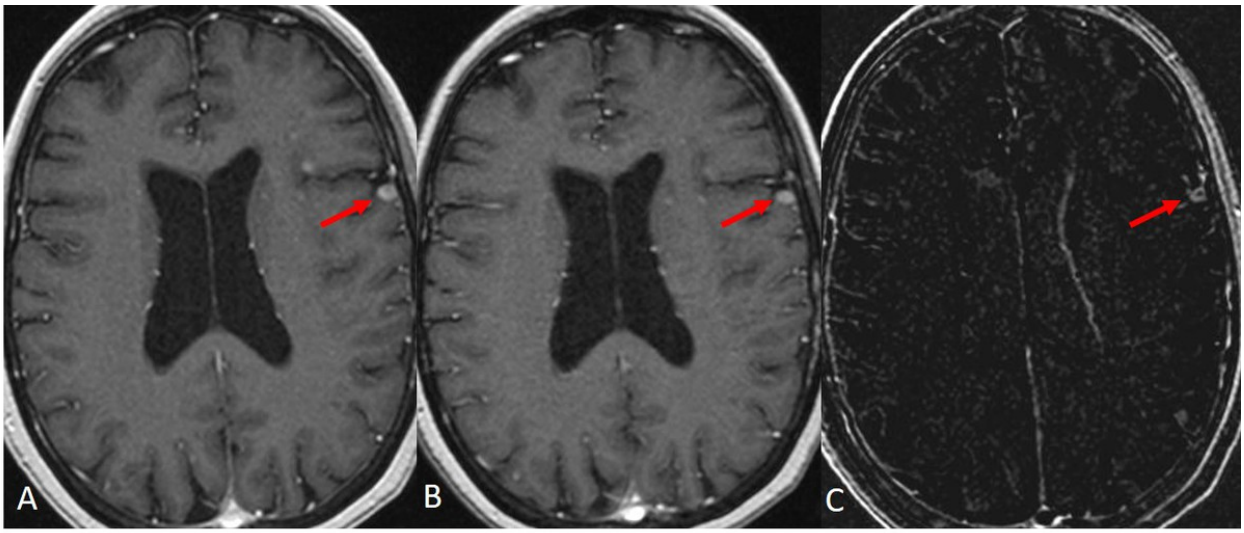

Fig. 27: T1 WI shows a spontaneous hyperintense leptomeningeal metastasis at the left Sylvian fissure. After gadolinium administration, there is a marked enhancement on T1 WI + Gd (B) and subtraction images (C).

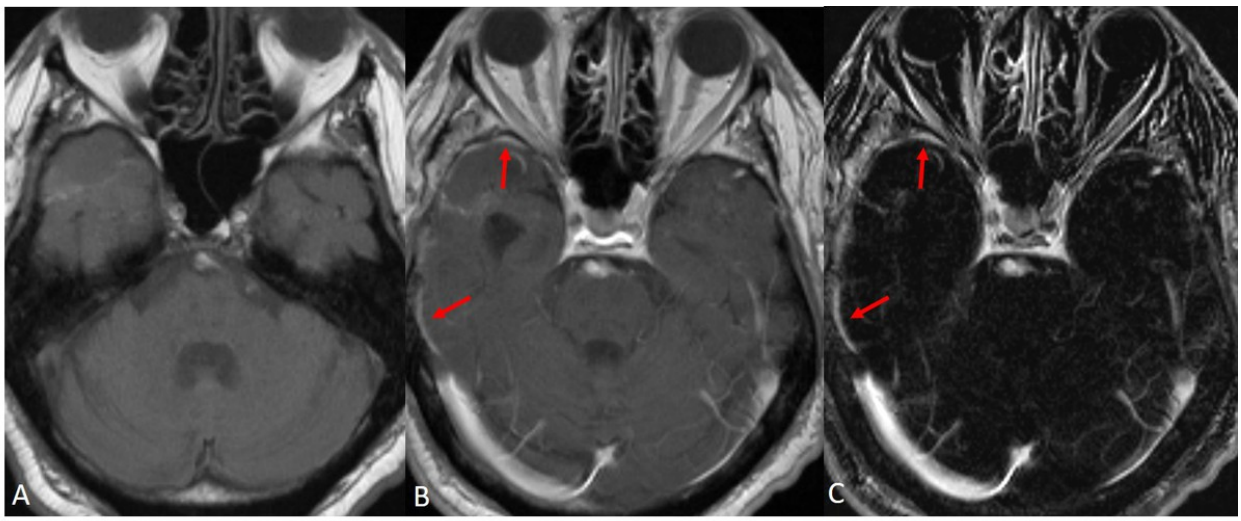

Fig. 28: Axial T1-WI before (A) and after administration of gadolinium (B) shows a diffuse enhancement (green arrows) of the leptomeninges of the right temporal lobe, which is clearly visible on the T1-WI subtraction images(C).

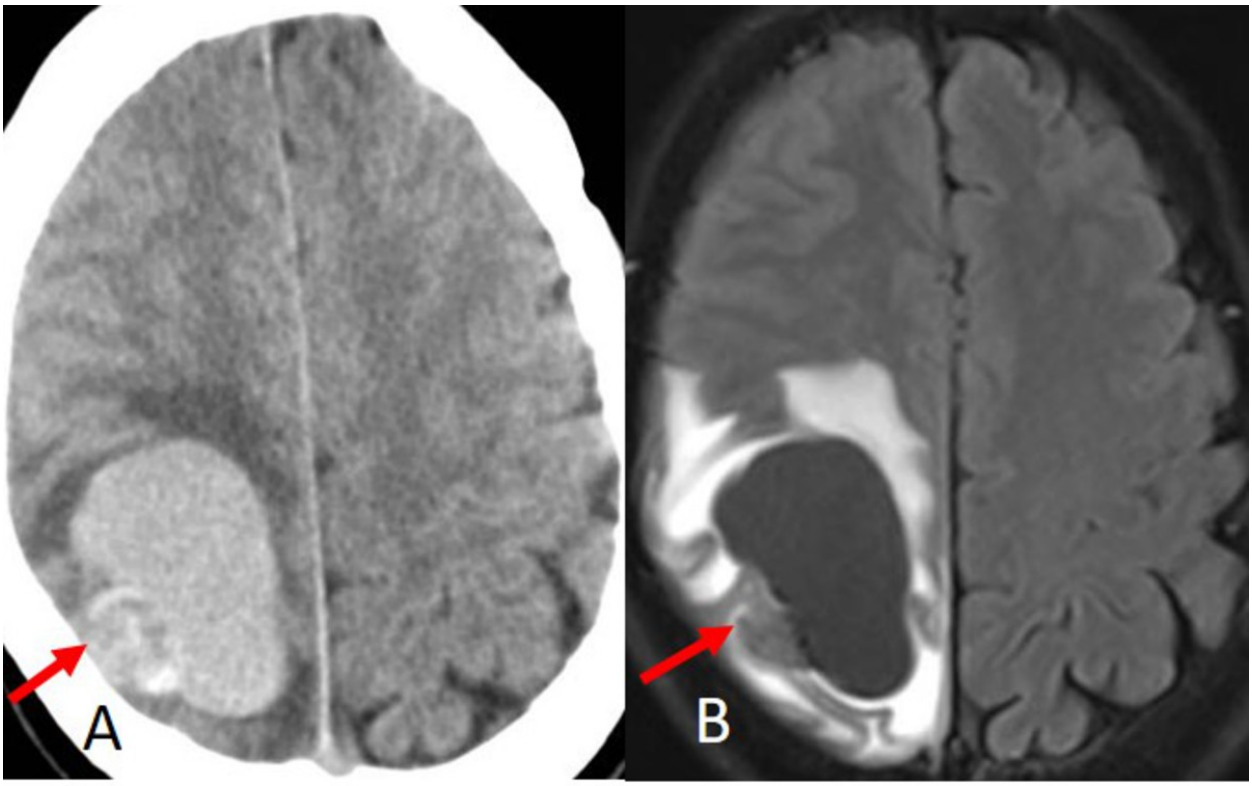

Fig. 29: CT and MRI of an acute intratumoral haemorrhage. Non-CE CT (A) shows a heterogeneous hyperdense lesion with associated haemorrhage and marked perilesional edema. T2-WI (B) confirms as a hypo- to isointense lesion with hyperintense surrounding edema. The haemorrhage is hypointense.

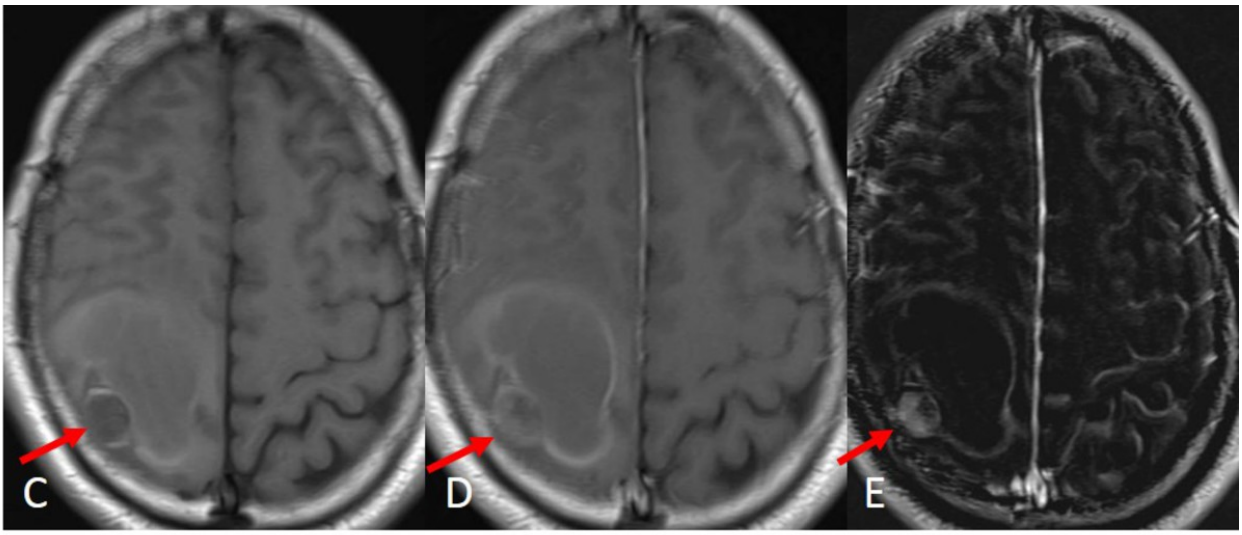

Fig. 30: T1-WI (C) shows a hypointense lesion with a peripheral hyperintense rim. The haemorrhage is hypo- to isointense. T1-WI after administration of gadolinium (D) shows heterogeneous and peripheral rim enhancement of the nodule and peripheral rim enhancement of the haemorrhage which is clearly seen on T1-WI subtraction images (E).

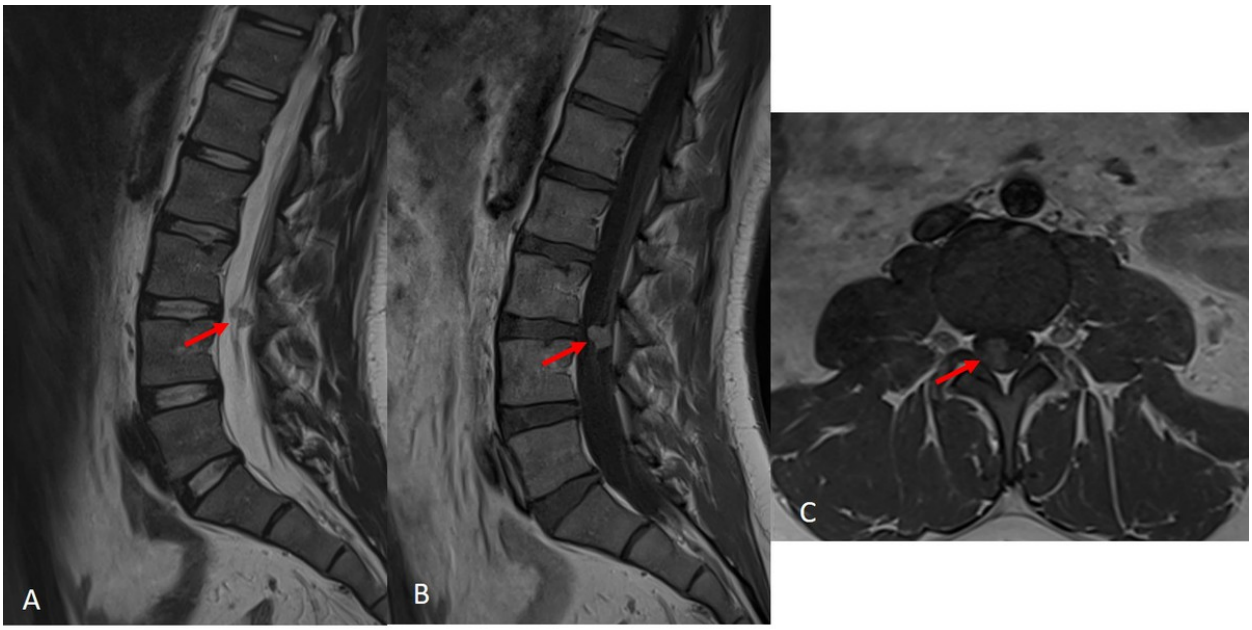

Fig. 31: T2-WI (A) shows an isointense leptomeningeal metastasis (red arrow) in the spinal cord, located at the cauda equina. Sagittal (B) and axial (A) contrast-enhanced T1-WI shows a marked enhancement (red arrow).

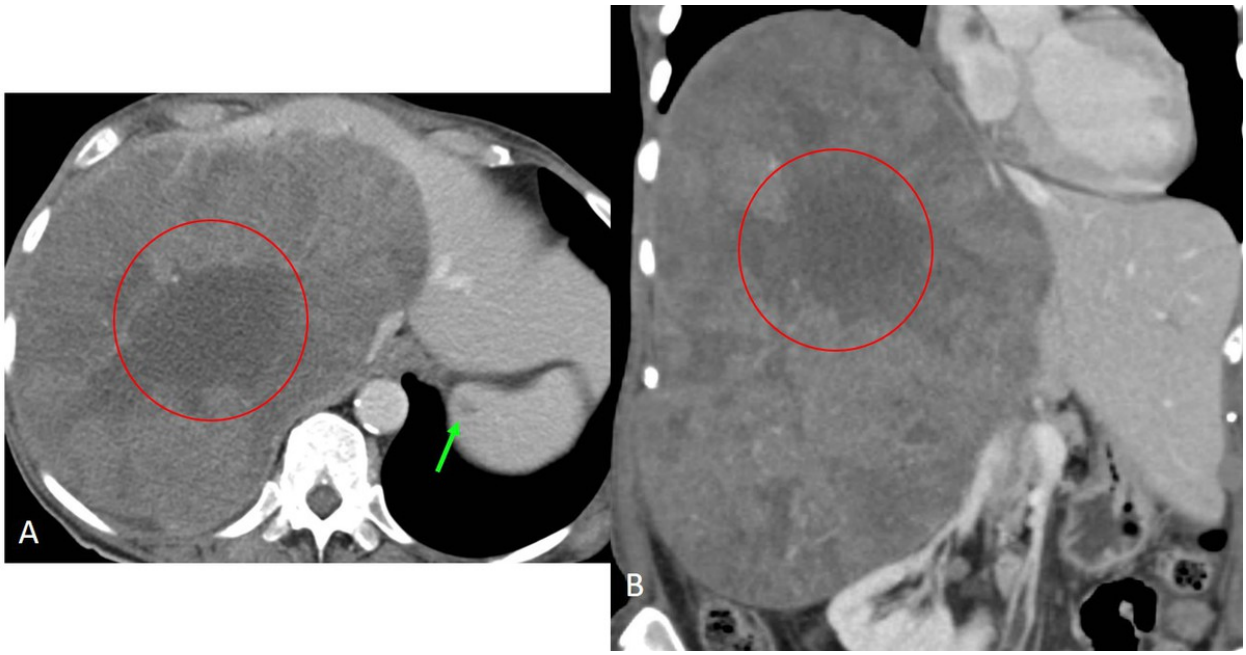

Fig. 32: Axial (A) and coronal (B) CE CT of the abdomen. A and B shows a large heterogeneous enhancing lesion in the liver. The lesion contains hypodense regions with no contrast enhancement in keeping with necrotic areas. The red circle indicates a large necrotic area. This patient had diffuse metastases with one large liver lesion. Mark the small metastasis in the spleen (green arrow).

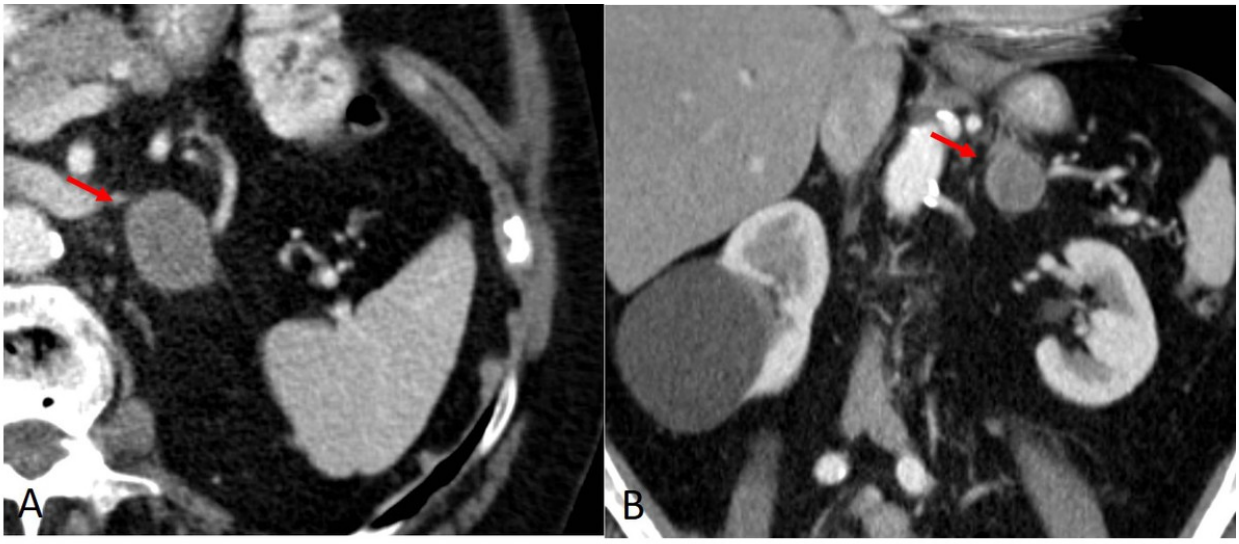

Fig. 33: Axial (A) and coronal (B) CE CT shows a metastasis in the left adrenal gland (red arrow).

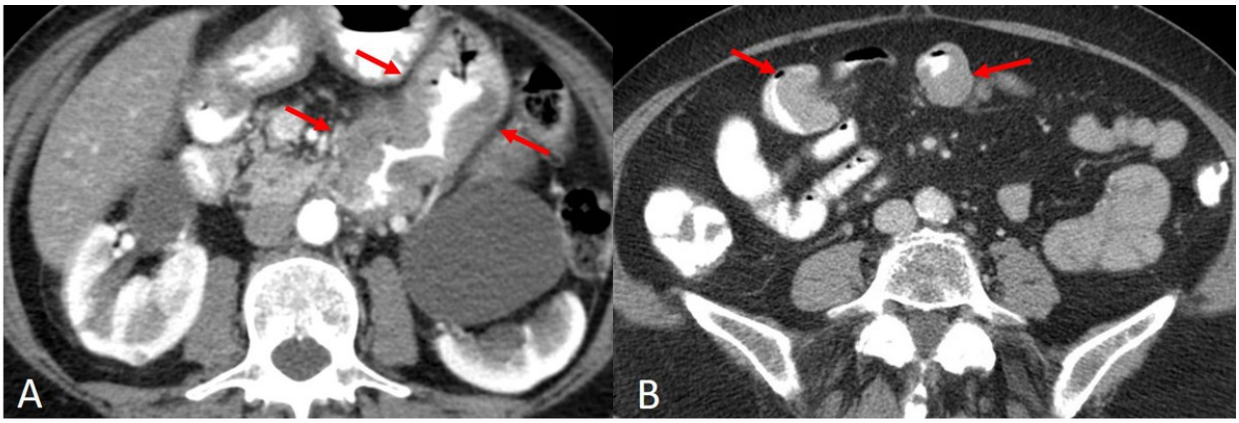

Fig. 34: Axial CE CT after administration of oral contrast shows small bowel metastasis. A shows a diffuse thickening of the jejunal wall (red arrows) and B shows multiple focal thickening of ileal bowel loops (red arrows).

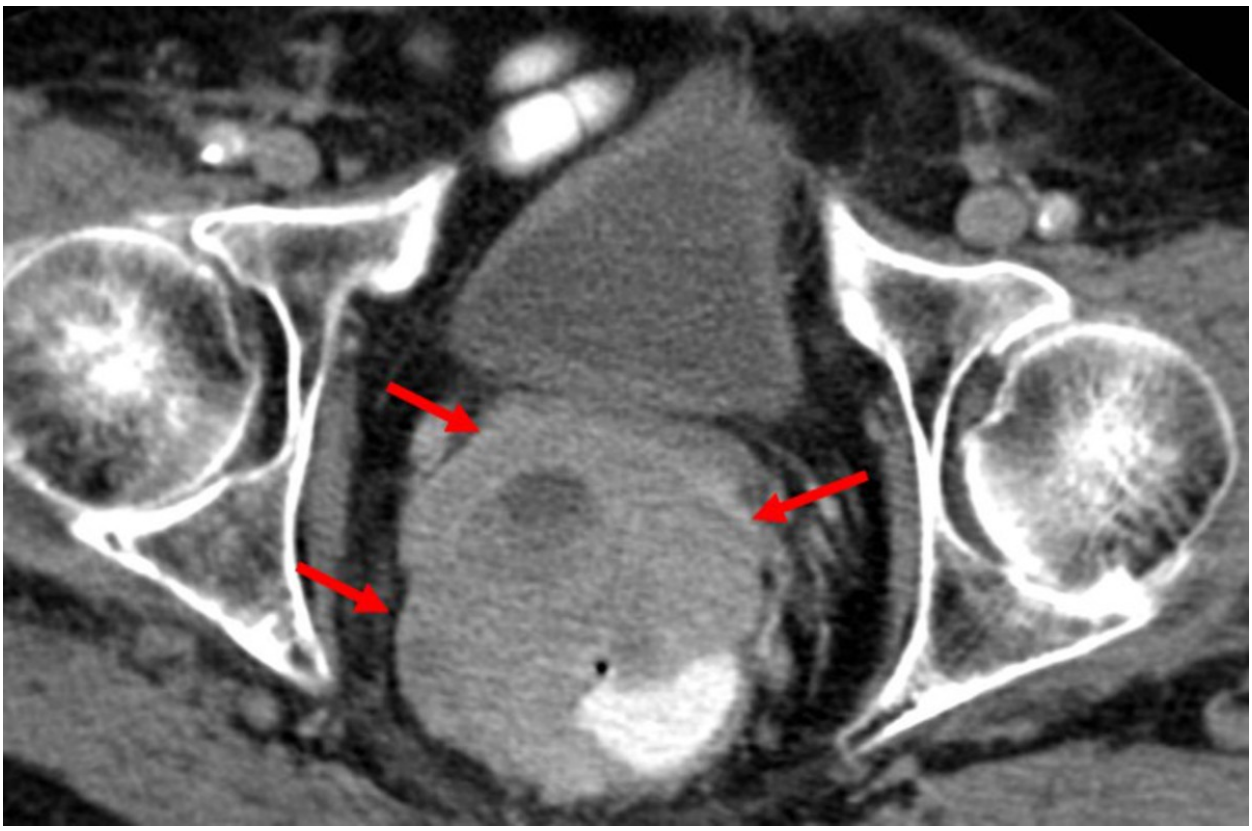

Fig. 35: Axial CE CT after administration of oral contrast shows an example of metastatic melanoma involving the rectum.

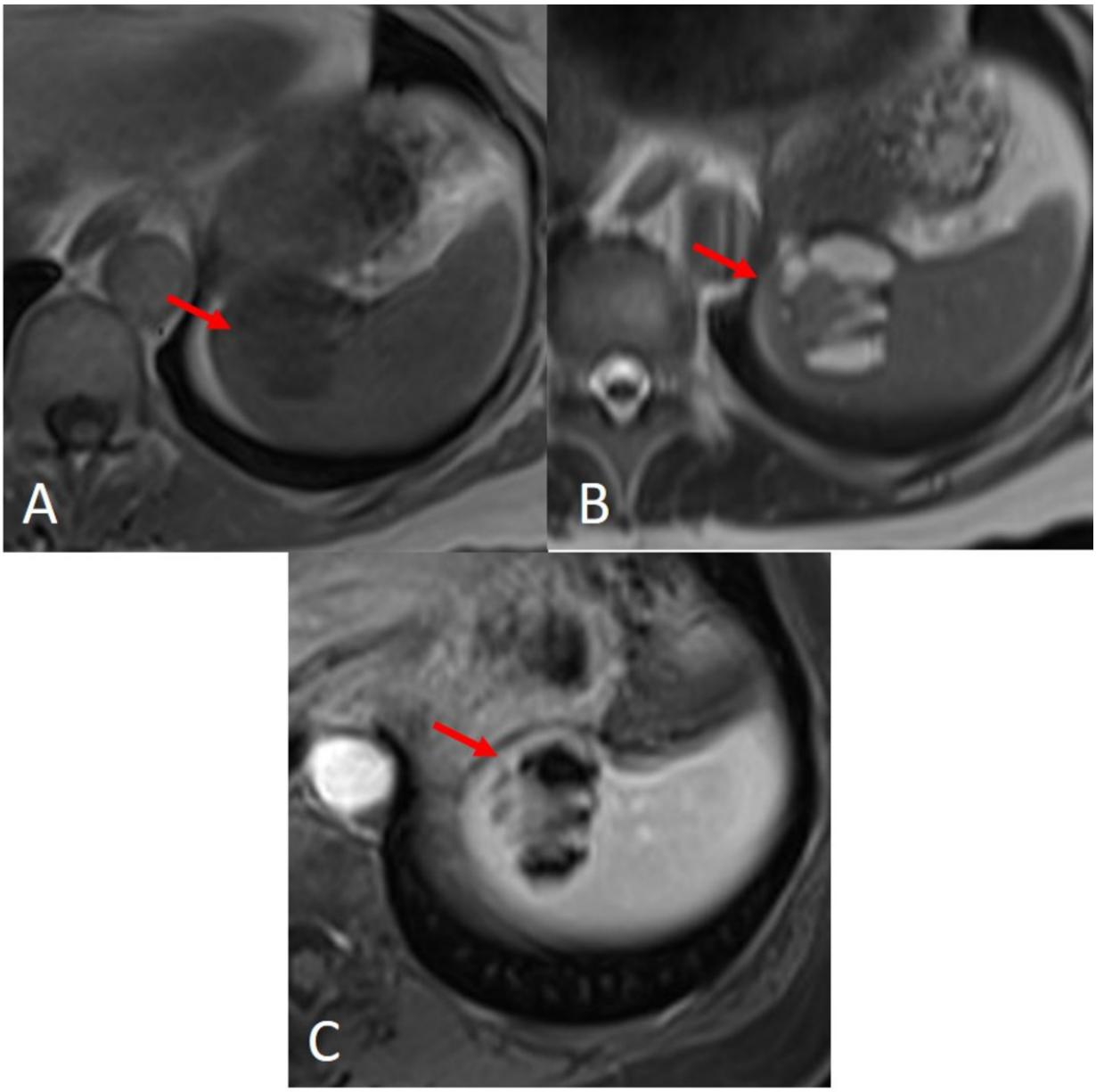

Fig. 36: T1-WI (A) shows a mass (red arrow) isointense to muscle in the spleen. On T2-WI (B) the mass has regions of iso- and hyperintensity. T1-WI after administration of gadolinium contrast (C) shows a heterogeneous enhancement of the mass.

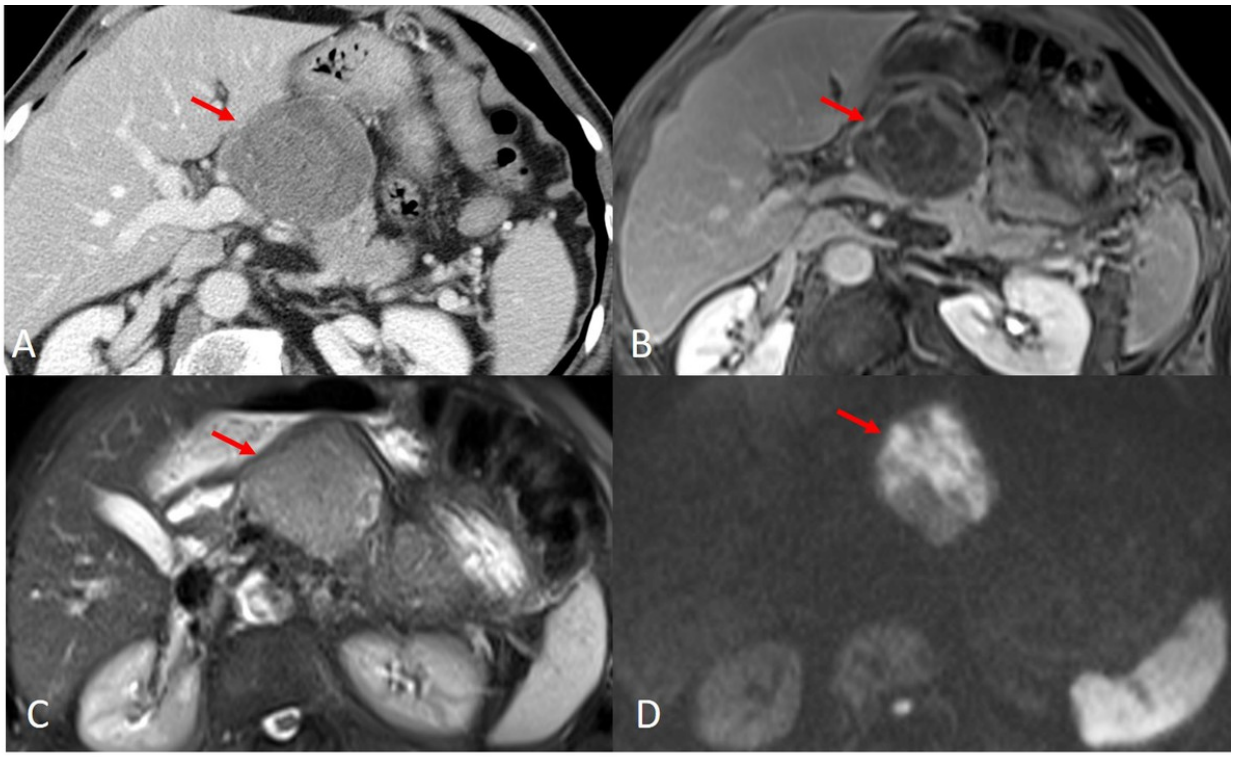

Fig. 37: Axial CT and MRI of the pancreas. CE CT (A) shows a heterogeneous enhancing mass in the pancreas. T1-WI (B) with FS shows a heterogeneous mass with regions of high and low intensity in the pancreas. The mass is hyperintense on T2-WI with FS (C). DWI (D) and ADC (not shown) shows marked diffusion restriction.

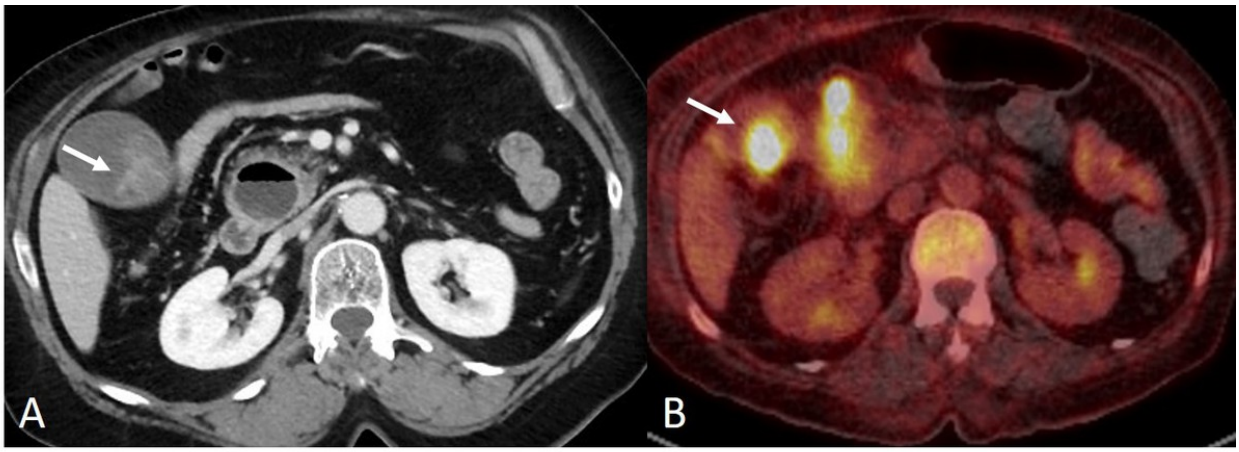

Fig. 38: Axial CE CT shows a heterogeneous enhancing mass in the gallbladder (white arrow). Fusion PET/CT shows a high metabolic activity in this lesion (white arrow). After surgical resection, histopathology showed a metastatic melanoma in the gallbladder.

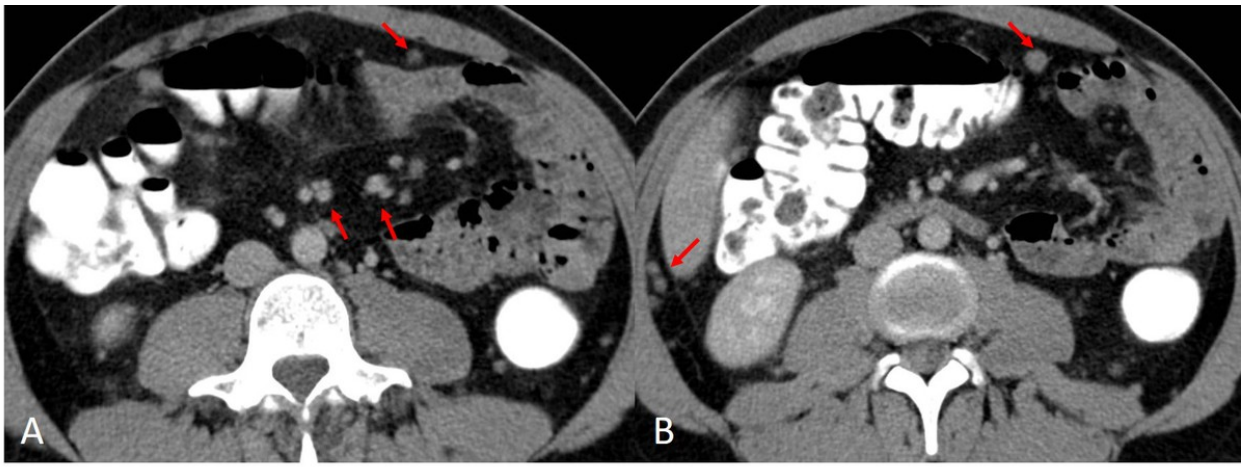

Fig. 39: Axial CE CT A and B shows multiple slightly enlarged lymph nodes located mesentery and retroperitoneal (red arrows).

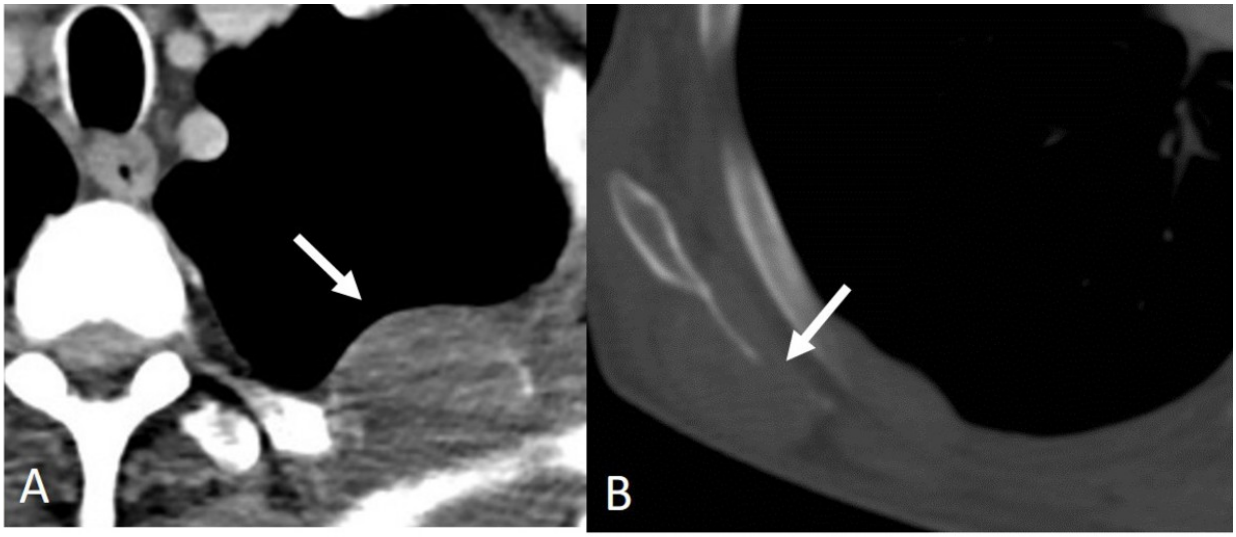

Fig. 40: CT of the chest shows an osteolytic metastasis with soft tissue component in the fourth left rib (A) and scapula (B).

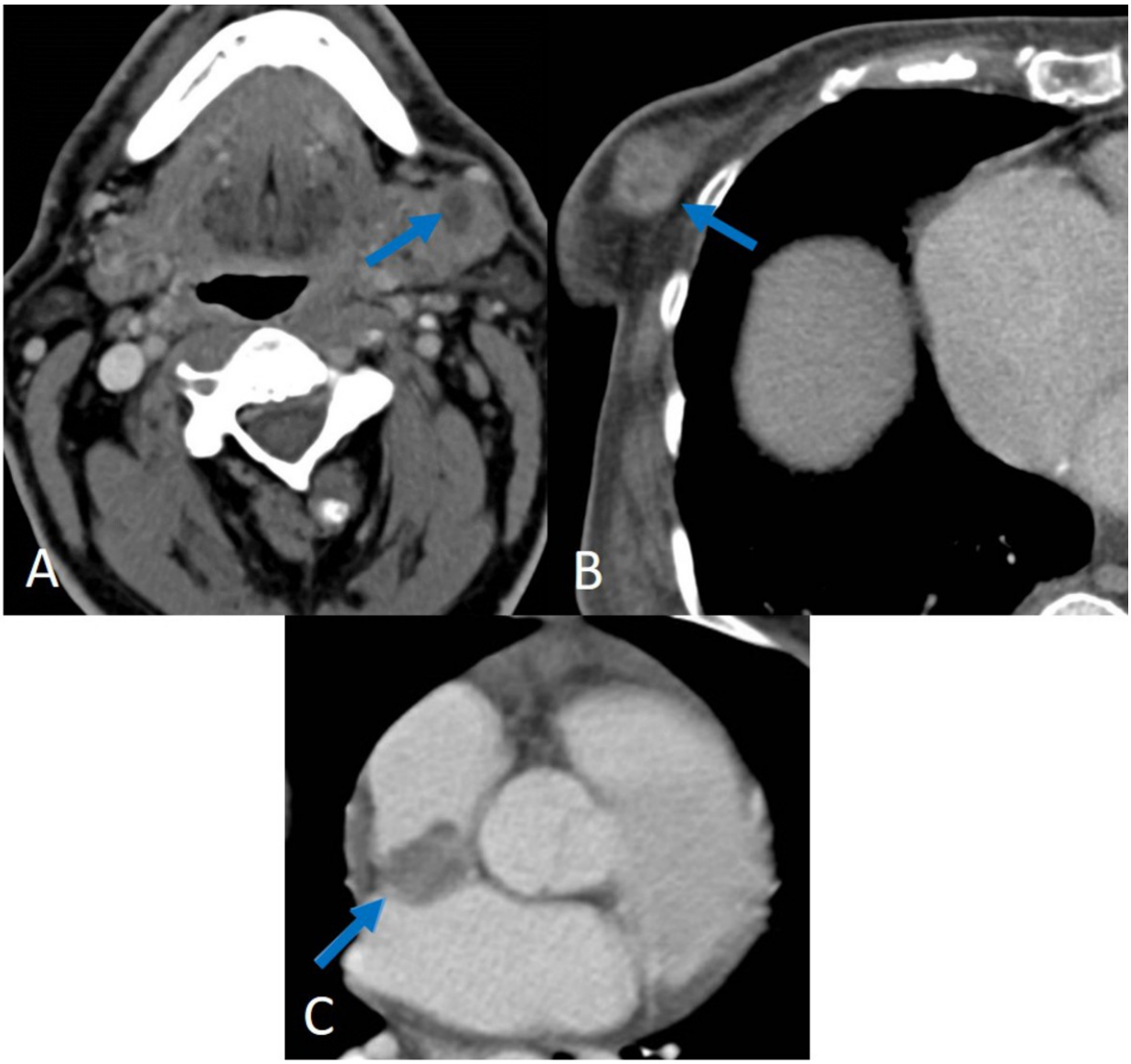

Fig. 41: CE CT shows a mass in the left submandibular gland (A), right breast (B) and heart (C).

Conclusion

- **The most frequent locations of metastasis are locoregional, lung, brain, liver or bones.**
- **US is used for superficial located lymphogenic spread for easily accessible areas. US is generally not used for hematogenous spread or deep locations.**
- **CT and PET/CT are the most used imaging modalities to evaluate hematogenous metastasis on most locations.**
- **MR is most sensitive and specific except for lung disease.**

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