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PROCEEDINGS OF THE OCTOBER SYMPOSIUM ON MRI IN ONCOLOGY: OLD TRUTHS AND NEW TRENDS*

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What does an oncologist want to know when he asks for a MRI?

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The basic questions for an oncologist when he thinks he needs a MRI are: is there something and what is it? In this presentation we review the use of the MRI at the level of diagnosis, staging and follow up in the following areas: Central nervous system, head and neck region, breast pathology, thoracic region, abdominal region, genitourinary system and musculoskeletal problems.

For the central nervous system it is evident that the MRI is the most performing imaging tool and it is stated that with the exception of suspicion of bleeding it is better to wait for the MRI than using a CT scan for diagnosis. The use in staging is limited to the situation of curable tumors. In the follow up situation asking for a MRI is only justified if it has an impact on treatment.

The use of MRI in breast cancer is limited to the situation of inconclusive mammography or US, suspicion of multifocal disease, axillary metastatic lymph node of unknown primary. In follow up situations MRI is indicated after autologous reconstruction.

Use of MRI in head and neck, thoracic, abdominal or genitourinary region is limited to specific situations linked to liver metastasis, rectal, bladder, prostate or cervical cancer.

On the other hand MRI is crucial in the diagnosis, staging and follow up of bone or soft tissue sarcomas. It also has an important role in the diagnosis of skeletal metastasis.

Maybe the most important conclusion of this presentation is the statement that correct us of MRI in oncology has always to be discussed between the MRI radiologist and the clinician.

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Magnetic resonance mammography in oncology

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General indications

Dynamic Magnetic Resonance Imaging (MRI) of the breast has become an important complementary examination in breast cancer management, thanks to the high sensitivity of 98% for invasive carcinomas and 80% for in situ carcinomas. Interpretation of MR images is based on morphology of enhancement after contrast administration and dynamics of enhancement.

Due to low specificity, with extremely variable reported rates of 37-97%, it may only be performed for selected indications (1).

Good indications are:

1. Staging of tumor extent within the breast and exclusion of multifocality or multicentricity in the same or contralateral breast
2. Assessment of scarring after breast-conserving therapy (preferentially 18 months after radiation therapy)
3. Evaluation after silicon implant
4. Problem solving early after surgery
5. Monitoring of neo adjuvant chemotherapy
6. Search for primary tumor when the primary tumor is unknown and breast cancer is suspected
7. Screening high risk patients

Staging of tumor extent within the breast and exclusion of multifocality, multicentricity in the same or contralateral breast

Breast cancer recurrence after breast conserving surgery is reported in 3 to 19% of patients and is mostly due to incomplete resection or multifocality. Furthermore, breast tumor recurrence is a risk factor for distant metastasis and mortality. Therefore, good preoperative staging before planning breast conserving surgery is important.

Reports have demonstrated that MR detects multifocal/multicentric carcinoma in up to 37% of breast cancer patients. However, of the enhancing lesions detected on MR only, 20% false positive lesions are reported (2). To avoid unnecessary wider surgery, histologic diagnosis must be performed of additional enhancing lesions. Second look ultrasound is able to detect 57-82% of additional cancers seen on MR.

Approximately 2 to 15% of women who appear eligible for breast conserving therapy have multicentric disease, detected on MRI. The presence of multicentric disease appears somewhat higher in patients with ductal carcinoma in situ (DCIS) (20-28%) or infiltrating lobular carcinoma (ILC) (17-40%). Due to its growth pattern, invasive lobular carcinoma is often difficult to detect on clinical examination, mammography and US, and MR is superior in determining the extent of ILC (3). Synchronous bilateral breast cancer accounts for 3-6% of breast cancers. The reported rates of MR-demonstrated but mammographically and clinically occult contralateral breast cancer varies between 5.7-24%.

Distinguishing postoperative scar vs. tumor (recurrence)

Breast MRI is useful in the evaluation of patients with a high clinical suspicion of local recurrence within the irradiated conserved breast. It is a sensitive method for detecting or excluding recurrence of malignant disease, with reported sensitivities of 93 to 100% (4). MR is therefore useful in patients who have breast characteristics limiting the sensitivity of mammography, i.e. dense breasts, implants or scarring after treatment.

However, MRI is not an adjunctive test for diagnosis of a suspicious lesion in order to avoid biopsy, if a lesion is suspicious on clinical examination, mammography or ultrasound, biopsy must be performed. MRI must be done 12-18 months after stop of radiotherapy to avoid false positives.

Problem solving early after surgery

It is best to perform MRI prior to breast conserving surgery. But it has been demonstrated that MR imaging can be used for breast cancer staging after excisional biopsy when there are positive margins of resection, although there are limitations: Reported false-negative rate was 27% and false-positive rate was 19% with 75% specificity and 86% negative predictive value, with an accuracy for the diagnosis of residual disease of 64%-88% (5).

Monitoring of neoadjuvant chemotherapy

Reduction in size occurs late in the course of chemotherapy; however, tumor vascularity decreases relatively early in responsive tumor. Contrast enhancement on MRI is related to tumor vascularity, thus, reduction in enhancement is a measure of early response to chemotherapy. Enhancement on MR correlates well with vital tumor (6).

After neoadjuvant chemotherapy, breast conserving surgery can be performed. MR is a useful modality for evaluating whether breast conserving surgery can be safely done in the neoadjuvant setting. The cases with concentric shrinkage are good candidates for breast conserving surgery, but tumors showing dendritic shrinkage often have positive margins.

The most important use of MRI would be to reliably identify those patients whose tumors do not respond. If these non-responders could be identified early during treatment, they could potentially

benefit from either a change in therapy or earlier surgery, rather than continuing completion of the planned course of treatment.

Search for primary unknown tumor when breast cancer is suspected

In patients with metastatic disease of unknown primary, MRI of the breast depicts the primary breast cancer in up to 94% of cases with normal conventional evaluation (7).

Screening of high risk women

Breast cancer is associated with or due to a genetic predisposition in 5-10% of the cases. Women with a strong family history of breast cancer are more likely to develop the disease at a young age, when breast density is higher. Mammography is less reliable, as sensitivity is lowered due to breast density. Additionally, the mean growth rate of a tumor slows down to half in each successive 10 years-older group. A high sensitive test that can be performed frequently is necessary in this group of patients.

Systemic reviews show that MR has a better sensitivity than mammography in screening high risk women (8).

MR cancers detected in high risk women are smaller than those in control groups and less patients have involved lymph nodes.

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MRI of rectal cancer

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Neoadjvant radiotherapy decreases the rate of local recurrence and increases survival after total mesorectal excision. Locoregional failure is associated with significant morbidity. MRI has a moderate accuracy for predicting tumor stage of rectal cancers. Selection of patients for neoadjuvant therapy is done on the basis of the circumferential resection margin (CRM), the smallest distance between the outer limit of the deepest tumor invasion and the mesorectal fascia. The CRM can be predicted with high accuracy on MRI. Overstaging is often caused by desmoplastic reactive tissue alteration surrounding the tumor. Staging is done on the axial T2 TSE high resolution images perpendicural to the tumor. Diffusion weighted imaging (DWI) has an added value in the evaluation of tumor response to neoadjuvant therapy. DWI increases the number of detected nodes and improves the PPV for identification of metastatic nodes.

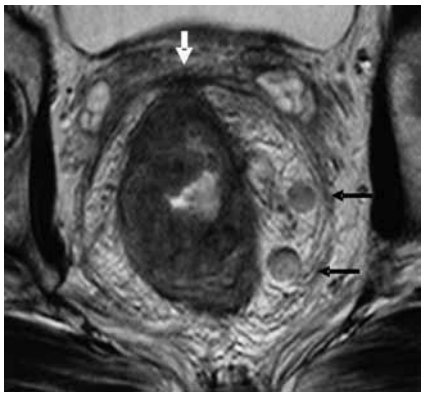

Fig. 1. - Mesorectal fascia with enlarged lymphnodes in the mesorectal fat (black arrows). Involvment of the mesorectal fascia (white arrow) by the rectal cancer.

MRI is currently the most advanced staging modality able to depict the mesorectal fascia and its relationship to the tumor margins, which affects the choise of treatment.

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Imaging of primary bone tumors

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The purpose of this presentation is to review the role of MR imaging (MRI) in the diagnosis, characterization, surgical staging and response to treatment of primary bone tumors.

Although initial detection of primary bone tumors still largely relies on plain radiographs, the use of MRI may increase due to the more widespread use of this imaging modality in the evaluation of musculoskeletal diseases. Moreover, cross-sectional imaging (both Computed Tomography (CT) and MRI) may be very useful in the detection of bone tumors located at complex anatomical areas, such as the spine, pelvis or skull base.

Imaging characterization of bone tumors is mainly done by combining clinical findings (age and location) and plain films (or CT-) findings. Analysis of a bone tumor should always start with meticulous analysis of basic plain film parameters such as the size of the lesion, matrix, margins transitional zone, cortical destruction and periosteal reaction. The main task of the radiologist is to distinguish benign (*"don't touch lesions"*) and aggressive (potentially malignant) lesions. The latter should be referred for further imaging, local and distant staging.

The additional role of MRI in potential characterization of a bone tumor is relatively limited, as most tumors are of low signal intensity on T1-weighted imaging (WI) and T2-WI. However, some lesions demonstrate more characteristic signal behaviour on MRI. High signal on T1-WI may be due to intralesional fat (e.g. intraosseous lipoma or quiescent haemangioma). On the other hand, low T2-signal may be due to hemosiderin deposition (e.g. giant cell tumor), the presence of fibrous tissue (e.g. non ossifying fibroma), osseous matrix, intralesional calcifications and flow voids (1). Morphological signs that may be helpful in tissue characterization on MRI are fluid-fluid levels (Fig. 1) (e.g. primary or secondary aneurysmal bone cysts but also rare teleangiectatic osteosarcoma), lobular appearance (e.g. chondroid tumors), sparing of the disc space in a spinal lesion (e.g. eosinophilic granuloma or chordoma).

In some scenarios, MRI may be misleading if CT or plain film findings are not taken into account (e.g. osteoid osteoma) (Fig. 2).

MRI should always been performed before biopsy in order not to alter characterization and local staging.

MRI plays a pivotal role in the local surgical staging of the tumor and is the imaging modality of choice to evaluate skip metastases, invasion of the adjacent joint and soft tissues, neurovascular bundle involvement and locoregional adenopathy. Sagittal or coronal images with a large field of view (or whole body MRI) are mandatory for evaluation of skip metastasis. STIR sequences seem to overstage the lesions. Rarely, skip metas-

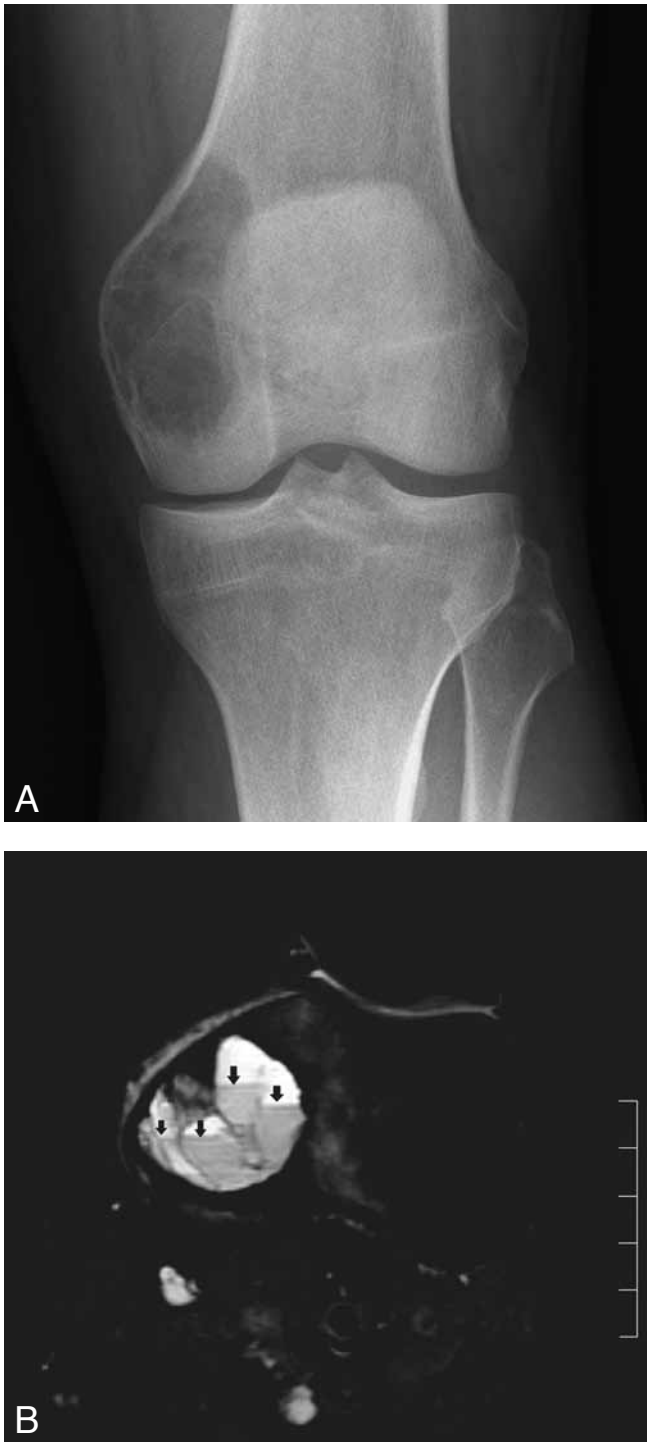

Fig. 1. — Aneurysmal bone cyst in an adult patient. Plain radiographs of the left knee (A) demonstrate an osteolytic lesion within the distal metaphysis of the femur with epiphyseal extension. On axial T2-weighted MR images (B) with special window setting fluid-fluid levels are seen within the lesion (arrows).

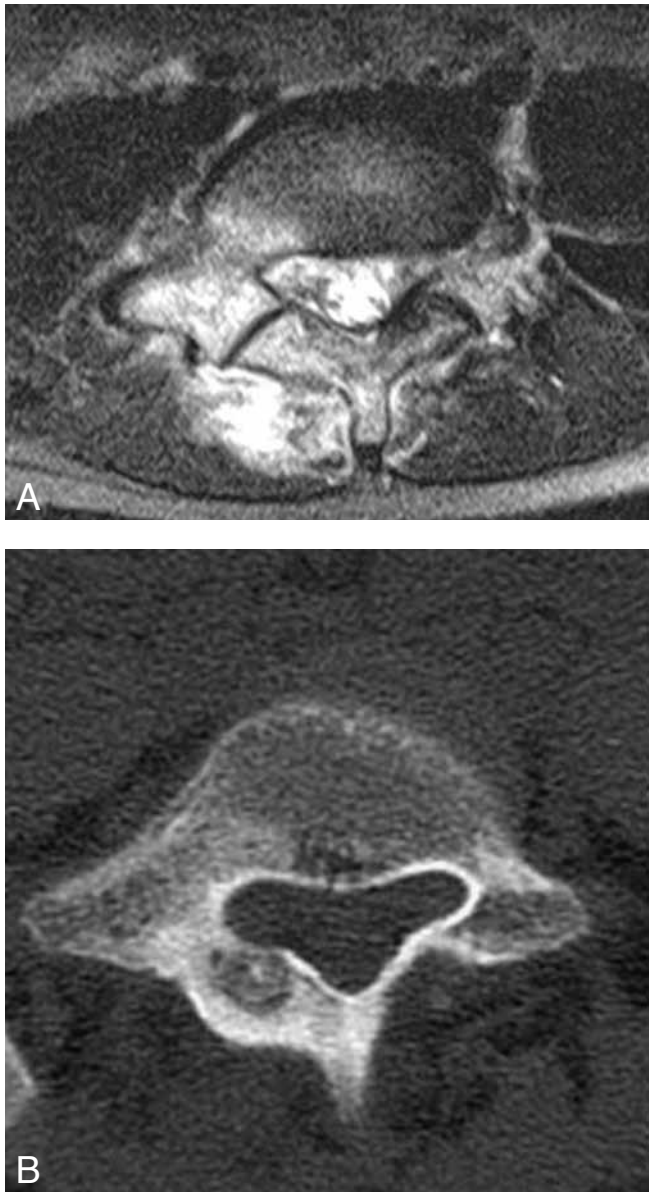

Fig. 2. — Osteoid osteoma of the lumbar spine in a 12-year-old female gymnast. Axial T2-weighted MR images (A) show non-specific bone marrow edema within the right pedicle and lamina of L5. Note also associated soft tissue edema. Differential diagnosis with other bone tumors or spondylosis could not be made. Axial CT-scan (B) shows nicely the nidus and surrounding sclerosis, which enables a specific diagnosis of an osteoid osteoma.

tases may cross the adjacent joint. Absence of joint fluid in peri-articular lesions has a high negative predictive value, but the presence of joint fluid doesn't necessarily indicate joint invasion. High resolution T2-WI are better suited than sagittal or coronal images to evaluate neurovascular bundle involvement.

Dynamic MR imaging after intravenous injection of gadolinium contrast is required for targetting viable tumor areas for biopsy, differentiation between tumor, necrosis and edema, monitoring of chemotherapy and detection of recurrence (2).

The expanding role of diffusion-weighted imaging (DWI) and whole body MRI in detection of multiplicity (e.g. Hereditary Multiple Exostoses Syndrome and multifocal lymphoma), distant staging (e.g. bone metastases) and treatment response has still to be determined (3, 4, 5). Evaluation of lung metastases is currently done by low dose CT of the chest. It is – however – important not to overcall every tiny pulmonary nodule on initial staging as a lung metastasis, as this may

dramatically change the management and therefore the patient's outcome.

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Whole body diffusion-weighted imaging at 3 Tesla in oncologic imaging

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At the time of diagnosis of malignancy, determination of locoregional disease extent and detection of potential distant metastases is important for treatment planning and assessment of patient prognosis. In the post-treatment phase, accurate and, preferably, timely assessment of the patients response to treatment is necessary in order to detect tumour recurrence at an early stage and thus enable salvage treatment with curative intent. Additionally, non-surgical treatment such as RT, chemotherapy and the novel generation of targeted cytotoxic and antivascular agents do not necessarily lead to a decrease of tumour volume as a result to treatment, especially in the early treatment phase requiring. As such, specific imaging biomarkers are required (Fig. 1,2).

Anatomical imaging may fall short in the early detection of tumoral recurrence as treatment induced inflammation and fibrosis are sometimes difficult to differentiate from tumoral tissue.

Similarly, in the non-surgical treatment of malignancy the response evaluation criteria in solid tumours (RECIST) may fall short to accurately separate responders from non-responders.

Early detection of treatment effects and thus the early separation or responding from non-responding lesions may help to guide treatment escalation or change of treatment strategy in case of non-favourable response, while toxic side-effects may be avoided in non-effective treatment. In this setting, diagnostic imaging modalities that probe the tumoral microstructure or metabolism may be useful as they do not depend on lesion morphology, size or volumetric changes.

In oncologic imaging, by integrating sequences with sufficient spatial and contrast resolution and optimizing contrast media dynamics for imaging of the different body regions, magnetic resonance imaging (MRI) is emerging as an efficient and non-invasive imaging modality for comprehensive cancer staging.

However, the sole use of anatomical imaging sequence harbours a number of potential disadvantages. The need to combine T1- and T2-weighed and contrast-enhanced sequences typically makes a whole-body MRI assessment time consuming. Moreover, the depend-

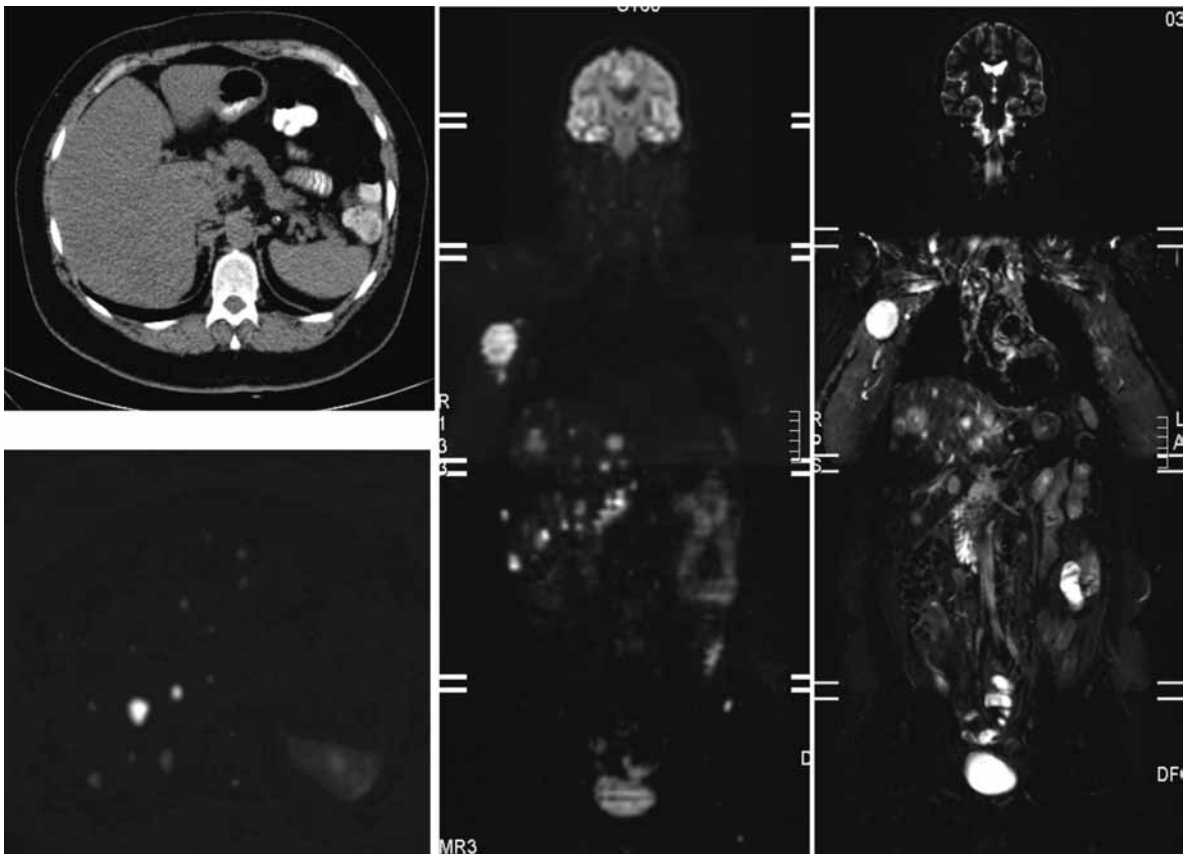

Fig. 1. — Patient with suspicion of metastatic melanoma and allergy to Iodinated contrast: (A) non-contrast enhanced CT cannot exclude liver metastases. (B) Diffuse liver metastases are visible as b1000 hyperintense lesions on transverse diffusion-weighted MRI. (C,D) Whole-body diffusion-weighted MRI in correlation to T2 fat-suppressed image shows diffuse metastatic spread to right axillary lymph nodes, liver and skeleton (left iliac wing and femur).

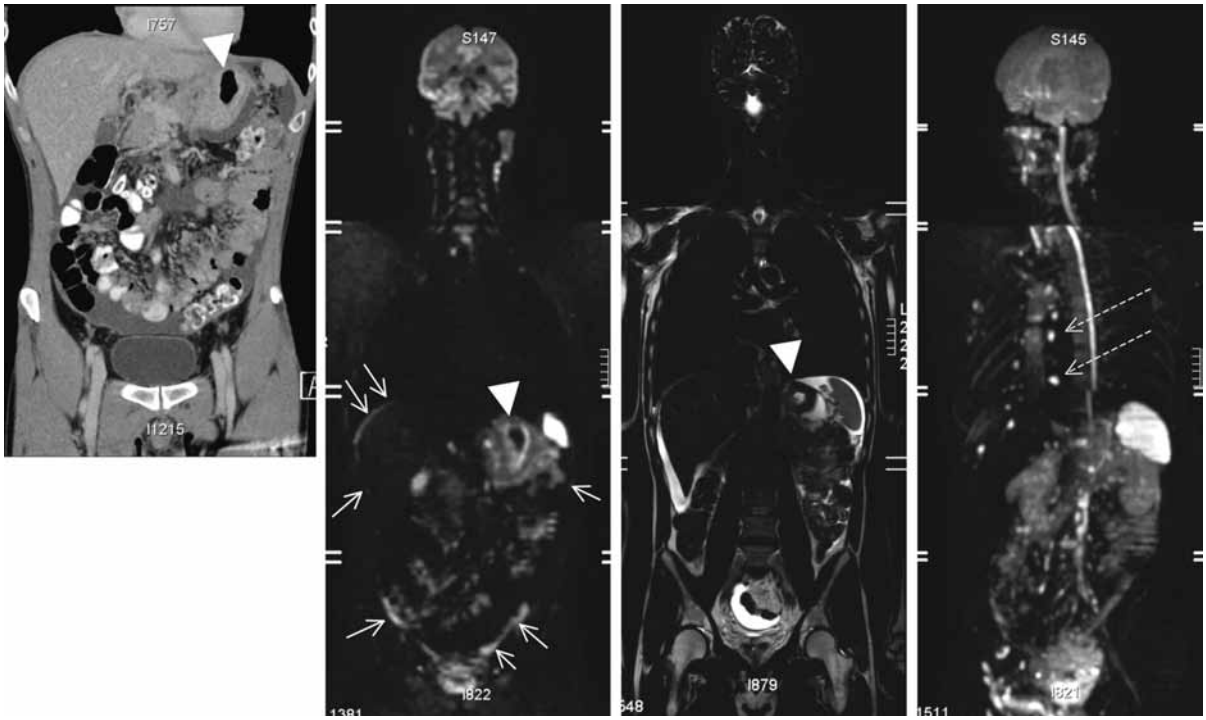

Fig. 2. — Abdominal shows large gastric tumor (arrowhead) and peritoneal fluid suspect of peritoneal dissemination. (B,C) Whole body diffusion-weighted MRI in correlation to T2-weighted image shows gastric tumor (arrowhead) and diffuse peritoneal metastases visible as b1000 hyperintense areas (arrows). (D) Diffusion-weighted MRI 3D MIP reconstruction also shows mediastinal metastatic adenopathies (arrows).

ency of morphological and size-related criteria – similar as for computed tomography (CT) – faces whole body MRI with limitations for nodal differentiation and treatment follow-up or early response assessment.

Diffusion-weighted magnetic resonance imaging (DWI) has already shown value for tumour differentiation, locoregional staging (primary tumour and regional lymph nodes), characterization of metastases and early assessment of treatment effects. Currently, DWI is often used for imaging of body-regions (for instance: liver, head and neck, pelvis,....) as a problem solving technique complementary to computed tomography (CT) or fluoro-deoxyglucose positron-emission tomography (FDG-PET); for instance, in the differentiation of liver metastases. However, rapid technological development has made the technique suitable for whole-body imaging. The major advantage of WB-DWI for tumour screening is that it possible obviates the need for a contrast-agent

The aim of the presentation is to give an overview of normal anatomy, basic clinical concepts of whole body–DWI (WB-DWI) and advanced applications for tumour staging and treatment follow-up.

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