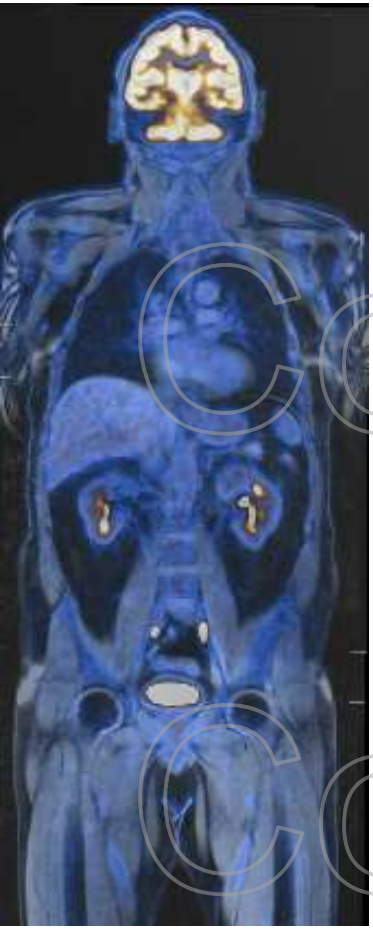
Actualités TEP-IRM en Oncologie: Apprendre de TEP-TD comment faire



JFMN 15, La Rochelle, May 29, 2015

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Acknowledgements:

Peter Crandall, MS*
Martin Huellner, MD
Anass Johayem, PhD
Nik Schaefer, MD
Edwin ter Voert, PhD
Gaspar Delso, PhD*
Lars Husmann, MD
Cäcilia Mader, MD
Paul Stolzmann, MD
Florian Wiesinger, PhD*

*GE Healthcare

Conflict of interest declaration

1. **Grant recipient Bayer, GE Healthcare, Guerbet, Lilly**
2. **Occasional speaker finanical support by GE Healthcare and others**
3. **Course Co-Director Intl. Diagnostic Course Davos www.idkd.org with educational support by several companies**

Contents

1. What is hybrid imaging?
2. Image acquisition
3. Image reconstruction and attenuation correction
4. Workflow, workflow, workflow
5. Towards an affordable PET/MR exam in oncology

What is hybrid imaging?

Imaging facts on hybrid data I

When we do imaging on a single modality, we try to optimze sensitivity and specificity for this modality.

CT: with and without CM, dynamic, multiple phase

MR: with and without CM, dynamic, multiple phase, many PS

Nuc: static, dynamic, multiple phase, various quant. Methods

Hybrid imaging: the sum of both exams has to be optimized regarding sensitivity and specificity

⇒ Exam protocols have to be reinvented for hybrid imaging

Imaging facts on hybrid data II

This reinvention is a problem, as there is resistance:

1. by imagers (who continue to push their favorite modality even in a hybrid environment)

2. by clinicians (who say e. g. CT images in PET are inferior)

The fact is: not all what is needed in single modality imaging, is needed in hybrid imaging

Example: we have learned that in many indications, CT in PET/CT does not need contrast medium

Imaging facts on hybrid data III

Any hybrid modality with A and B can provide

1. **Complementary information**
   (e. g. see it on PET, but not on CT)
2. **Confirmatory information**
   (e. g. present but unclear on PET, clear on CT)
3. **Redundant information**
   (e. g. present and obvious on PET and on CT)

Imaging facts on hybrid data IV

Here MR is at best confirmatory

Example:

liver metastases

MR > CT ≠

PET/MR > PET/CT

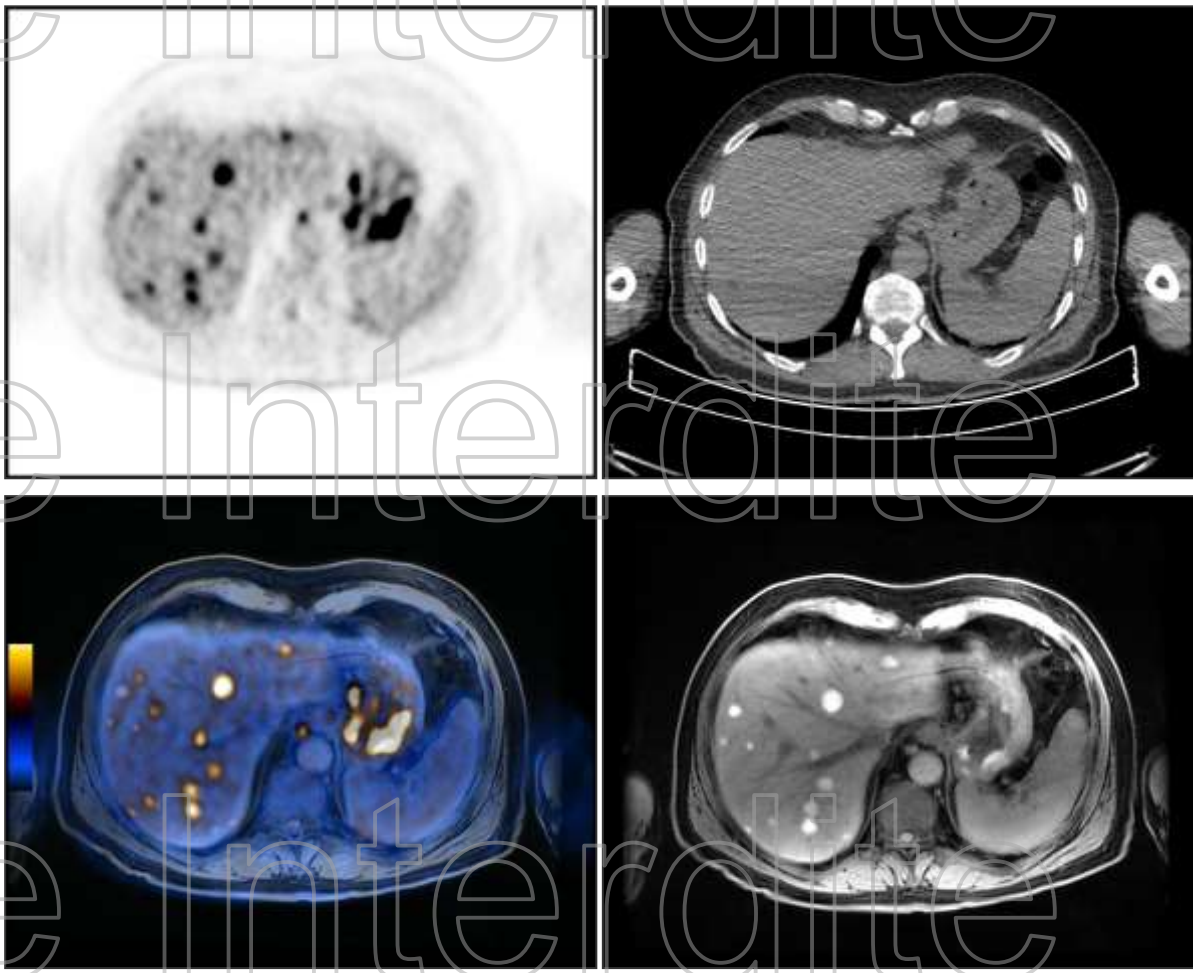
In this case:

MR > CT, but

PET/MR = PET/CT

(all lesions seen on PET,

MR info redundant



A hybrid system is a single modality!

Consequences

1. **minimize redundant hybrid imaging information**
   relatively simple in PET/CT, complex in PET/MR (=mist!)

2. **PET data acquisition options limited**
   static or dynamical mapping of tracer distribution
   Note: richness of PET and SPECT are in the tracer choice

3. **CT and MR data acquisition options much higher:**
   - variations in CT moderate: early / late contrast enhancement (ce)
   - variations in MR high: pulse sequences / ce / Diffusion etc

⇒ **Renivent CT or MR for hybrids PET/CT and PET/MR**

What do we expect from hybrid imaging ?

Consequences

1. **One-stop shop exam**
   - *ease for patient*
   - *all data are more easily integrated*
   - *synergy (like attenuation correction /anat. correlation)*

2. **Answers clinically relevant questions**
   - *these differ depending disease and organ*
   - *oncology: essentially «rule-out metastases» exam*

⇒ **usefulness is disease- and organ- dependent**

Image acquisition

Options of image acquisition

1. **Several systems available**
   - integrated PET/MR (Siemens)
   - integrated TOF-PET/MR (GE)
   - separate one room PET and MR (Philips)
   - two room shuttle connected PET/CT-MR

2. **No compromise in image quality should be accepted**
   compared to single systems or in PET/MR vs PET/CT

3. **A lot of protocols available, particularly in MR**
   - task has to be to optimize protocols for clinical question

Contents

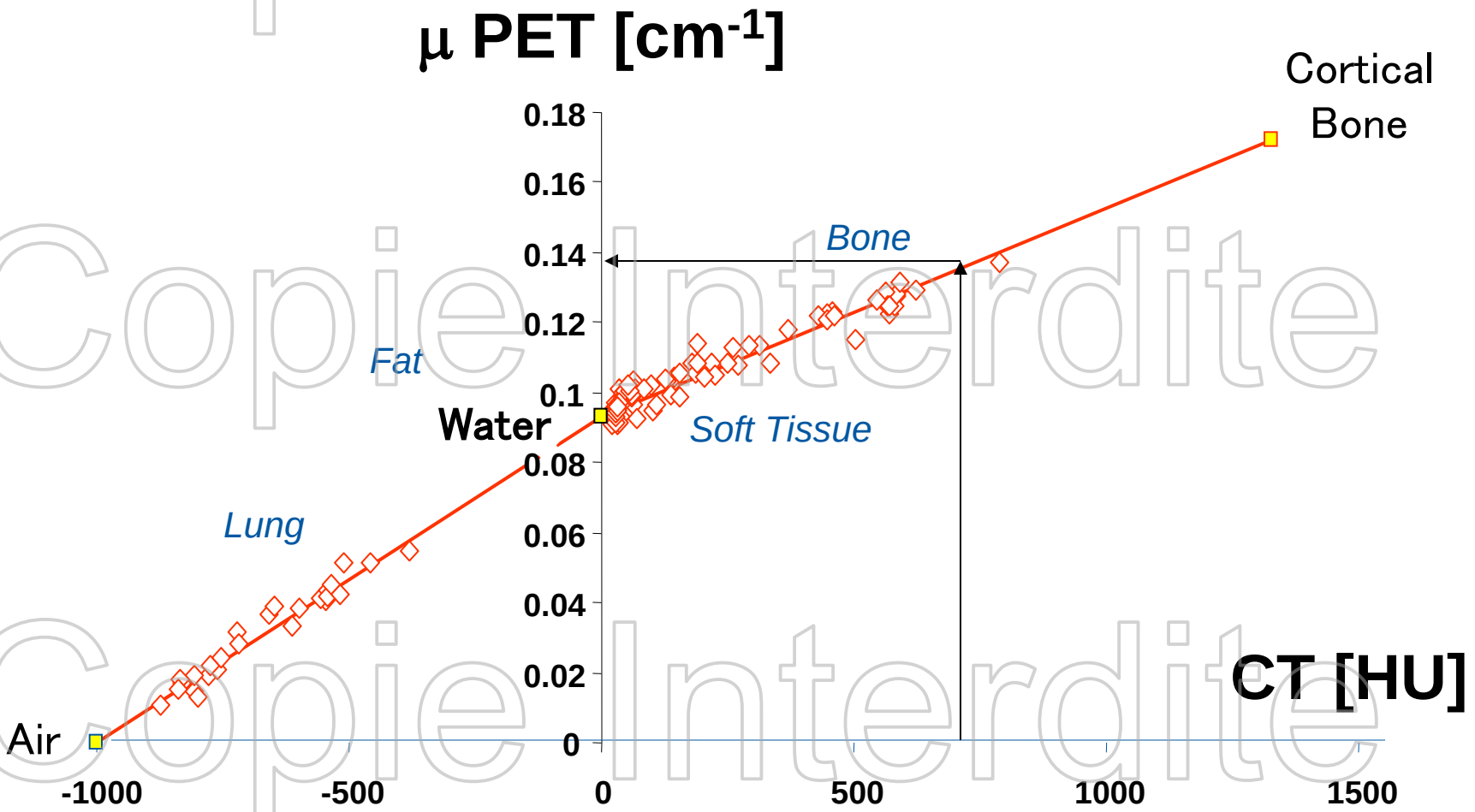
Image reconstruction

and

attenuation correction

Attenuation Correction in PET/CT

Burger C, Goerres GW, Schoenes S, Buck A, Lonn AHR, von Schulthess GK. Europ J Nucl Med 2002; 29,7:922-927



Problems with MR based AC in PET/MR

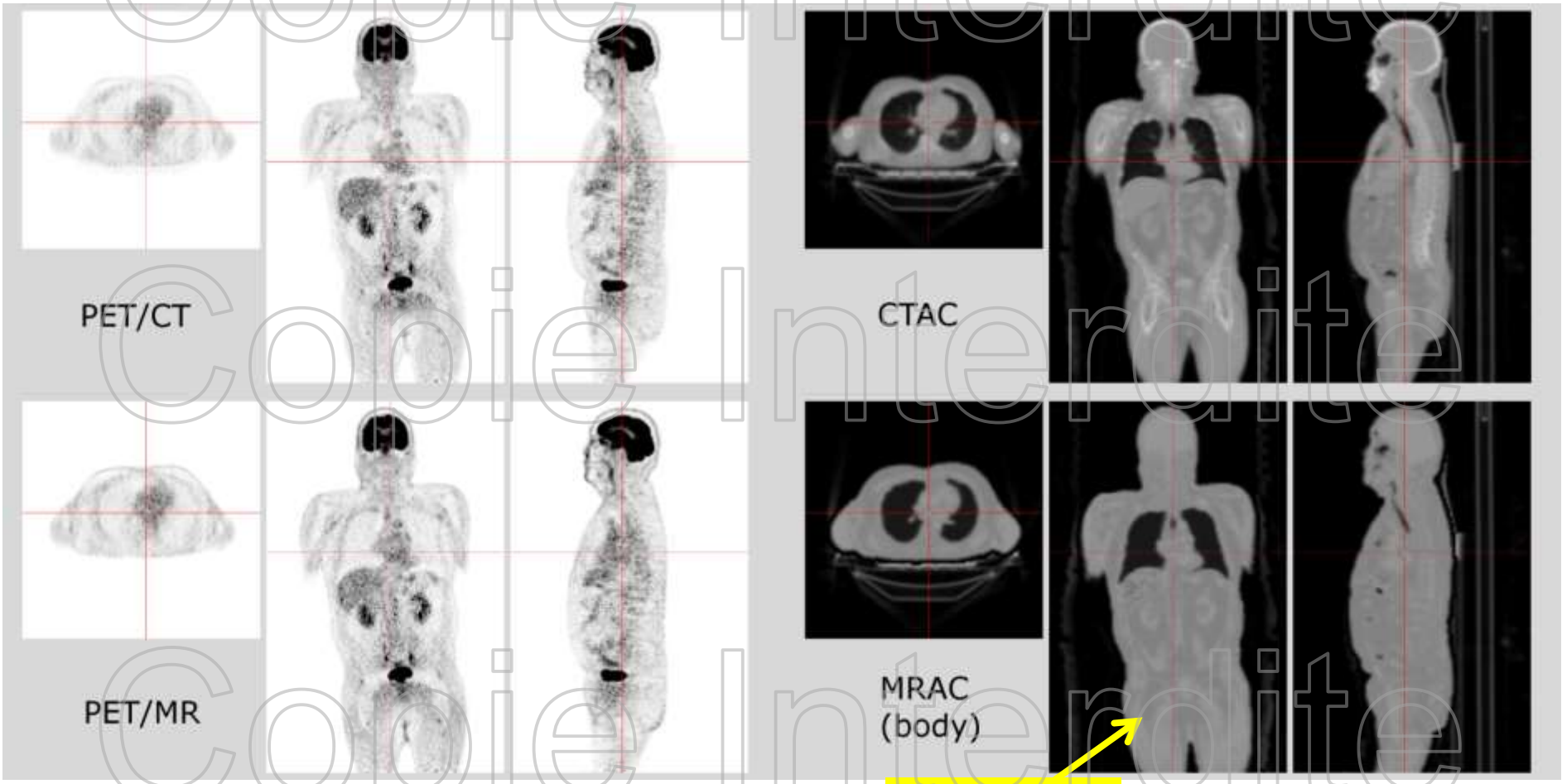
MR provides no X-ray/gamma-ray density maps

1. **Bones (compact bone) is black on MRI**
   => it cannot be differentiated from air
   => attenuation correction errors

2. **Metals in MRI can (or cannot) cause large signal voids**
   => pulse sequence dependent
   => cannot be differentiated from air
   => attenuation correction errors
   => also caused by local coils in MR

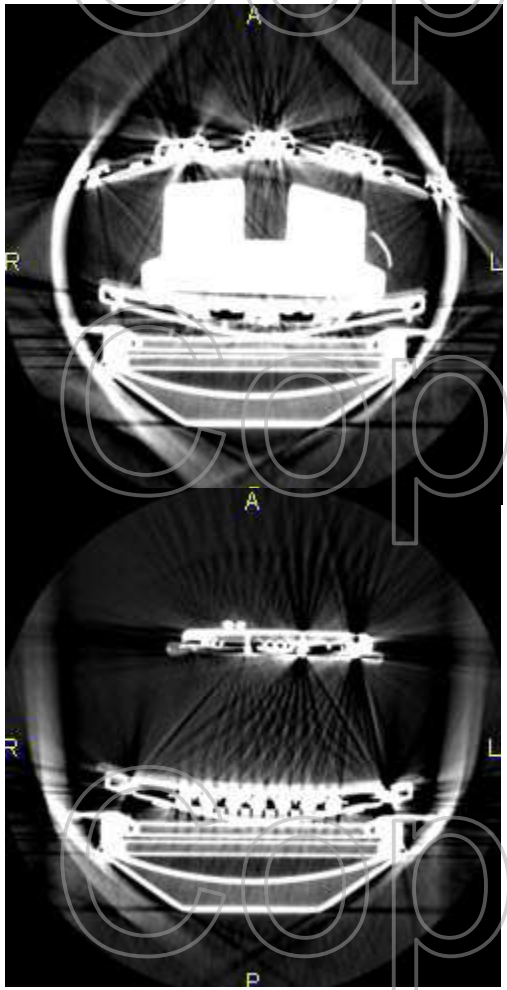
Whole Body Imaging

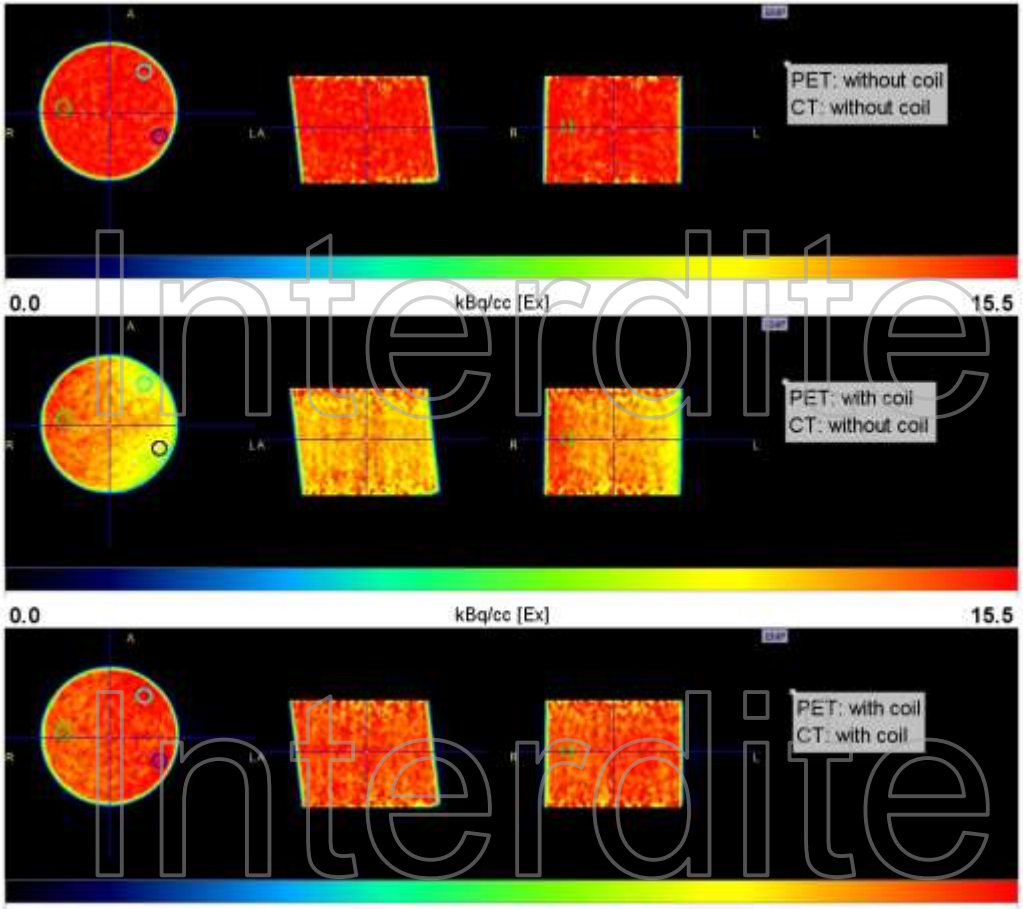
CT- and MR based attenuation correction



Externe Metall-enthaltende Objekte

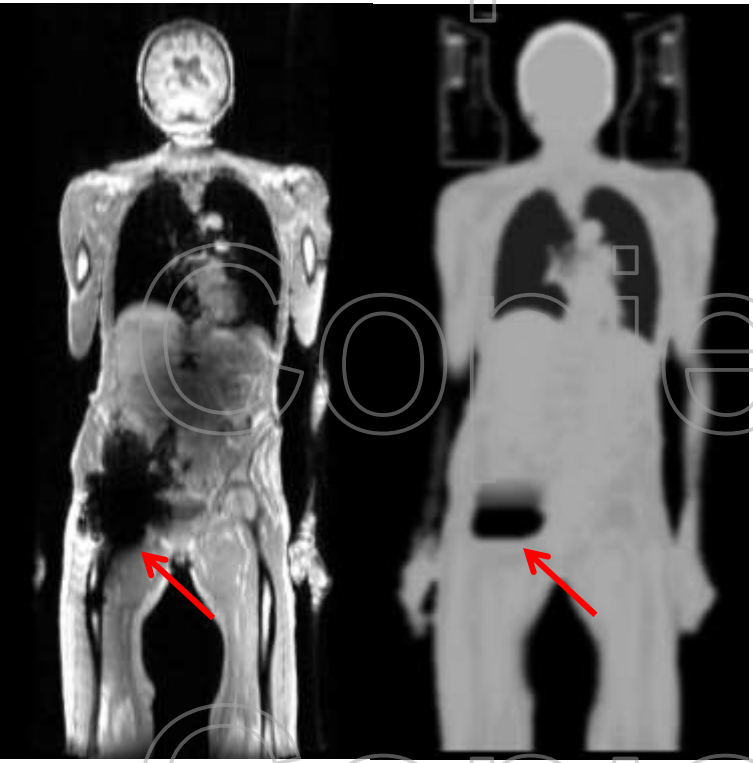
Interferenz von Oberflächenspulen mit γ- und Rö-Strahlen



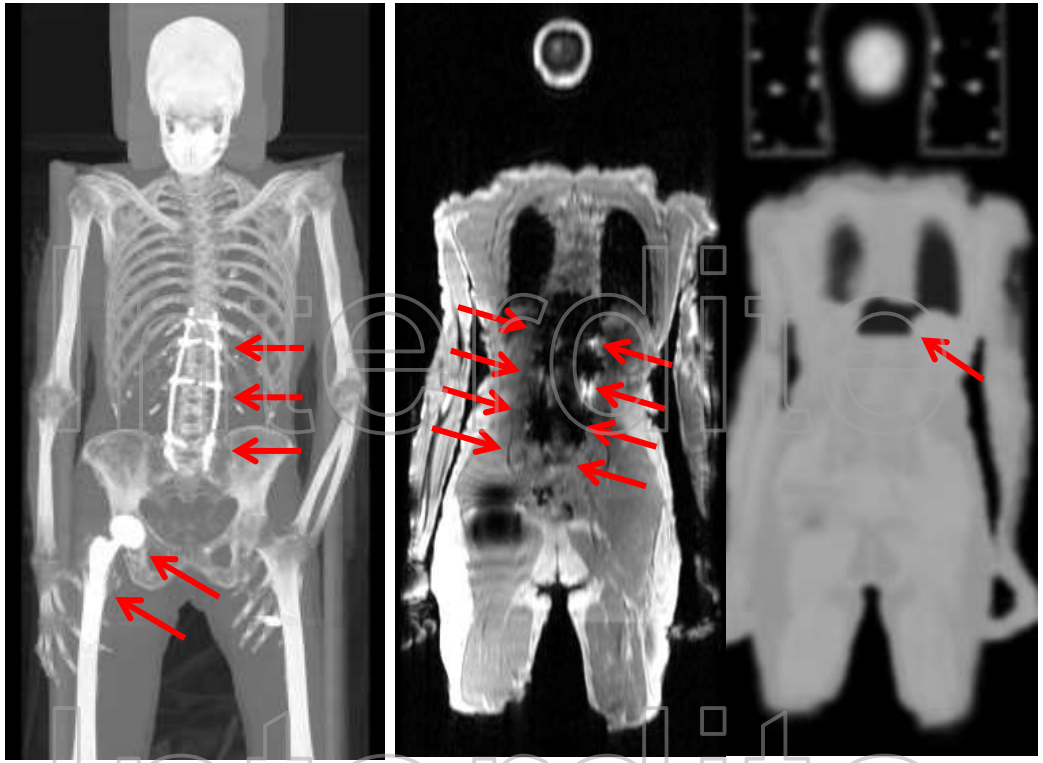


Artifacts due to metal implants

MR MR-AC map

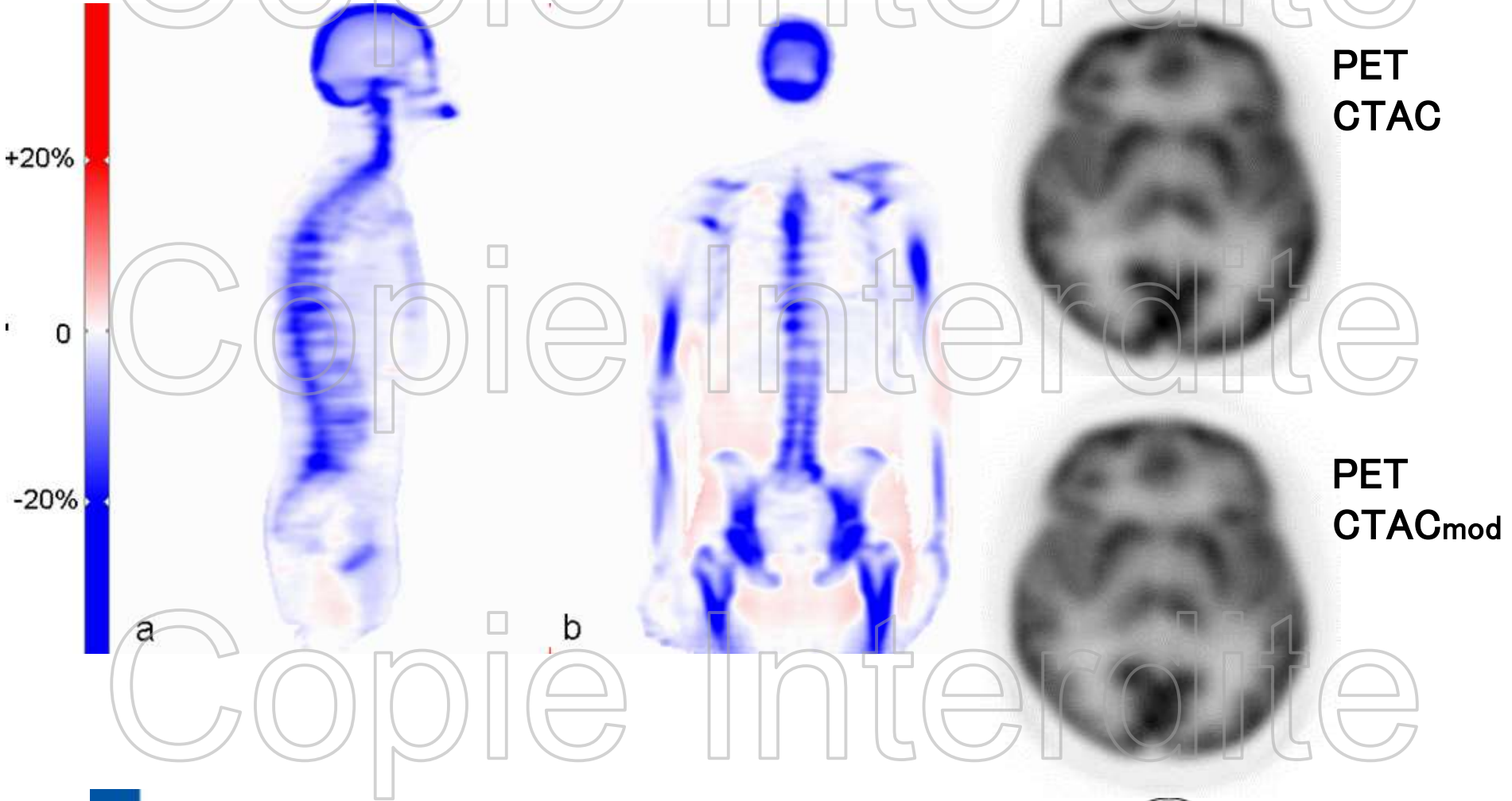


MR MR-AC map



jAttenuation Correction using MR: MR-AC

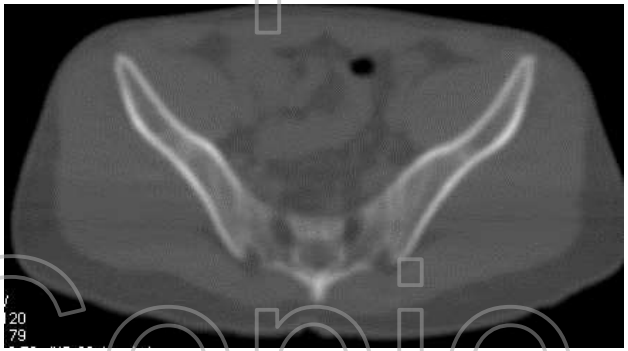
Simulation with CT-AC: replacement of bone by soft tissues

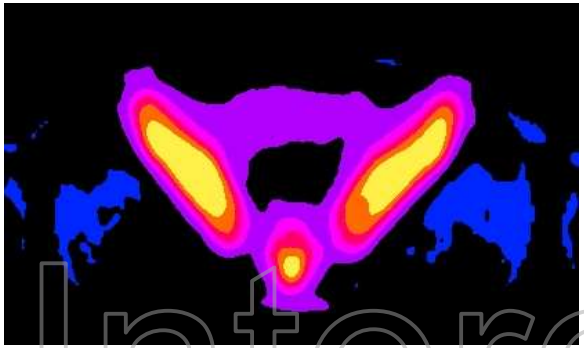


MR Attenuation Correction: MR-AC

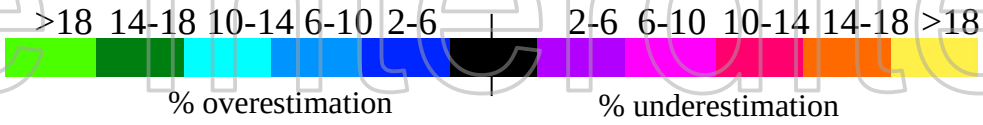
Correction with replacement of bones by soft tissues

CT

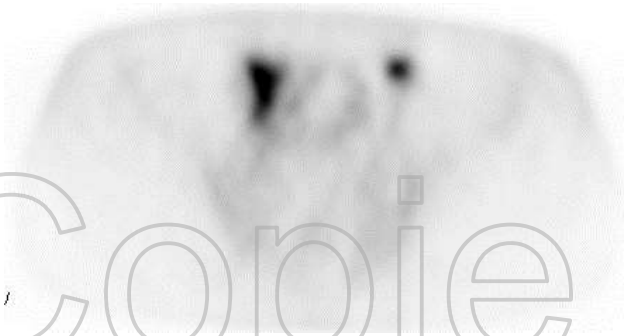


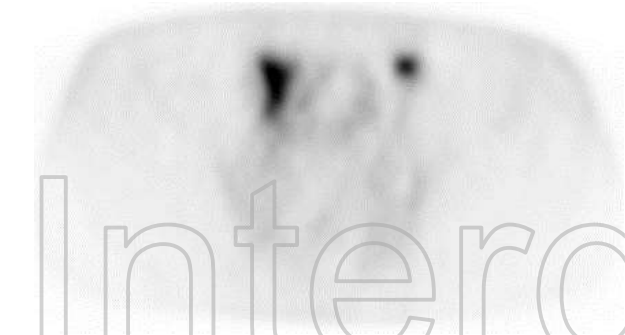


$$\frac{(PET_{bone}-PET_{st})}{PET_{bone}}$$



PET
CTAC





PET
CTAC$_{mod}$

MR attenuation correction: data*

using soft tissue – fat – air - background as AC-map

1. **Brain AC requires bone correction => error 5-10%**
2. **Body soft tissue AC ok => error < 5%**
3. **AC next to bone (10 mm) => error < 10%**
4. **AC of bone lesions (in bone) => error < 25%**

⇒ **for therapy monitoring, bone must be used for AC**

⇒ **severe drawback of PET/MR at this time**

⇒ ***e. g. Samarin A et al: EJNMMB 2012**

Quality of MR in PET/MR

Appenzeller et al, Insights Imaging 2013, Zurich

Insights Imaging. 2013 Aug;4(4):481-90. doi: 10.1007/s13244-013-0247-7. Epub 2013 May 15.

PET/CT versus body coil PET/MRI: how low can you go?

Appenzeller P[1], Mader C, Huellner MW, Schmidt D, Schmid D, Boss A, von Schulthess G, Veit-Haibach P.

1. Evaluation of whether PET/MRI with one sequence using body coil is diagnostically sufficent compared with PET/CT

2. PET/MRI with body coil does not match entirely the diagnostic accuracy of standard low-dose PET/CT

3. PET/MRI might only serve as a backup solution in patients

Current solutions for AC in PET/MR

MR provides no X-ray/gamma-ray density maps

Current solutions

1. Ignore bone (replace bone by soft tissues)
   => still AC-errors leading to SUV-errors

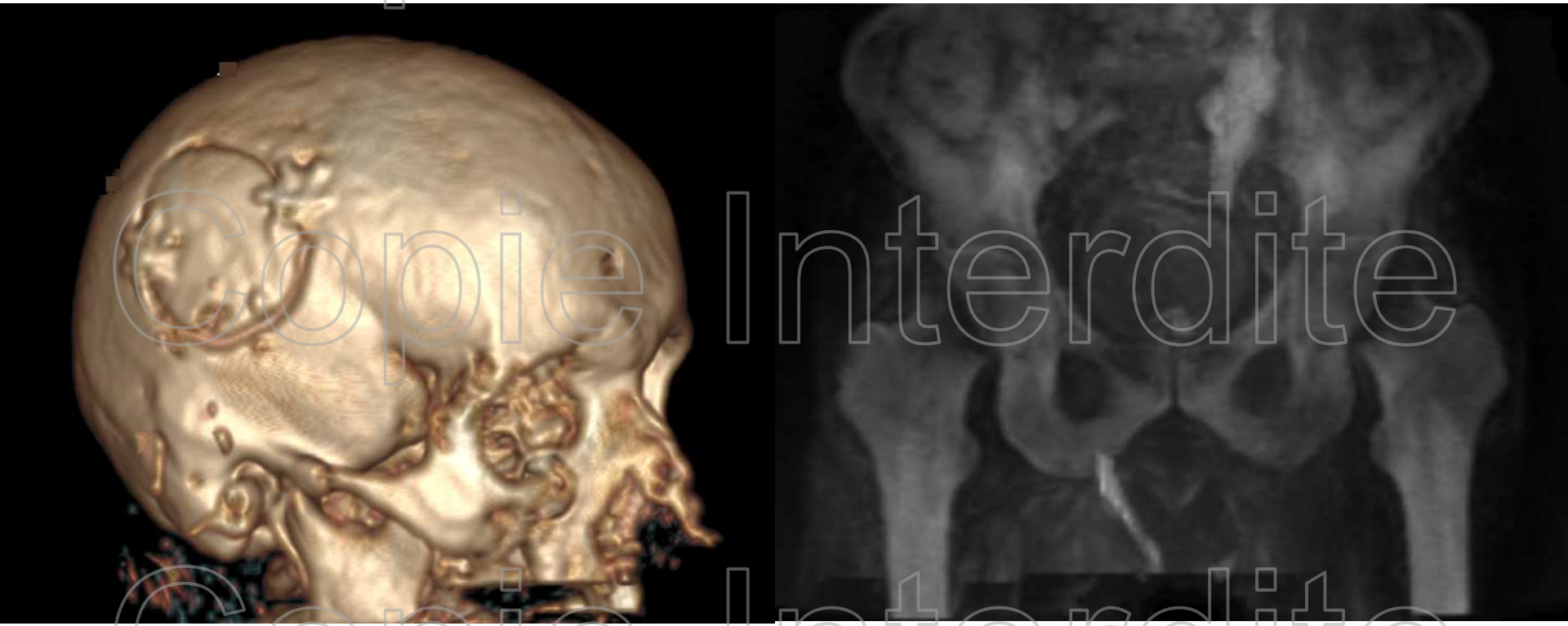
2. Atlas-based identification of bone in MR images
   => cumbersome, can cause misclassifications

3. Better bone MR imaging with ZTE sequences

4. Better localization with TOF-data

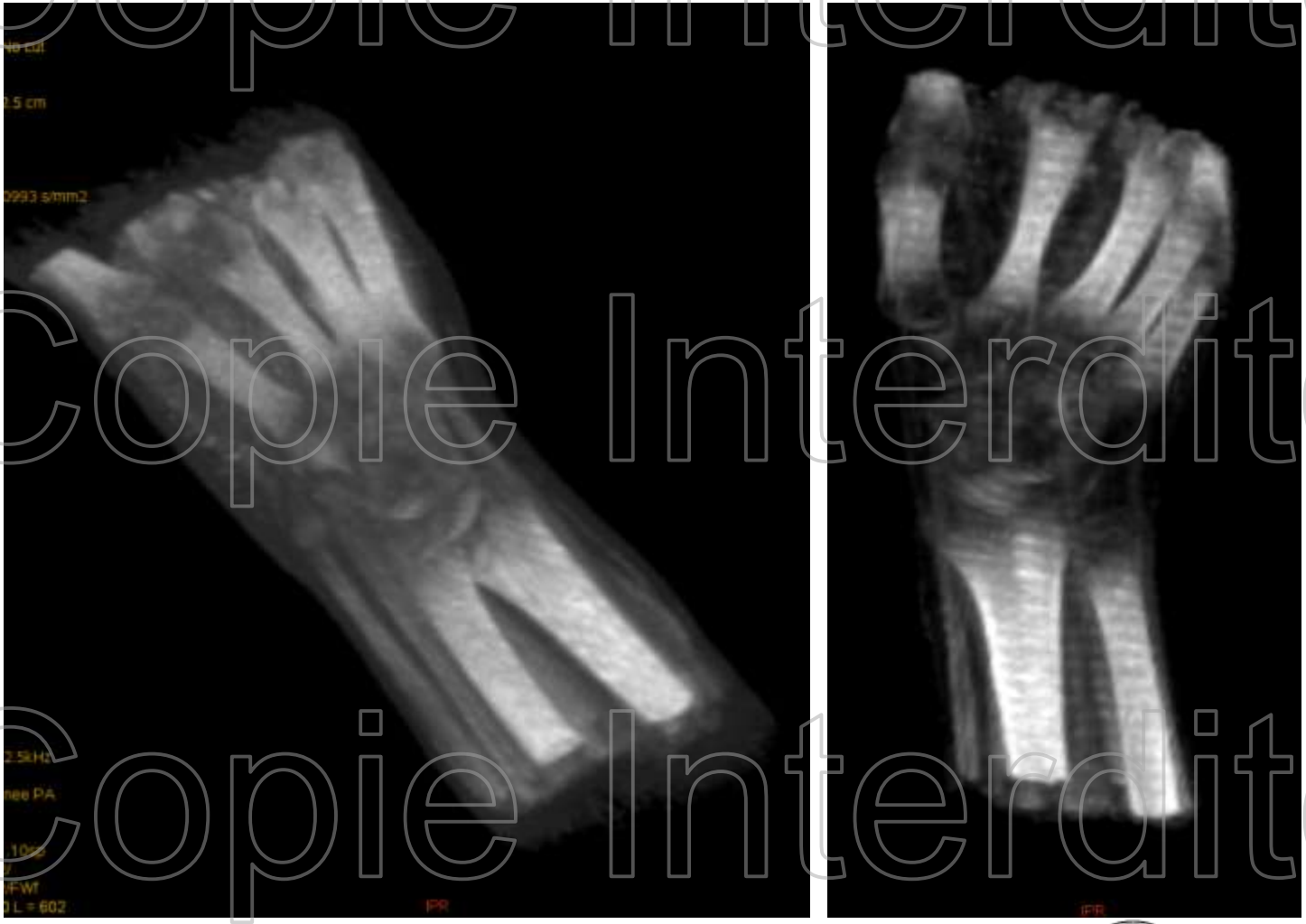
Solutions for the MR AC Problem

Ultrashort (UTE)/Zero Echo Time (ZTE) Sequences



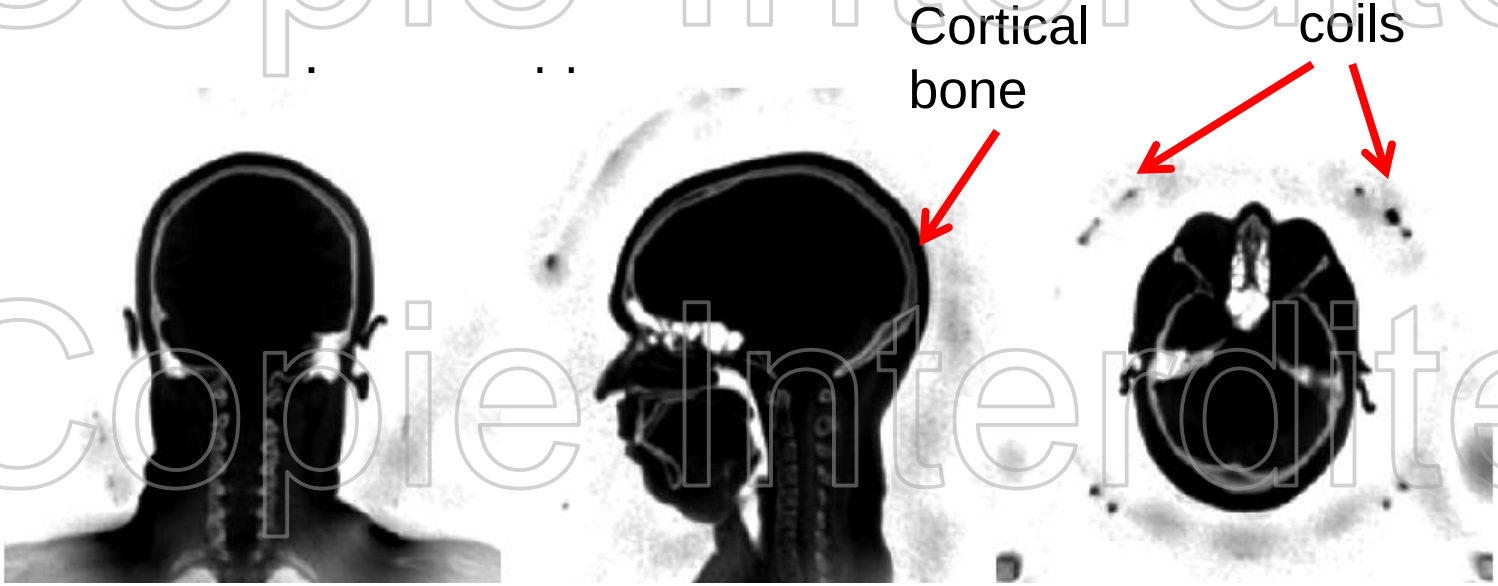
Solutions for the MR AC Problem

Ultrashort (UTE)/Zero Echo Time (ZTE) Sequences



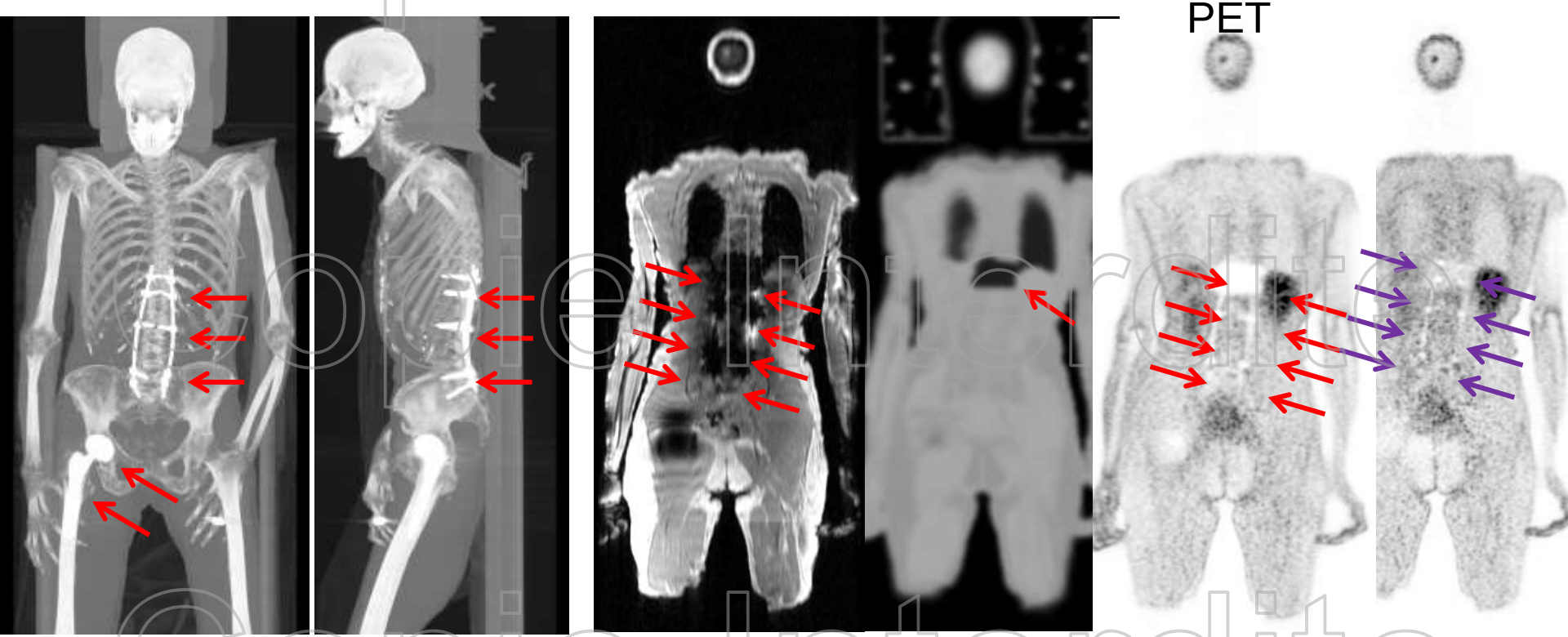
Solutions for the MR-AC problems with metals

Short (UTE) or zero echo time (ZTE) sequences



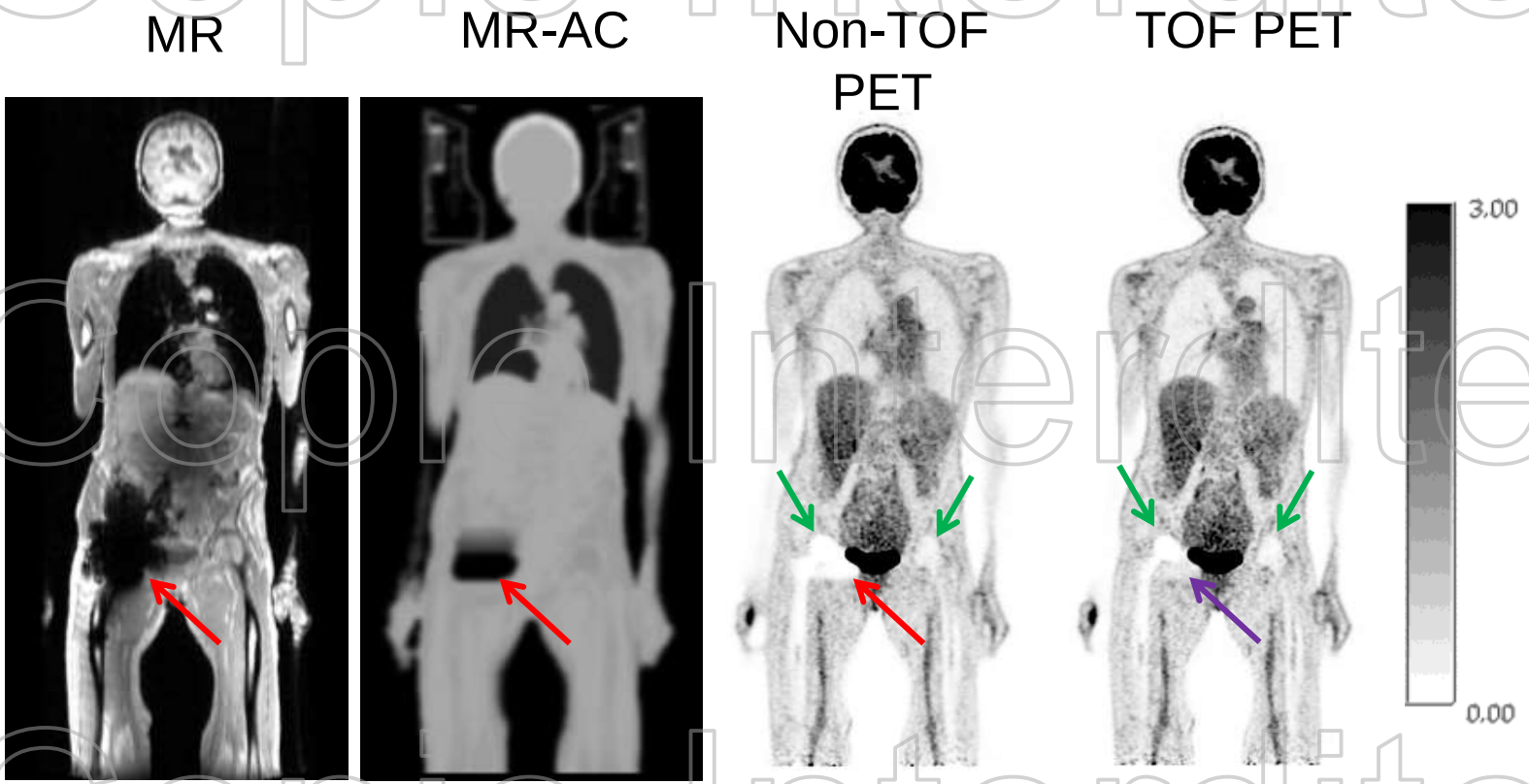
Artifact Reduction with TOF-PET

Data reconstruction with TOF on and off



Artifact Reduction with TOF-PET

Data reconstruction with TOF on and off



Workflow, Workflow, Workflow

Workflow, workflow, workflow

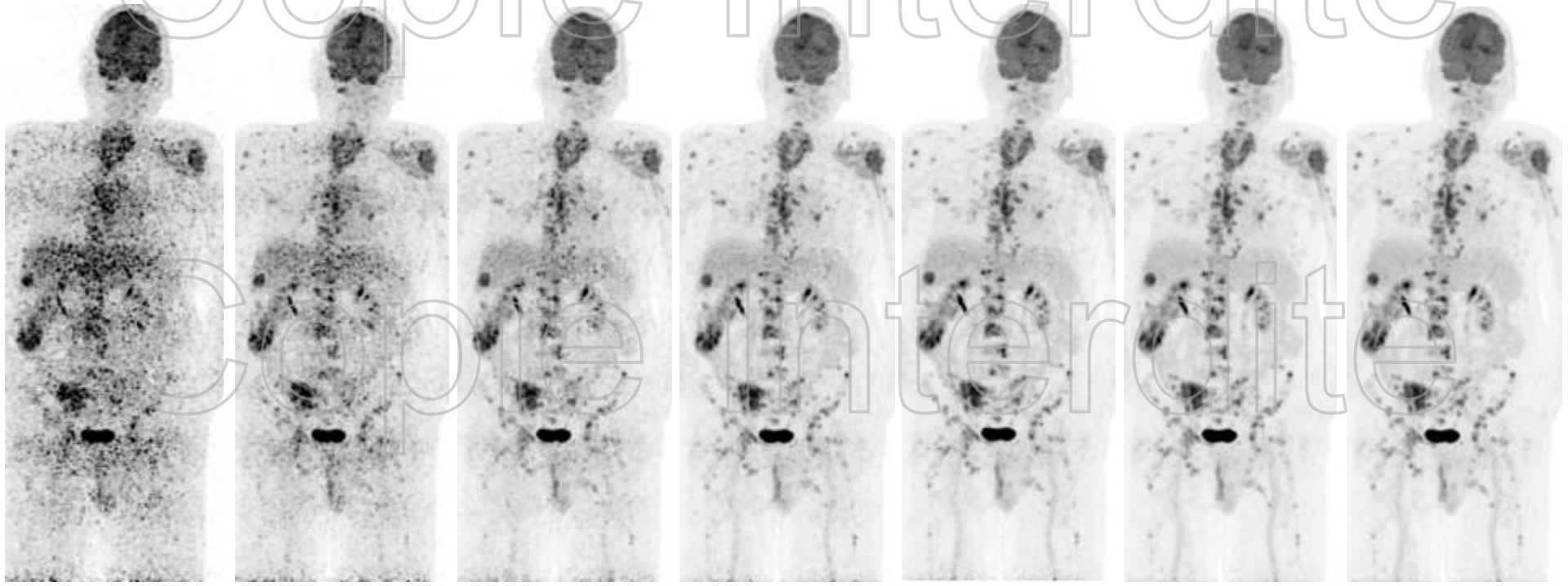
1. If a PET scan takes 15 minutes and an MR 45 minutes
   => a PET/MR scanner is an expensive MR scanner!

2. Zurich rule: if $t_{MR} > t_{PET} + 15$ minutes,
   limit MR acquisition in PET/MR and do separate MR

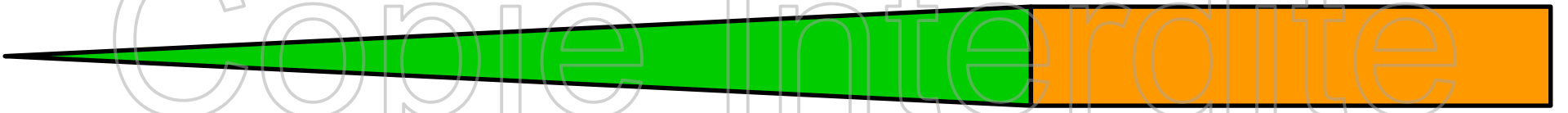
3. Eliminate MR pulse sequences with info redundant to PET
   => optimize sensitivity and specificity for entire system
   => cut as many MR pulse sequences as you can

Longer PET measurements add no information!

In this scanner, 80 sec measurements per cradle are ok



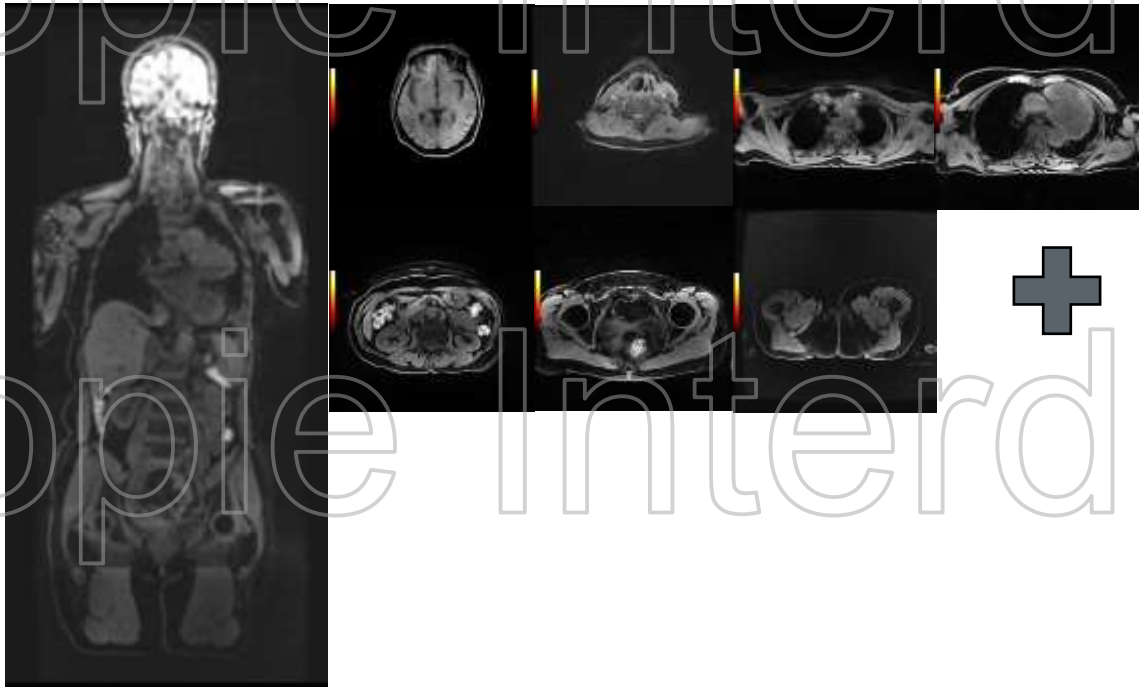
A 5 s **B** 10 s **C** 20 s **D** 40 s **E** 80 s **F** 120 s **G** 180 s

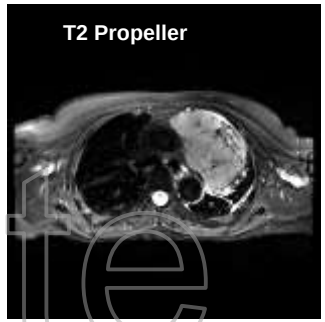


«Low-Dose» PET/MRI

= PET + LavaFlex + T2 Propeller in chest/upper abdomen

Basic PET/MRI





ceMRI in area of interest

Workflow, workflow, workflow

Much clinical research to be done on PET/MR must strive to:

1. Identify useful sequences
   - Dixon water-fat GRE, T2w (Propeller, Blade)

2. Suppress sequences which do not add additional info
   - conflicting data, what to omit
   - DWI (as it looks like FDG-PET, but less specific)
   - STIR

=> Minimize redundancy

Towards affordable PET/MR examinations

Clinical data

1. Much time (literature) has been spent on dealing with the shortcomings of PET/MR (which is necessary)

2. Much time has been spent on saying: hey, let us play with PET/MR a bit !

3. Much research has been done using protocols with 20' worth of PET and 80' worth of MR = not contributory, because unrealistic !

4. Little focus has been put on analyzing where – e. g. in oncology – PET/MR may be really superior than PET/CT AND
   can be run with cost-effective protocols

⇒ **unfortunately, there is not that many clinical data yet**

Clinical applications of PET/MR

1. PET/CT in oncology is successful, as it effectively rules out the presence of metastases, but in one place, it DOES NOT WORK!

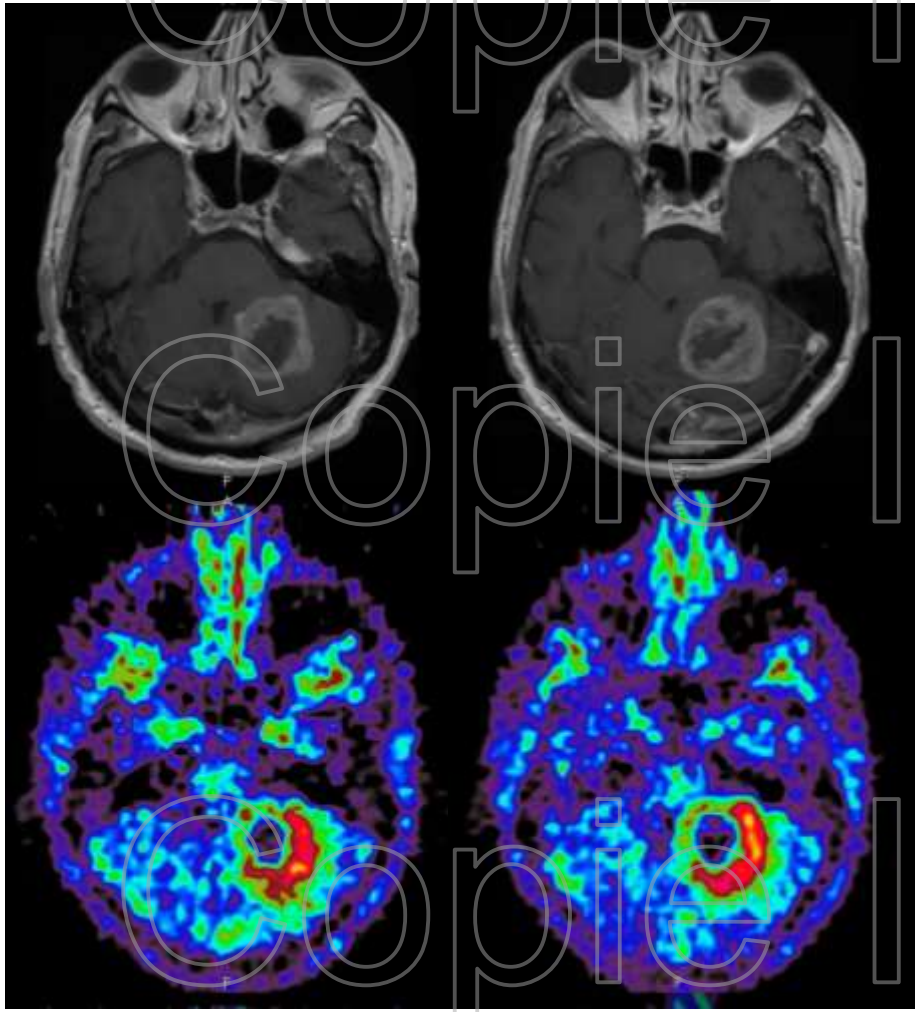
THE BRAIN

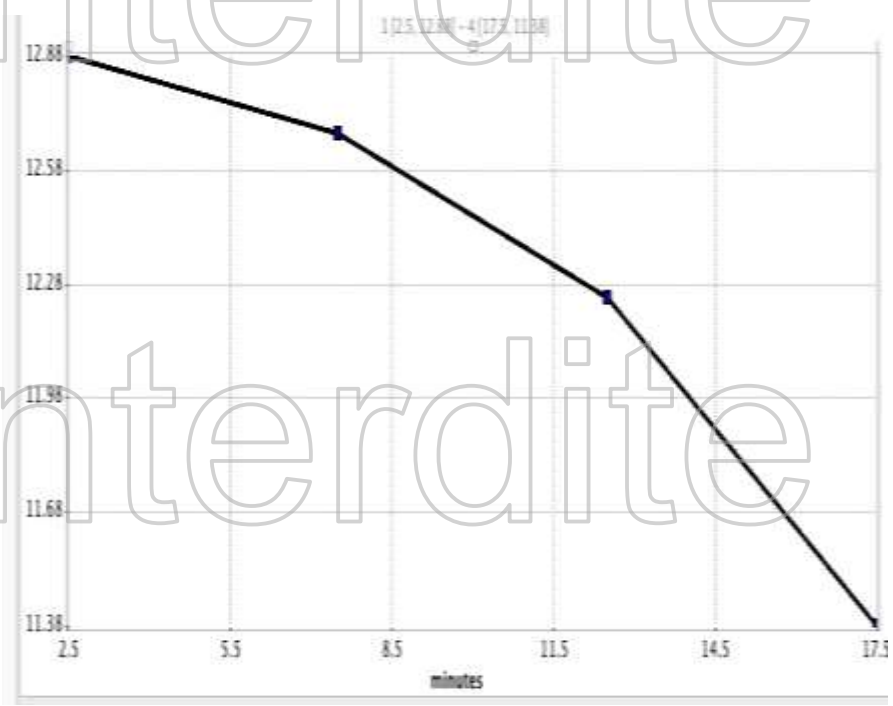
2. Hence, PET/MR may be superior to PET/CT in primary brain tumors and those, where there is a preponderance for brain metastases
   - lung cancer
   - advanced stage breast cancer
   - melanoma

3. PET/MR also needs to safely detect lung metastases !

Brain tumor PET with F-18-ethyl tyrosine

tumor grading

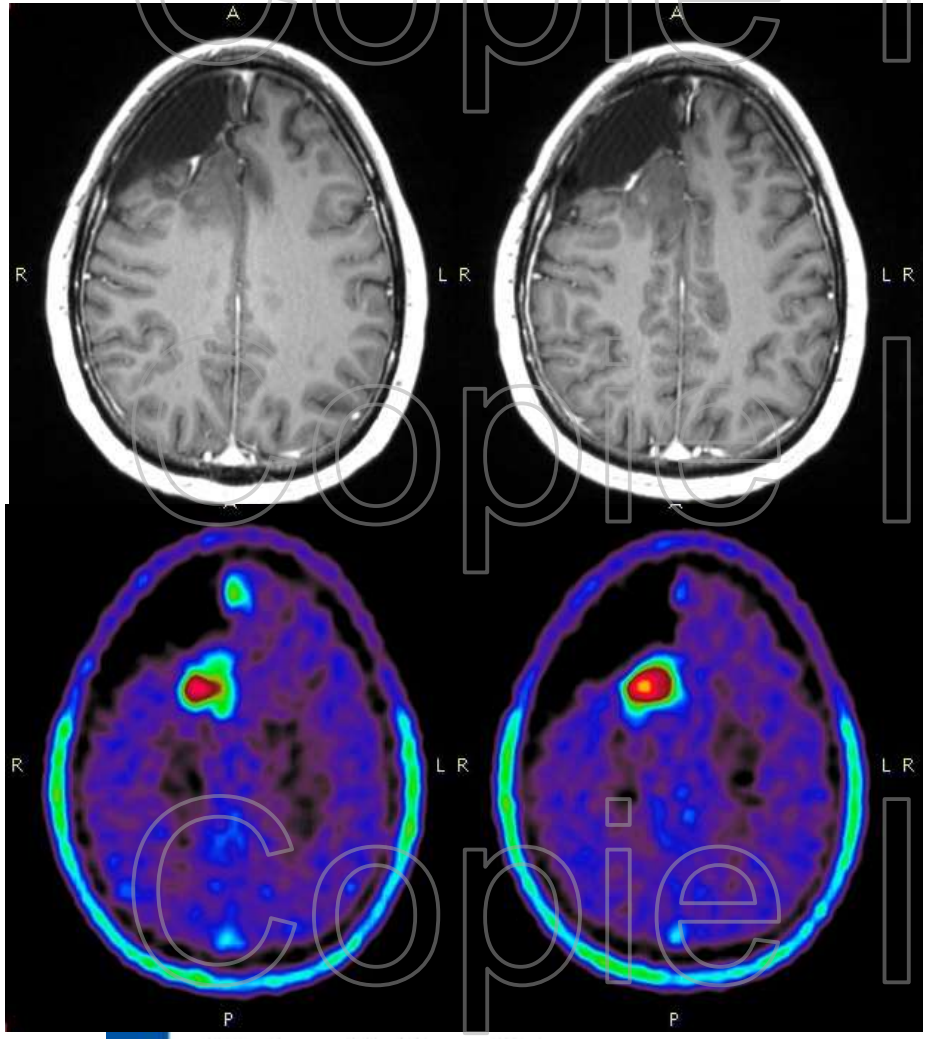


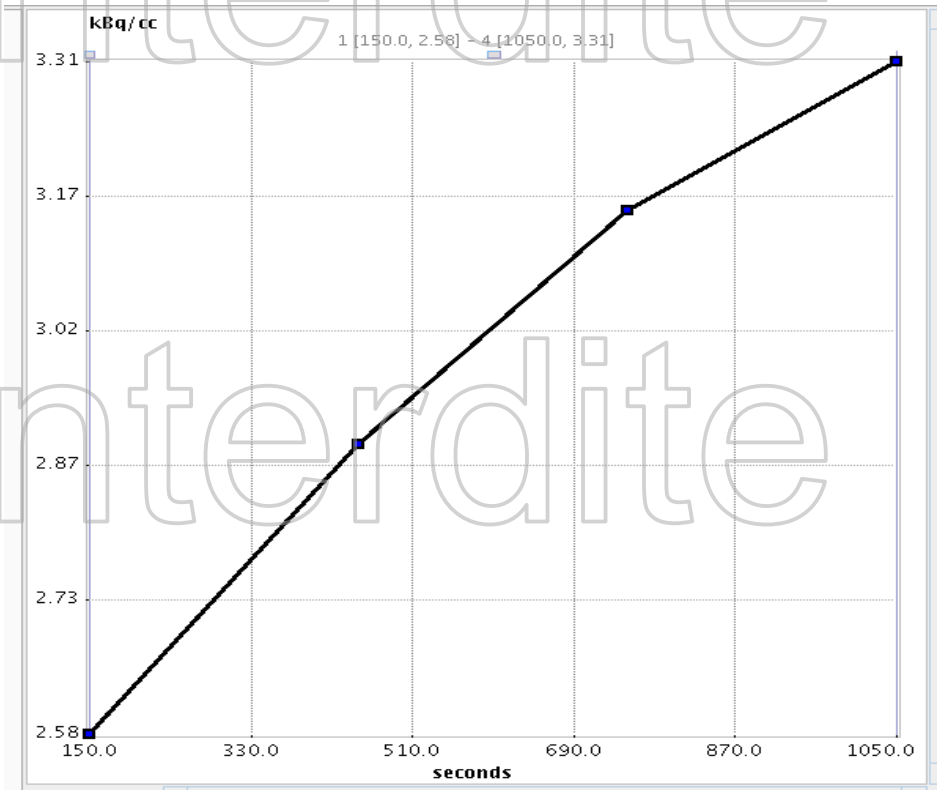


FET PET:
primary brain tumor
Grade III - IV

Brain tumor PET F-18-ethyl tyrosine

tumor grading





FET PET:
recurrent brain tumor
Grade I - II

PET/MR in brain tumors

1. Prime potential application for PET/MR
   ? Literature ?

2. Much can be accomplished by image fusion
   - most patients get MR first, so repeating MR may not be useful

3. FET studies are dynamic and require around 30’ scan time
   => enough time to do extended MR unlike in body oncology

PET/MR in tumors with brain metastases

1. First and foremost:
   is lung MR adequate enough for lung metastases

2. If this is the case:
   comparative value of PET/MR vs. PET/CT in the body
   in the brain we know that PET/MR is better !

Detectability of lung lesions

Stolzmann et al. Invest. Radiol., Zurich

Invest Radiol. 2013 May;48(5):241-6. doi: 10.1097/RLI.0b013e31826f2de9.

Detection rate, location, and size of pulmonary nodules in trimodality PET/CT-MR: comparison of low-dose CT and Dixon-based MR imaging.

Stolzmann P[1], Veit-Haibach P, Chuck N, Rossi C, Frauenfelder T, Alkadhi H, von Schulthess G, Boss A.

Author information

Abstract

OBJECTIVE: The objective of this study was to prospectively compare the detection rate, the location, and the size of pulmonary nodules in low-dose computed tomography (CT) and in magnetic resonance (MR) imaging with a 3-dimensional (3D) dual-echo gradient-echo (GRE) pulse sequence using a

Conclusions:

1. Dixon based dual-echo GRE PS may be suitable for lung imaging in PET/MRI

2. However, detection rate is lower on a lesion-by-lesion basis

=> We are not quite good enough yet with this

Respiratory gated MR (and PET)

PROPELLER (BLADE, etc.) is the sequence!

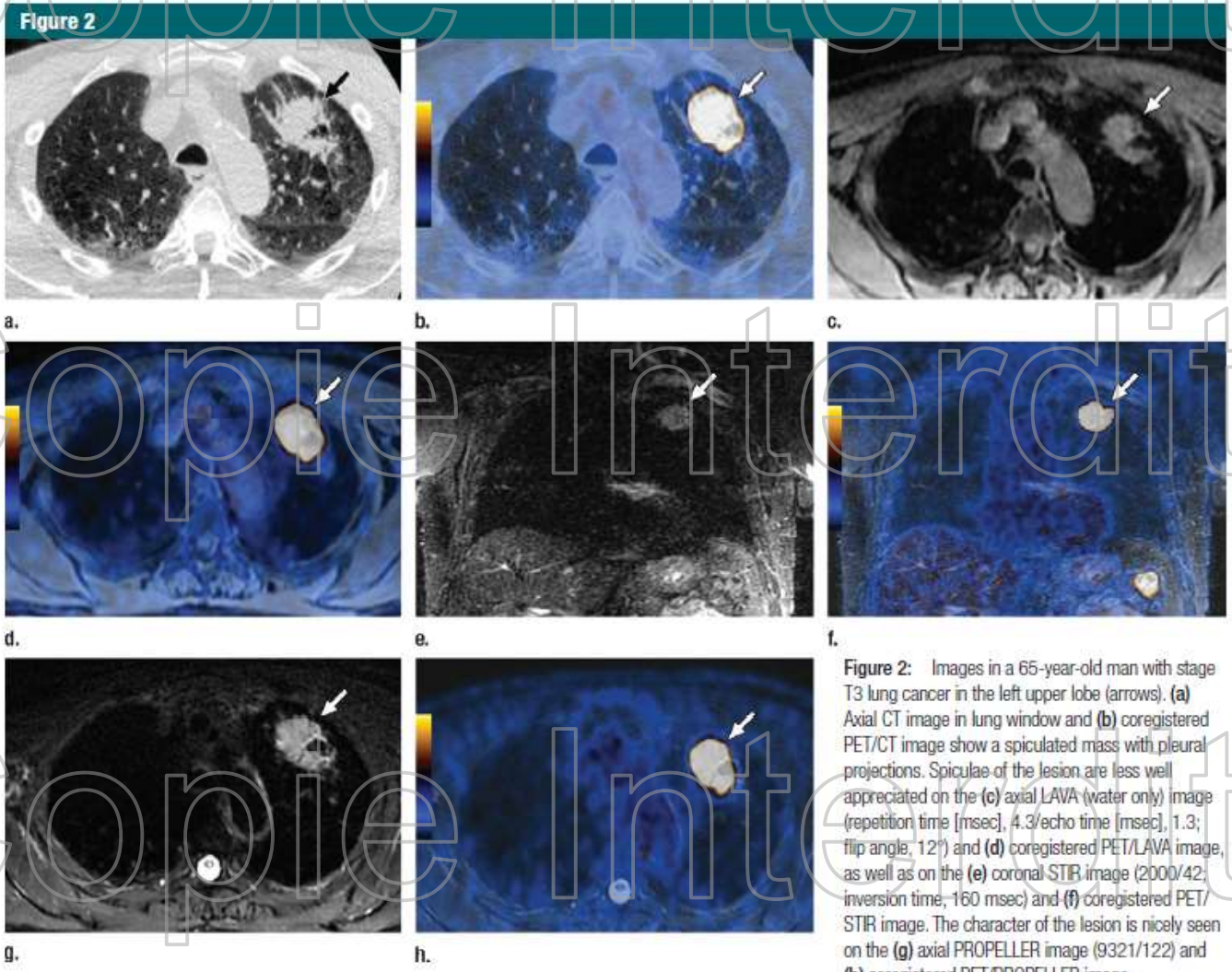


Figure 2: Images in a 65-year-old man with stage T3 lung cancer in the left upper lobe (arrows). **(a)** Axial CT image in lung window and **(b)** coregistered PET/CT image show a spiculated mass with pleural projections. Spiculae of the lesion are less well appreciated on the **(c)** axial LAVA (water only) image (repetition time [msec], 4.3/echo time [msec], 1.3; flip angle, 12°) and **(d)** coregistered PET/LAVA image, as well as on the **(e)** coronal STIR image (2000/42; inversion time, 160 msec) and **(f)** coregistered PET/STIR image. The character of the lesion is nicely seen on the **(g)** axial PROPELLER image (9321/122) and **(h)** coregistered PET/PROPELLER image.

Metastasis detection in general

Huellner M et al. Radiology 2014, Zurich

Radiology. 2014 Dec;273(3):859-69. doi: 10.1148/radiol.14140090. Epub 2014 Aug 6.

Whole-body nonenhanced PET/MR versus PET/CT in the staging and restaging of cancers: preliminary observations.

Huellner MW[1], Appenzeller P, Kuhn FP, Husmann L, Pietsch CM, Burger IA, Porto M, Delso G, von Schulthess GK, Veit-Haibach P.

Author information

Findings

1. STIR and LAVA < CT,
2. PROPELLER ≈ CT
3. PROPELLER > CT for distant metastases
4. Subanalysis of lung lesions: similar results
5. Lesion classification more confident with PET/MR than PET/CT
6. PET/CT shows more incidental (irrelevant) findings in the lung
7. MR had more (irrelevant) artifacts than CT

Detectability of lung lesions

Schaarschmidt BM et al. EJR 2015, Düsseldorf

Eur J Radiol. 2015 Apr 18. pii: S0720-048X(15)00182-5. doi: 10.1016/j.ejrad.2015.04.008. [Epub ahead of print]

Oncological whole-body staging in integrated 18F-FDG PET/MR: Value of different MR sequences for simultaneous PET and MR reading.

Schaarschmidt BM[1], Grueneisen J[2], Heusch P[3], Gomez B[4], Beiderwellen K[2], Ruhlmann V[4], Umutlu L[2], Quick HH[5], Antoch G[6], Buchbender C[6].

Author information

Conclusions

Ts, TIRM, and contrast-enhanced T1 provide a high quality of lesion detectability and anatoical allocation of FDG-avid foci. Thier perfomance ist at least comparable to contrast-enhanced -PET/CT. Non-enhanced T1 may be omitted and the necessity of DWI should be further investigated for specific questions, such as assessment of the liver.

Detectability of lung lesions

Fraioli F, et al. EJNMMI 2015, London

Eur J Nucl Med Mol Imaging. 2015 Jan;42(1):49-55. doi: 10.1007/s00259-014-2873-9. Epub 2014 Aug 15.

Non-small-cell lung cancer resectability: diagnostic value of PET/MR.

Fraioli F[1], Screaton NJ, Janes SM, Win T, Menezes L, Kayani I, Syed R, Zaccagna F, O'Meara C, Barnes A, Bomanji JB, Punwani S, Groves AM.

Author information

Abstract

PURPOSE: To assess the diagnostic performance of PET/MR in patients with non-small-cell lung cancer.

METHODS: Fifty consecutive consenting patients who underwent routine (18)F-FDG PET/CT for potentially radically treatable lung cancer following a staging CT scan were recruited for PET/MR imaging on the same day. Two experienced readers, unaware of the results with the other modalities, interpreted the PET/MR images independently. Discordances were resolved in consensus. PET/MR TNM staging was compared to surgical staging from

50 patients, 33 undergoing surgery
TNM staging with PET/CT and PET/MR

Conclusions

in lung cancer patients PET/MR appears to be a robust technique for preoperative staging

Lung cancer

«*Rule-out» lung metastases protocol*

1. **PET/MR: 2’ – 5’ – 5’ – 2’ – 2’ protocol**
   - Dixon water-fat sequence for AC and T1w imaging anatomic correlation
   - in lung and upper abdomen enough time for Propeller

   => comparable to CT in PET/CT

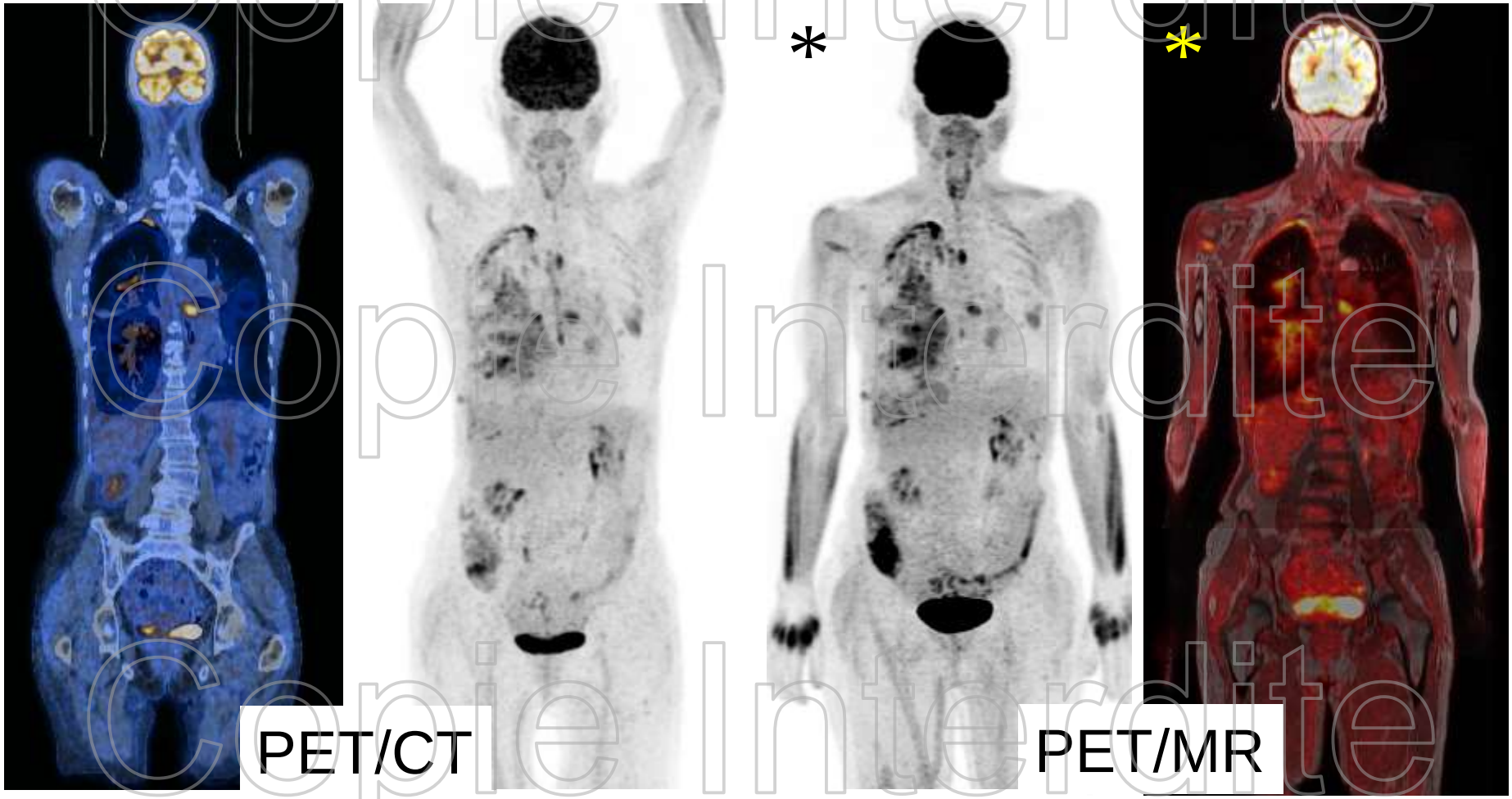
2. **< 15’ MR-only protocol (sufficient to rule-out brain mets.)**
   - CM enhanced axial and coronal brain imaging

   => far better than CT in PET/CT

=> Better hybrid exam than PET/CT

Case: (Alk+) Adenocarcinoma of the lung

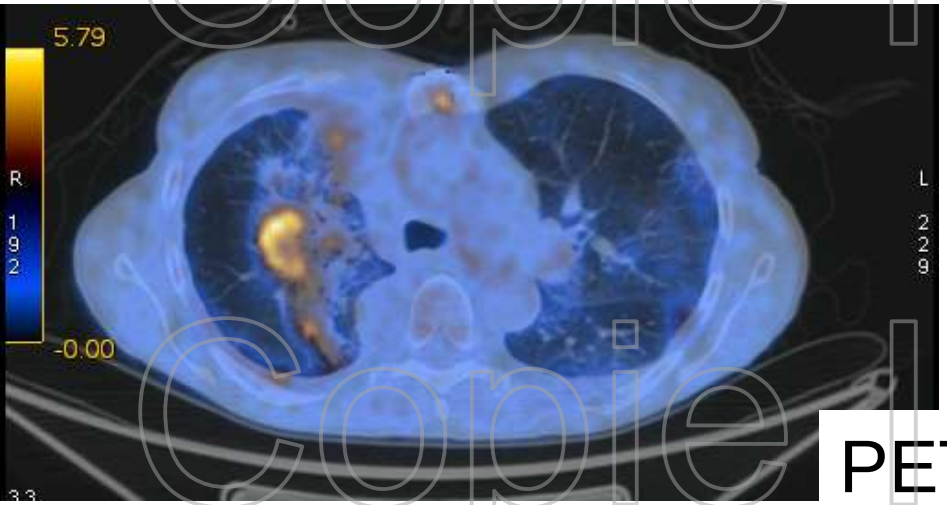
PET/CT vs. PET/MR

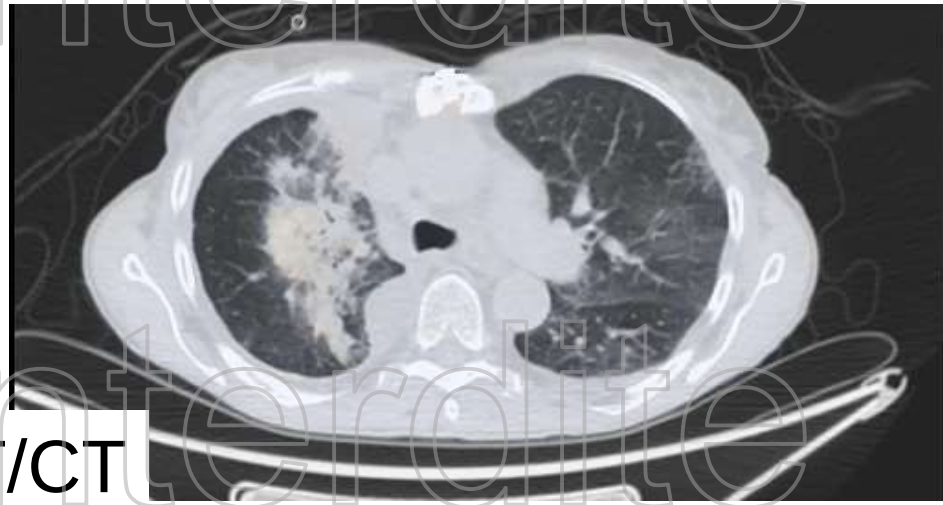


*data from experimental system

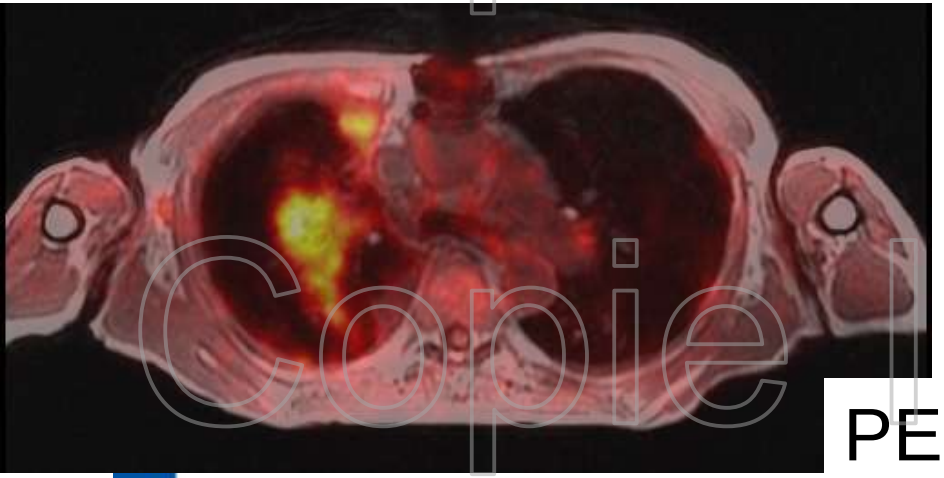
Case: (Alk+) Adenocarcinoma of the lung

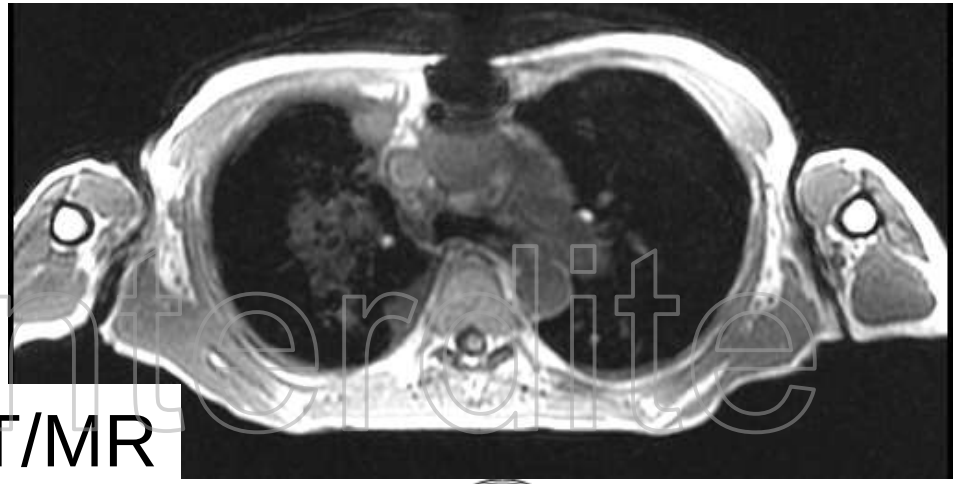
PET/CT vs. PET/MR





PET/CT

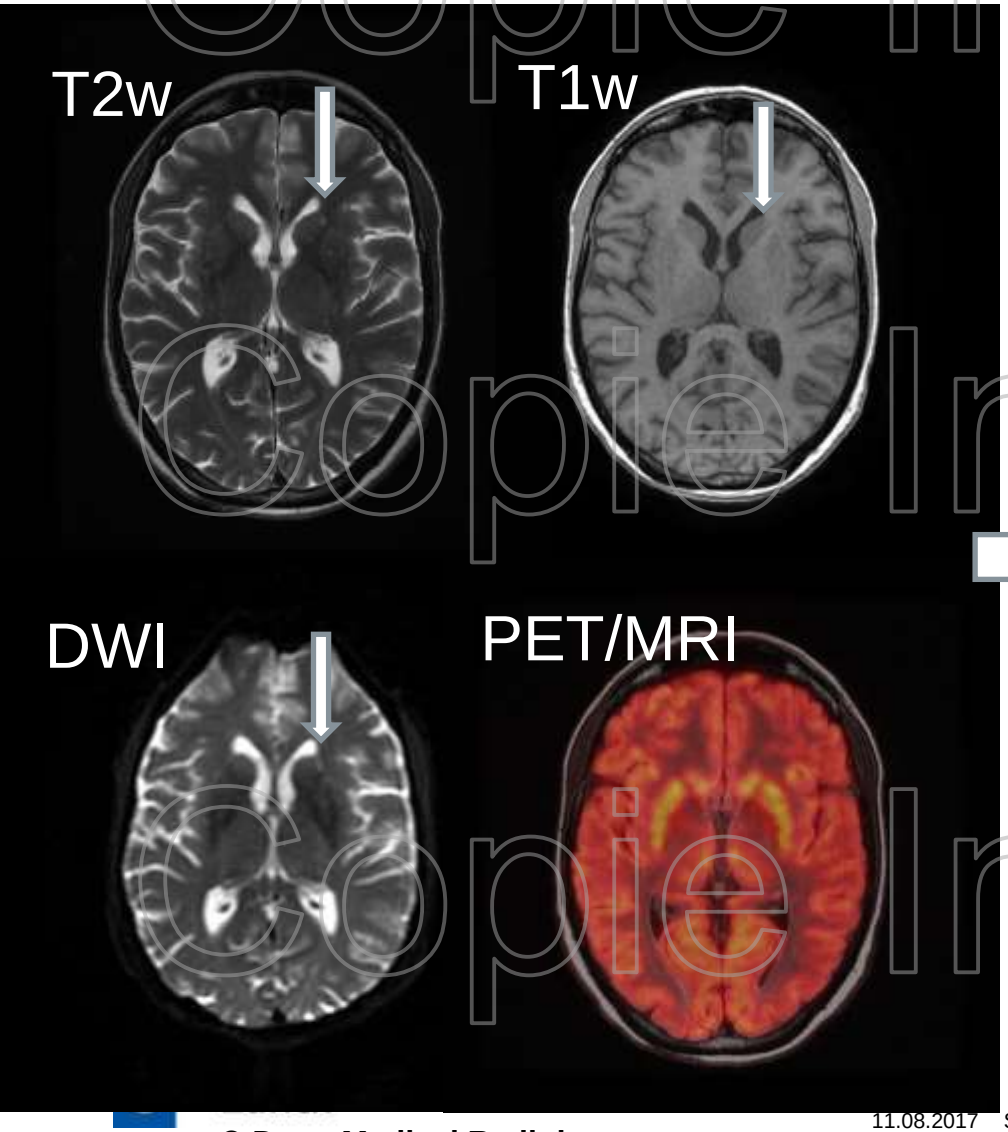


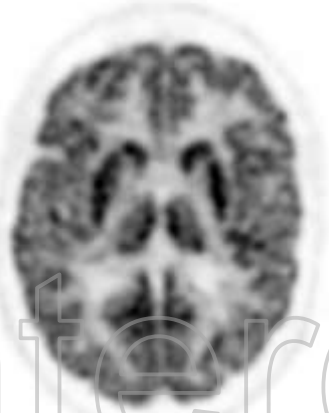


PET/MR

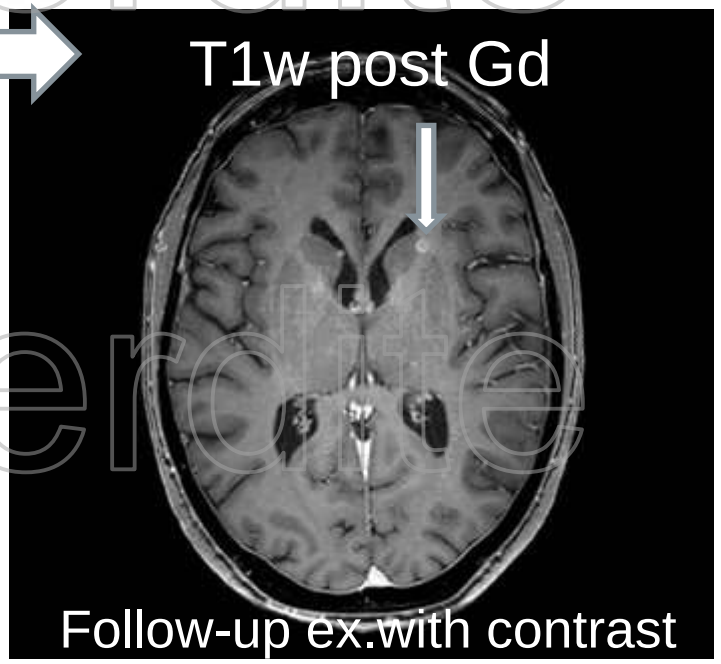
Case: (Alk+) Adenocarcinoma of the lung

PET/CT vs. PET/MR

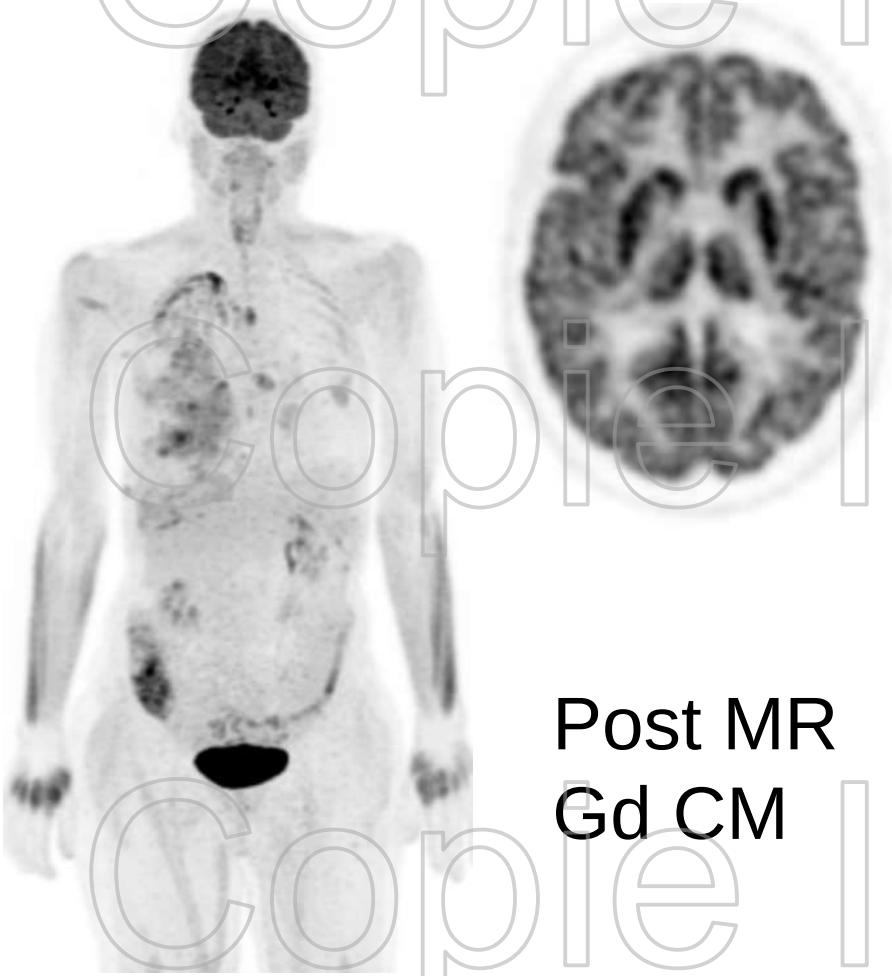


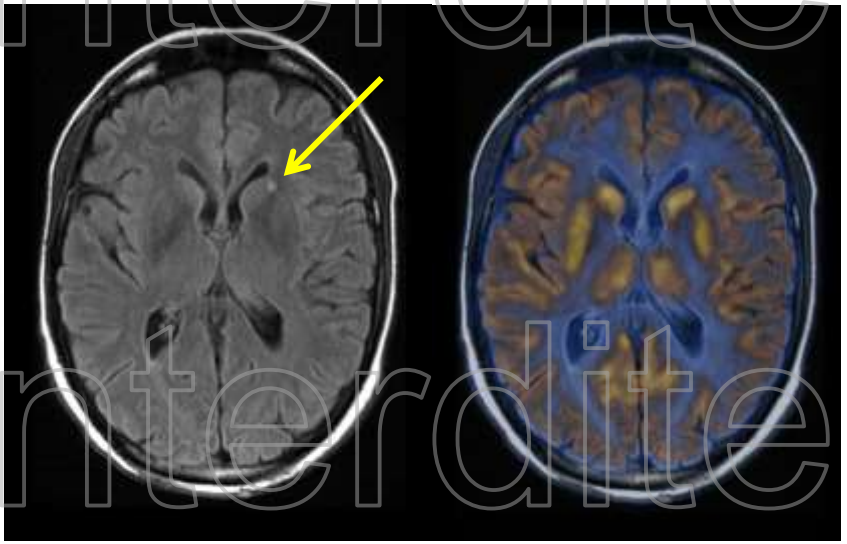


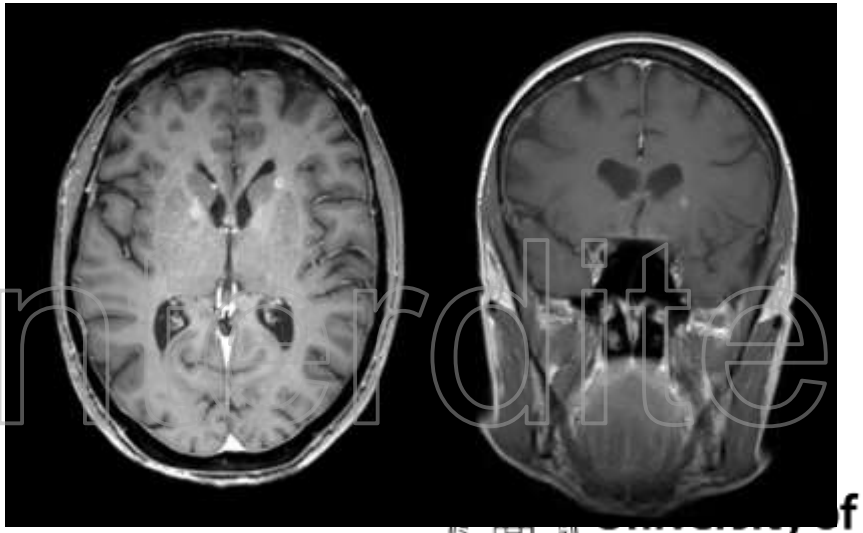
PET from PET/MRI



One stop shop rule out metastasis protocol







Post MR
Gd CM

Clinical applications of PET/MR

1. In imaging of head and neck cancer many imagers favor MR over CT and MR adds information to PET/CT.

THE NECK

2. Hence, imaging of HNSSC may be a good application for PET/MR

Head- and Neck cancer

MR vs low dose CT

J Nucl Med. 2014 Feb 3. [Epub ahead of print]

Contrast-Enhanced PET/MR Imaging Versus Contrast-Enhanced PET/CT in Head and Neck Cancer: How Much MR Information Is Needed?

Kuhn FP, Hüllner M, Mader CE, Kastrinidis N, Huber GF, von Schulthess GK, Kollias S, Veit-Haibach P.

CONCLUSION: The results of the present study provide evidence that PET/MR imaging can serve as a legitimate alternative to PET/CT in the clinical workup of patients with head and neck cancers. Intravenous MR contrast medium may be applied only if the exact tumor extent or infiltration of crucial structures is of concern (i.e., preoperatively) or if perineural spread is anticipated. In early assessment of the response to therapy, in follow-up examinations, or in a whole-body protocol for non-head and neck tumors, T2w PET/MR imaging may be sufficient for coverage of the head and neck. The additional MR scanning time may instead be used for advanced MR techniques to increase the specificity of the hybrid imaging examination.

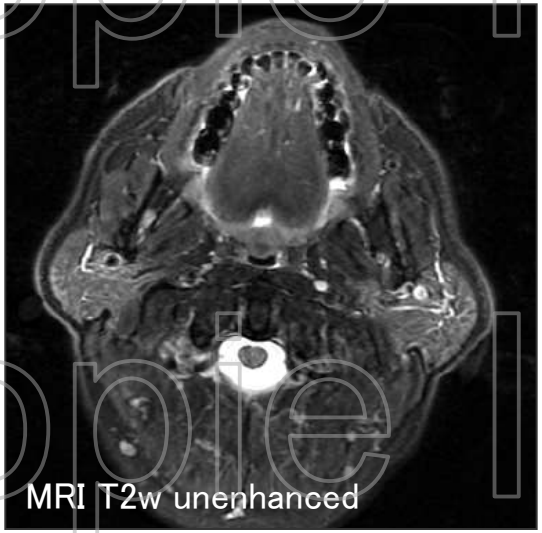
N=150

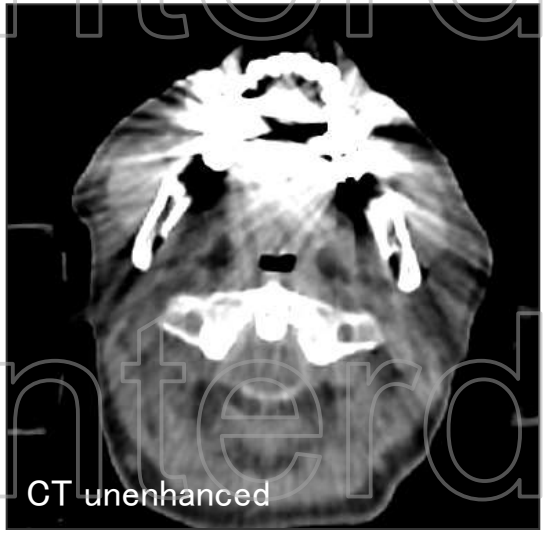
Conclusions

- PET/MR superior in pharynx
- PET/CT better in larynx

Integrated diagnostics H & N: PET-MR > PET/CT

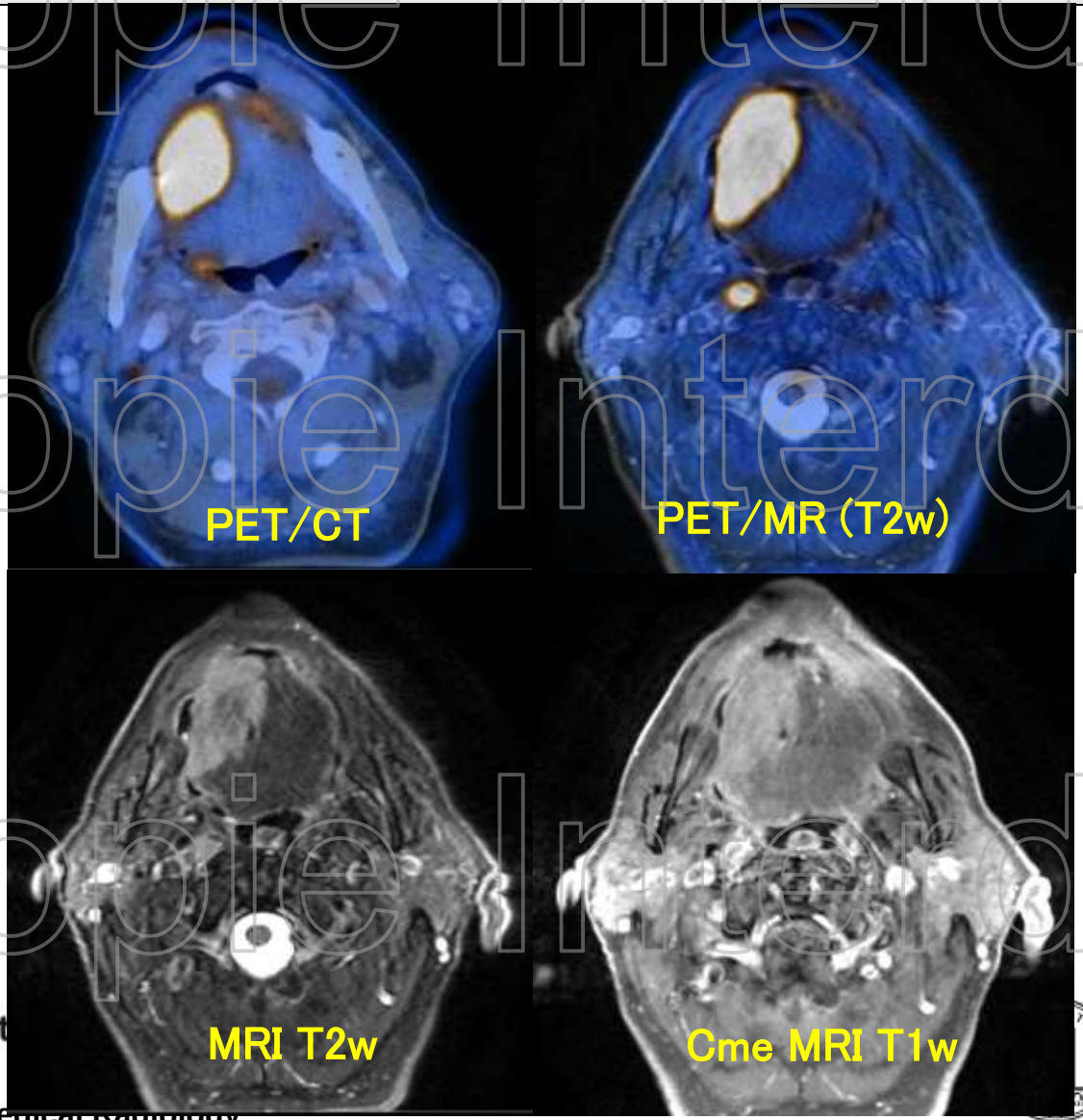
MR produces fewer artefacts?





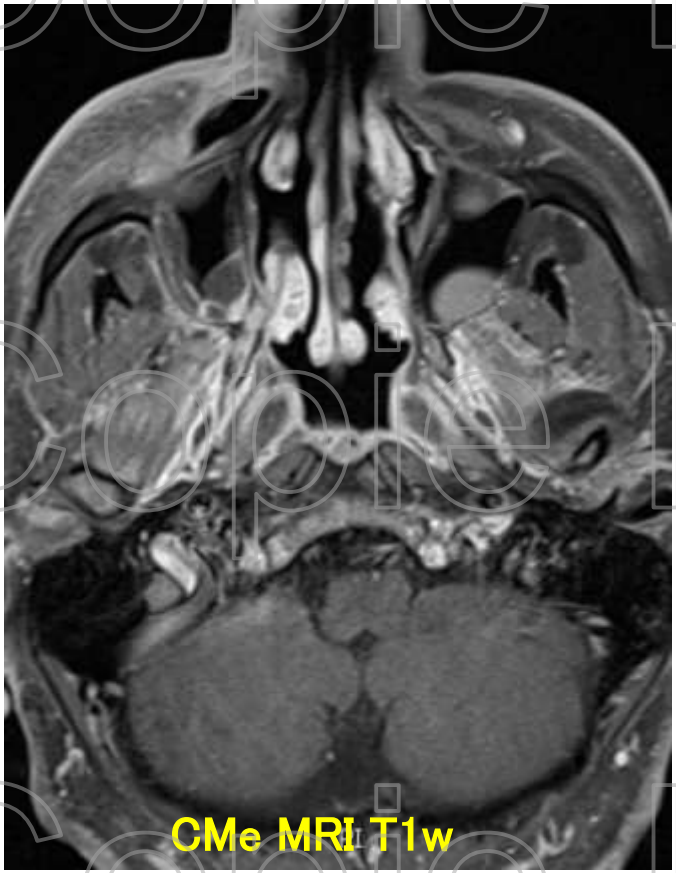
SCC of the tongue

MR produces fewer artefacts in the pharynx



Cystic carcinoma of hard palate

Perineural tumor spread in head and neck cancer



Clinical applications of PET/MR

1. There are other areas, where MR outperforms CT and where integrated PET/MR may eventually prove superior

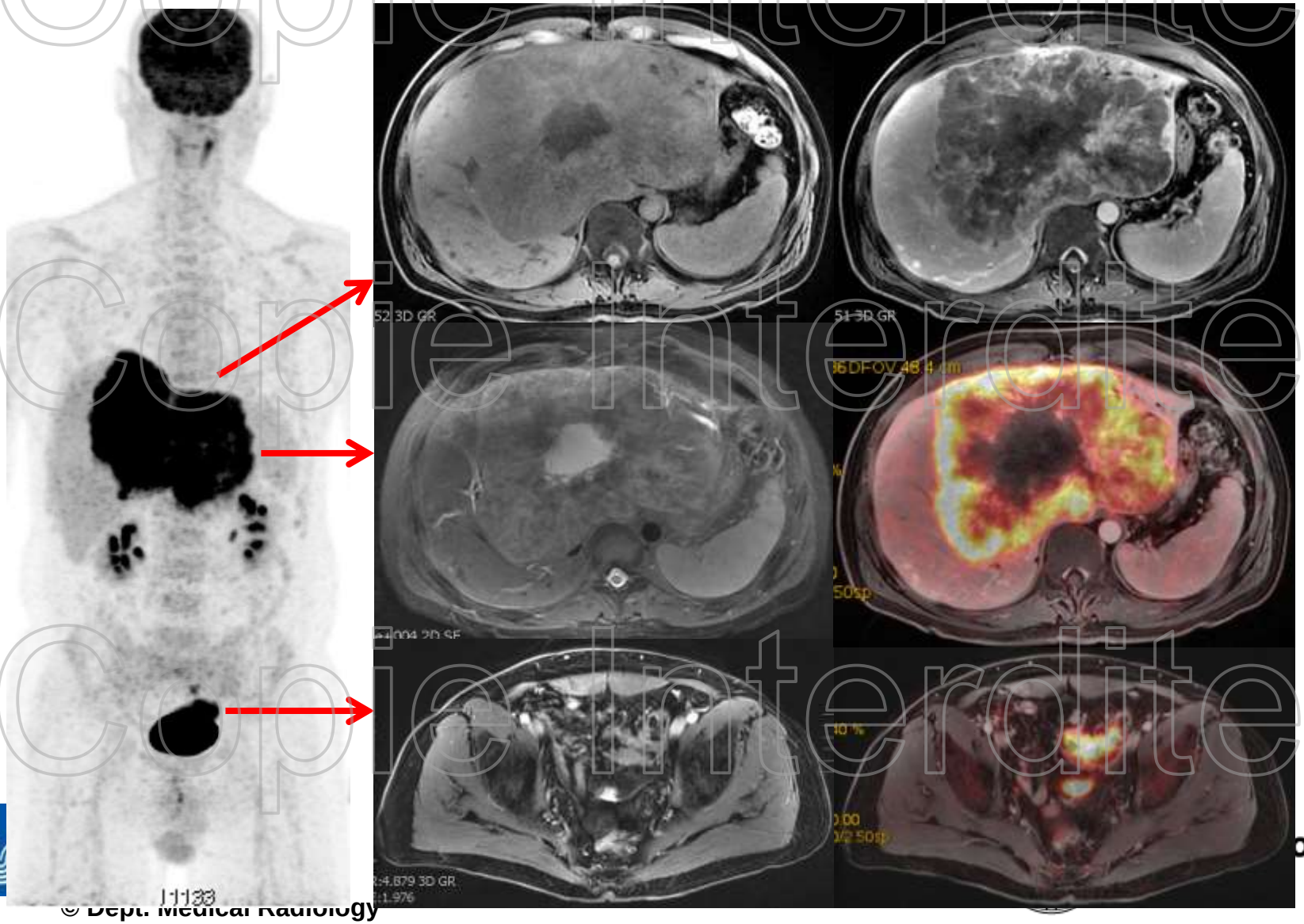
THE LIVER

THE BONE MARROW

2. Therefore in oncologic applications of PET/MR, these may be the prime target diseases where PET/MR should be evaluated against PET/CT

PET/MR in sigmoid cancer: staging

Potential: dentifying small liver lesions not seen on PET



Breast cancer: PET/MR vs. PET/CT

Catalano et al. Br. J. Cancer 2015, multicenter study

Br J Cancer. 2015 Apr 28;112(9):1452-60. doi: 10.1038/bjc.2015.112. Epub 2015 Apr 14.

Comparison of CE-FDG-PET/CT with CE-FDG-PET/MR in the evaluation of osseous metastases in breast cancer patients.

N = 109 patients with breast cancer,

25 had mets.

Reference standard: prior and follow-up imaging

CE-PET/CT: 90 mets (1 FP) in 22 patients (88%)

CE-PET/MR showed 141 mets in 25 patients (100%)

Conclusions

CE-PET/MR detected a higher number of osseous metastases than did same day CE-PET/CT, and was positive for 12% of the patients deemed osseous metastasis-negative on the basis of CE-PET/CT

Conclusions

1. Integrated imaging is „one imaging modality“
   => sens. and spec. have to be optimized for both together

2. Unsolved technical issues: mainly attenuation correction

3. Clinical workflows are emerging, which suggest that PET/MR may be run effectively from a clinical point of view

4. Early data are emerging which indicate superiority of PET/MR in some areas over PET/CT
   - brain metastases in tumors likely to metastasize to brain
   - liver and bone metastases

Prostate cancer with C-11 Choline

Souvatzoglou et al, EJNMMI 2013, Munich

Eur J Nucl Med Mol Imaging. 2013 Oct;40(10):1486-99. doi: 10.1007/s00259-013-2467-y. Epub 2013 Jul 2.

Comparison of integrated whole-body [11C]choline PET/MR with PET/CT in patients with prostate cancer.

Souvatzoglou M[1], Eiber M, Takei T, Fürst S, Maurer T, Gaertner F, Geinitz H, Drzezga A, Ziegler S, Nekolla SG, Rummeny EJ, Schwaiger M, Beer AJ.

Author information

Abstract

PURPOSE: To evaluate the performance of conventional [(11)C]choline PET/CT in comparison to that of simultaneous whole-body PET/MR.

METHODS: The study population comprised 32 patients with prostate cancer who underwent a single-injection dual-imaging protocol with PET/CT and subsequent PET/MR. PET/CT scans were performed applying standard clinical protocols (5 min after injection of 793 ± 69 MBq [(11)C]choline, 3 min per bed position, intravenous contrast agent). Subsequently (52 ± 15 min after injection) PET/MR was performed (4 min per bed position). PET images were reconstructed iteratively (OSEM 3D), scatter and attenuation correction of emission data and regional allocation of [(11)C]choline foci were performed using CT data for PET/CT and segmented Dixon MR, T1 and T2 sequences for PET/MR. Image quality of the respective PET scans and PET alignment with the respective morphological imaging modality were compared using a four point scale (0-3). Furthermore, number, location and conspicuity of the detected lesions were evaluated. SUVs for suspicious lesions, lung, liver, spleen, vertebral bone and muscle were compared.

Conclusions

- 32 patients with prostate ca.
- Anatomic localization better with PET/MR than with PET/CT especially in bone and pelvis

Breast cancer

Pinker K. et al., Clin Cancer Res 2014, Vienna

Clin Cancer Res. 2014 Jul 1;20(13):3540-9. doi: 10.1158/1078-0432.CCR-13-2810.

Improved differentiation of benign and malignant breast tumors with multiparametric 18fluorodeoxyglucose positron emission tomography magnetic resonance imaging: a feasibility study.

Pinker K[1], Bogner W[2], Baltzer P[1], Karanikas G[3], Magometschnigg H[1], Brader P[1], Gruber S[2], Bickel H[1], Dubsky P[4], Bago-Horvath Z[5], Bartsch R[6], Weber M[3], Trattnig S[2], Helbich TH[7].

Author information

Abstract

PURPOSE: To assess whether multiparametric (18)fluorodeoxyglucose positron emission tomography magnetic resonance imaging (MRI) (MP (18)FDG PET-MRI) using dynamic contrast-enhanced MRI (DCE-MRI), diffusion-weighted imaging (DWI), three-dimensional proton MR spectroscopic imaging (3D (1)H-MRSI), and (18)FDG-PET enables an improved differentiation of benign and malignant breast tumors.

EXPERIMENTAL DESIGN: Seventy-six female patients (mean age, 55.7 years; range, 25-86 years) with an imaging abnormality (BI-RADS 0, 4-5) were

Findings

1. Improved differentiation of benign and malignant breast tumors by PET/MRI
2. PET/MRI may lead to reduction of breast biopsies

Breast cancer

Taneja S et al., Europ J. Radiology 2014, New Dehli

Eur J Radiol. 2014 Dec;83(12):2231-9. doi: 10.1016/j.ejrad.2014.09.008. Epub 2014 Sep 28.

Simultaneous whole-body ^{18}F-FDG PET-MRI in primary staging of breast cancer: a pilot study.

Taneja S[1], Jena A[2], Goel R[3], Sarin R[4], Kaul S[5].

N = 36 patients, 25 surgery, 11 systemic therapy

PET found 91 metastatic lesions

MRI found 105 metastatic lesions

Authors conclude, that combined imaging may make sense

for both and a false negative rate of 6.7% on MRI and 40% on PET. Kappa co relation analysis between PET and MRI for all the lymph nodes detected revealed fair agreement by the two modalities (κ=0.337; P=0.000). Combined PET-MRI increased diagnostic confidence for nodal involvement (median DC 5, range 4-5; P<0.05). Distant metastases were found in 8/36 (22%) patients at the time of diagnosis with a total of 91 metastatic lesions on PET (DC≥4) and 105 on MRI (DC≥4), the difference being statistically significant (P=0.001) while Kappa co relation analysis showed significant agreement between the two modalities (κ=0.667; P=0.000). Overall PET-MRI led to a change in management in 12 (33.3%) patients.

CONCLUSION: In this pilot study, simultaneous (18)F-FDG PET-MR, has been found to be useful in whole-body initial staging of breast cancer patients.

Metastasis detection in general

Al Nabhani et al, JNMMI 2014, London

J Nucl Med. 2014 Jan;55(1):88-94. doi: 10.2967/jnumed.113.123547. Epub 2013 Dec 12.

Qualitative and quantitative comparison of PET/CT and PET/MR imaging in clinical practice.

Al-Nabhani KZ[1], Syed R, Michopoulou S, Alkalbani J, Afaq A, Panagiotidis E, O'Meara C, Groves A, Ell P, Bomanji J.

Author information

Abstract

The aim of this study was to prospectively compare whole-body PET/MR imaging and PET/CT, qualitatively and quantitatively, in oncologic patients and assess the confidence and degree of inter- and intraobserver agreement in anatomic lesion localization.

METHODS: Fifty patients referred for staging with known cancers underwent PET/CT with low-dose CT for attenuation correction immediately followed by PET/MR imaging with 2-point Dixon attenuation correction. PET/CT scans were obtained according to standard protocols (56 ± 20 min after injection of an average 367 MBq of (18)F-FDG, 150 MBq of (68)Ga-DOTATATE, or 333.8 MBq of (18)F-fluoro-ethyl-choline; 2.5 min/bed position). PET/MR was performed with 5 min/bed position. Three dual-accredited nuclear medicine physicians/radiologists identified the lesions and assigned each to an exact anatomic location. The image quality, alignment, and confidence in anatomic localization of lesions were scored on a scale of 1-3 for PET/CT and PET/MR imaging. Quantitative analysis was performed by comparing the standardized uptake values. Intraclass correlation coefficients and the

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Conclusions

- PET/MT = PET/CT in anatomic lesion localization
- Superior MR soft tissue resolution in H&N, pelvic and CR cancers
- Superior CT lesion detectability of lung lesions

Copie Interdite

cancers and of CT in lung and mediastinal nodal disease points to future tailored use in these locations.