Strategies and Technical Challenges for Imaging Oligometastatic Disease: Recommendations from the EORTC Imaging Group.

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Abstract: Patients with oligometastases (OMD) often have controllable symptoms and cures are possible. Technical improvements in surgery and radiotherapy have introduced the option of metastasis-directed ablative therapies as an adjunct or alternative to standard-of-care systemic therapies. Several clinical trials and registries are investigating the benefit of these therapeutic approaches across several cancer sites. This requires that patients are correctly included and followed with appropriate imaging. This article discusses the evidence and offers recommendations for the implementation of standard-of-care (Response Evaluation Criteria in Solid Tumours [RECIST] measurements on Computerized Tomography [CT], Magnetic resonance Imaging [MRI], bone scintigraphy) and advanced imaging modalities (functional, metabolic, radionuclide targeted) for identifying and following-up patients with OMD.

Imaging requirements for recognising OMD vary with tumour type, metastatic location, and timing of measurement in relation to previous treatment. At each point in the disease cycle, (diagnosis, response assessment and follow-up), imaging must be tailored to the clinical question and the context of prior treatment. The differential use of whole-body approaches such as ^{18}F-FDG-PET/CT, diffusion-weighted MRI, ^{18}F-Choline-PET/CT and ^{68}Ga-PSMA–PET/CT require rationalization depending on clinical risk assessment. Optimal standardized imaging approaches will enable OMD trials to document patterns of disease progression and outcomes of treatment. Quality assured and quality controlled imaging data included in databases such as the EORTC Imaging platform for the Oligocare trial (a prospective, large-scale observational basket study being set up to collect outcome data from patients with OMD treated with radiation therapy) will establish a large and high-quality imaging warehouse for future research.

Introduction:

The recognition that a solitary or a "few" metastases represent a better prognostic group than if metastases are numerous and widespread has led to the definition of an oligometastatic state.[1] Oligometastatic disease (OMD) has been defined as the presence of 1 and 5 distant metastases in <2 organs,[2-4] although the exact number of metastases that should be considered remains debatable. Patients with OMD often have symptomatology that is easier to control, and cures are potentially obtainable particularly because of improved locally ablative surgical or radiation therapy.[5-7] Correct recognition of OMD and precise tumour delineation are therefore imperative to offer patients optimal management strategies based on their risk of further recurrence or progression.

Correct identification of OMD is not trivial. Although serum biomarkers such as PSA or CA125 or cfDNA signal the likely presence of cancer and molecular techniques using micoRNAs have been shown to distinguish lung cancer metastases with high and low rates of progression[8], metastasis screening using whole-body *in vivo* imaging is the only real option for OMD detection. Limitations in the sensitivity of the selected imaging techniques mean that disease may be missed. Validation by biopsy of multiple visualised lesions is impractical and unacceptable to patients. Learning from prospective registries and clinical trials is the most pragmatic option but it requires prospective data collection in a multinational, multivendor European registry. Clinical trials (within the EORTC network, such as Oligocare, as well as those outside it) are being set up to monitor OMD and address the benefit of metastasis-directed therapy[9-12] particularly with regard to radiation therapy.[13, 14] Collection of meaningful imaging data in these trials would offer a unique opportunity to establish response patterns, and outcomes of treating OMD. This article therefore describes the optimal strategies for imaging OMD based on the sensitivity of the imaging techniques

and gives recommendations for their implementation in 4 cancer types with a known predilection for developing OMD (lung, breast, prostate and gastrointestinal (GI)) initially being studied in Oligocare.

Imaging Data Collection:

The recognition of OMD may require different imaging approaches at different points in the disease cycle: namely at initial diagnosis, at response assessment, and at follow-up to identify metastatic recurrence. At each point, the type of imaging needs tailoring to the clinical question and to the therapeutic options that are available, especially in the context of prior treatment. At each point, the imaging needs to accurately determine the location, extent and ideally quantify the character of the metastases, so that treatment response can be assessed. An imaging working group enables specific common imaging requirements to be addressed across OMD trials and standard operating procedures for imaging to be proposed for implementation in a robust and reliable manner across multiple sites contributing to trial databases. Oligocare, a joint initiative between the ESTRO and the EORTC, is one such trial. It is a prospective, large-scale observational basket study being set up to collect outcome data from patients with OMD treated with radiation therapy. It seeks to address multiple unanswered questions around OMD. Those requiring imaging data include patterns of disease progression and characteristics of the tumour that influence both management and outcome.

Imaging modalities routinely used as standard-of-care may be inadequate. Several “standard” imaging modalities have been superseded by more technologically “advanced” imaging with better sensitivities and specificities. The utility of the advanced modalities

depends not only on the modality itself, but also is often cancer type-specific, so that judicious selection of the best technique(s) requires adapting for a specific situation. The following sections summarize the preferred approaches for imaging based on modality-specific considerations, as well as the evidence for their use in specific cancer types.

Consensus imaging recommendations are summarized in Table 1.

Imaging modality-specific requirements:

To ensure maximal sensitivity for OMD detection, contrast between tumour and background is critical. For soft tissues, contrast is superior with MRI as it depends on altered water relaxation and diffusion properties, rather than on density alone, as with CT. Tumour-to-background contrast may also be generated through externally administered agents, taken up by vascular or metabolically active tumour or tumour stroma, or by targeting tumour cell surface receptors with the imaging agent. Spatial resolution determines the minimum size of a detectable lesion and is a trade-off between coverage and scan time. In PET, it also depends on the energy of the radiotracer used for imaging.

Cross-sectional anatomic and functional imaging: CT and MRI are the mainstay of whole-body morphological imaging; functional techniques in MRI provide additive data. CT delineates lymph nodes and other soft-tissue sites of disease albeit with limited accuracy (a metaanalysis of 24 studies in prostate cancer gave a pooled sensitivity of 42%, pooled specificity 82%)[15] but is even less sensitive for bony disease which relies on later stage cortical and trabecular destruction. Therefore, in cancers with a known predilection for bone metastases, CT scans are supplemented by bone scintigraphy with its high sensitivity but poor specificity.[16, 17] Whole body (WB-) MRI with conventional T1, T2 and short tau

inversion recovery (STIR) sequences provide high tissue contrast for metastasis detection. The addition of diffusion-weighting (DW) allows quantification of tumour.[18, 19] Inter-observer agreement for reading of WB-MRI images that include DW is very good (K = 0.87 [0.66; 1.00]).[20, 21] Automated measurements of the global volume of metastatic disease through a course of treatment also can be derived from DWI sequences to evaluate response and assess prognosis.[22-24] A small single-centre study looking at the inter-observer variability in quantifying global ADC on WB-DW-MRI reported excellent inter-observer agreement (Intraclass Correlation Coefficient 0.99 (0.89-0.99).[24] However, to pool quantitative data from multicentre trials, standardization of image acquisition and analysis and a system for rigorous quality assurance and quality control through the life of the trial is imperative.[25]

Metabolic and Receptor-specific imaging: Bone scintigraphy (BS) and positron emission tomography (PET) employ radionuclides. BS relies on a bone-seeking radiopharmaceutical and only assesses the skeleton, while PET is a whole-body technique that visualizes many different metabolic functions depending on the chosen radiopharmaceutical. The most commonly used PET radiopharmaceuticals for assessing metastatic disease are radiolabelled glucose (^{18}F-FDG), the bone-seeking tracer fluoride (^{18}F-NaFluoride, which exchanges with hydroxyl groups on hydroxyapatite at areas of bone turnover[26]), membrane-specific compounds such as choline (^{11}C- and ^{18}F-, radiolabeled versions of choline, a precursor of phosphatidylcholine, the key component of cell membrane lipogenesis), or a peptide ligand binding to the prostate specific membrane antigen (PSMA), which is a type II transmembrane glycoprotein highly expressed on prostate cancer cells. Sensitivity and specificity for bone metastases with ^{18}F-FDG, ^{18}F Na-Fluoride and radiolabelled PSMA ligands

vary substantially by tumour type and situation (e.g. primary vs recurrent disease, histological type and disease aggressiveness). To secure reproducible imaging procedures and guarantee minimal acceptable standards, requirements have been defined for bone scintigraphy,[27] ^{18}F-FDG PET imaging[28] as well as for the recently introduced PSMA-compounds.[29] These procedure guidelines emphasize the need for a standardized patient preparation, image acquisition parameters, start and time of acquisition and image reconstruction. The high interobserver agreement of PET studies as recently reported for ^{68}Ga-PSMA 11 (kappa-values of 0.62, 0.74 and 0.88 for T-, N- and M-staging) is advantageous and impressively applies when including readers with less than 30 previously read ^{68}Ga-PSMA-PET scans.[30] This is in line with studies focused on other PET tracers.[31] Nevertheless, challenges have to be addressed to successfully achieve harmonization:[32] programs using ^{18}F-FDG PET as a quantitative imaging biomarker in clinical trials require a specific set of quality control experiments to overcome algorithm and reconstruction variability across PET systems.

Cancer specific recommendations for detecting OMD

Lung cancer, the leading cause of cancer-related death, presents with distant metastases in more than half of patients, frequently to the adrenal glands, liver, brain, bones. Survival rate at 5 years in this subgroup of patients is near 5%.[33] Evidence has emerged that patients with limited metastatic disease, both intracranial and extracranial, treated with curative intent with radiotherapy or surgery have prolonged survival.[34, 35] Whole-body ^{18}F-FDG-PET/CT is the most reliable imaging technique in assessing extracranial metastases[36] as lung cancer lesions display increased FDG uptake with few exceptions (ground glass opacities,

lesions <1cm diameter and endocrine tumours). Importantly, staging work-up that includes ^{18}F-FDG-PET/CT has prognostic implications: a 5-year overall survival rate for ^{18}F-FDG-PET/CT vs. CT staged patients has been reported to be 58% and 33%, respectively ($p = 0.01$).[37] However, variations by histology may need to be considered when interpreting ^{18}F-FDG findings: notably, small cell carcinomas and squamous cell carcinomas show higher ^{18}F-FDG uptake than adenocarcinomas.[38, 39] Among adenocarcinoma subtypes also, uptake characteristics may vary.[40] The American College of Surgeons Oncology Group (ACOSOG) trial reports a sensitivity, specificity, positive and negative predictive value of 83%, 90%, 36% and 99%, respectively, for M1 disease assessment with ^{18}F-FDG-PET/CT.[41] Due to intense physiological FDG uptake in the brain, MRI is indicated in patients with signs or symptoms of central nervous system disease, as well as in asymptomatic patients with stage III disease being considered for aggressive local therapy.[42]

Follow-up surveillance guidelines in lung cancer recommend the use of chest CT. Due to the aggressive nature of the disease and to the fact that metastatic patients are a high-risk group by definition, imaging follow-up, at least every 3 months after first-line therapy with curative intent, is optimal but the exact timing should be individualized.[43] ^{18}F-FDG PET/CT in this circumstance is not first-line because misinterpretation is possible within 3-6 months and even up to 24 months. False positives after treatment occur from radiation-induced lung disease or inflammatory findings after surgery. However, when restaging is needed, or when suspicion for recurrence arises[44-46] from other imaging modalities or after clinical examination, ^{18}F-FDG-PET/CT is mandatory for confirmation of disease extent.

Prostate Cancer: As metastases in prostate cancer, typically arise in nodal or skeletal sites, techniques that address both these locations optimally are sought. Conventional imaging

modalities (e.g. CT, MRI, BS), as recommended by current guidelines, systematically underestimate the extent of metastases in prostate cancer.[26, 47] For detection of OMD therefore, molecular imaging techniques that utilize PET/CT are required[47]; PET/MR may be a future option.

In untreated intermediate or high-risk disease at presentation where nodal and bone disease is considered jointly, radiolabeled choline has been proposed as a promising imaging technique. However, a metaanalysis using choline PET/CT gave a pooled sensitivity of 49% and pooled specificity 95%.[48] Poor sensitivity is largely due to non-recognition of early bone metastases, so the WB-MRI, which outperforms ^{18}F-choline, is preferred. Alternatively, bone-seeking agents such as ^{18}F-NaF PET/CT have superior accuracy, (96.2% vs. 81.4% for WB-MRI and 64.6% for BS).[49] To rationalize imaging, and deliver a single technique with high accuracy at all anatomic locations, molecular imaging agents targeting PSMA are becoming first-line for simultaneous N and M staging. A variety of such agents are now available in both ^{68}Ga and ^{18}F- labelled formats (^{68}Ga-PSMA-11; ^{18}F-DCFBC; ^{18}F-DCFPyL; ^{18}F-PSMA-1007). In an early study comparing ^{68}Ga-PSMA with MRI for detecting lymph node metastases, accuracy per patient was 92% for PSMA and 67% for MRI. When compared at an individual lymph-node level, PSMA also performed significantly better (accuracy 95% vs. 90% for MRI).[50] Data from other studies is similar[51, 52] even with earlier ^{64}Cu labelled PSMA tracers.[53]

For recurrent disease the picture is very different; when PSA ranges between 2-5 ng/ml, choline PET/CT detection rate is ~70%.[54] At higher PSA (5<PSA<10 ng/ml), where likelihood of recurrence is high, detection rate is unsurprisingly higher (80-90%).[54] Choline PET/(CT) is currently recommended when PSA >5 ng/ml, with a pooled sensitivity and specificity for all

recurrent sites of disease of 86% and 93%, [48, 55]. At lower PSA levels, ^{68}Ga-PSMA outperforms ^{18}F/^{11}C-Choline for both nodal and bone recurrence. For a PSA between 0.2-1 ng/ml, 1-2 ng/ml and >5 ng/ml, PSMA-ligand positivity is 58%, 76% and 95%, respectively,[56] representing the imaging technique of choice. An "all-in-one" approach combining WB-MRI and prostate-specific MRI is useful for the combined detection of local recurrence, regional lymph nodes and distant metastases, being efficient at very low PSA levels.[57, 58]

Breast Cancer: As with other tumour types, between 1 and 10% of metastatic breast cancer patients have OMD, and are eligible for receiving surgery and/or radiotherapy with curative intent.[59] Anatomic sites for extracranial breast cancer metastases are widespread and include lymph nodes, skeleton, viscera particularly hepatic and lung metastases. Brain metastases occur in 0.4% of patients at presentation, but in 20 times that number (~8%) when other extracranial metastases are present,[60] indicating that brain imaging (MRI) is only warranted in the presence of extracranial disease.

Currently, ^{18}F-FDG-PET/CT is the most easily accessible and sensitive imaging diagnostic tool with a sensitivity between 90 and 94% and an accuracy rate ranging between 83 and 90%[61, 62]. MRI is superior for correct depiction and characterization of liver lesions when compared to ultrasound, CT and ^{18}F-FDG PET/ CT.[63, 64] As with all small liver metastases (<1 cm in diameter), the sensitivity of ^{18}F-FDG-PET is limited due to liver motion during image acquisition and poor spatial resolution. WB-MRI, like ^{18}F-FDG-PET/CT offers the advantage of multi-organ evaluation. Although some studies have emphasized the sensitivity of WB-MRI, they have also highlighted its poor specificity (with as many as 82% of lesions being considered false-positive compared to 11% on ^{18}F-FDG PET/CT).[65] In a study of 33 patients with 186 lesions which used clinical and radiological follow-up as a standard of reference,

sensitivity was 93% for WB-MRI and 91% for ^{18}F-FDG PET/CT, specificity was 86% and 90% respectively,[66] indicating the equivalence of these techniques. Logistically and economically, WB-MRI is currently less available than PET. In future, PET/MR would address the limitations of each technique individually. A study of 51 patients, 30 of whom had a total of 282 distant metastases, PET/MR imaging yielded better sensitivity for liver and possibly bone metastases, while PET/CT remained best for pulmonary metastases.[67] Furthermore, ^{18}F-FDG PET/MR offers better classification of malignant vs. benign lesions,[68] compared with ^{18}F-FDG PET/CT, an important consideration in disease recurrence.

In the context of response evaluation to systemic therapies, ^{18}F-FDG-PET/CT has the unique advantage of identifying oligometastatic disease resistant to treatment very early on. Adding locoregional ablative treatment for these resistant OMD could have a favourable clinical impact.

Gastrointestinal Cancer: In the gastrointestinal tract, OMD mainly occurs in colorectal cancer. The commonest site is in the liver, in which metastases occur in nearly one fourth of patients at initial diagnosis, but OMD also occur in the lungs and peritoneum. Because of the portal venous drainage of the colon, the liver may be the only metastatic site of colorectal cancer and so may be effectively treated with surgery. Imaging for M staging of colorectal cancer is classically based on thoraco-abdominal contrast-enhanced CT although ^{18}F-FDG PET/CT has been recommended to search for extra-hepatic metastases.[69-72] PET/CT alone is accurate at a patient level, but analysis by lesion indicates poorer results. In a metaanalysis, the pooled sensitivity and specificity of PET/CT on patient basis were both 93%, but corresponding values for a lesion based analysis were 60% and 79%, respectively.[73] For the assessment of liver metastases, MRI has superior diagnostic accuracy relative to CT

and ^{18}F-FDG PET, especially for small lesions (≤1 cm). A metaanalysis of 39 studies with over 3000 patients gave sensitivity estimates of CT, MR imaging, and ^{18}F-FDG PET on a per-lesion basis of 74%, 80%, and 81%, respectively.[74] Liver MRI should include contrast-enhanced imaging and diffusion-weighted imaging (DWI) for optimal sensitivity and specificity.[75, 76] Using hepato-specific contrast agents may improve the diagnostic performance and cost-effectiveness of liver MRI in patients with suspected colorectal liver metastases compared to MRI with extracellular contrast agents and contrast enhanced CT.[77, 78]

Developments in WB-MRI techniques indicate that it compares favorably with ^{18}F-FDG-PET for detection of distant metastases.[64] PET-MRI provides at least equal diagnostic accuracy relative to PET-CT with substantially reduced radiation dose[63, 79-81] but its cost-effectiveness remains to be determined.

Extraction of quantitative biomarkers from the images further helps define disease aggressiveness and indicate the likelihood of OMD vs a polymetastatic disease state. A data-driven radiomic approach harvests multiple image features that go beyond the traditional tumour size criteria (RECIST) to include features from perfusion, diffusion and biomechanical parameters at MRI and standard uptake values at ^{18}F-FDG-PET.[82] Assessing tumour heterogeneity with texture analysis or unsupervised machine learning offers new opportunities to assess the prognosis and response to treatment.[83, 84] Future efforts are needed to validate and standardize this radiomics analysis.[85, 86]

Quality Assurance (QA) and Quality Control (QC) in clinical trials:

Evidence-based data to inform a validated change in practice for OMD demands quality assured data [87]. QA and QC programs therefore constitute the pillars on which to deliver therapeutic progress. Particularly in the context of advanced imaging, adequate imaging

QA/QC is central to achieving assessable and reliable data. Imaging QA/QC requirements depend on the information required from the imaging, feasibility, and potential variability of the imaging readout. Operational support through the entire conduct of the trial is essential[88]. Conforming with regulatory requirements on security and data protection requires a dedicated imaging platform for data transmission, tracking, and reporting. The EORTC Imaging platform provides a customised QA approach for protocols, and ensures that potential misconduct is avoided in trial quality procedures.

Summary and Conclusions:

The correct recognition of OMD is heavily dependent on imaging. Optimal imaging strategies are therefore vital. Different approaches at different points in the disease cycle are required. Correct classification of patients for inclusion in OMD trials such as Oligocare (which initially will address OMD in lung, prostate, breast and colorectal cancer, to determine patterns of care and outcomes) demands that the most appropriate imaging is performed to recognize and monitor patients with OMD. Current evidence indicates that ^{18}F-FDG-PET/CT is optimal in lung cancer, ^{68}Ga-PSMA in prostate cancer (although WB-MRI and choline PET/CT may be used depending on clinical circumstance), ^{18}F-FDG PET/CT is favoured in breast cancer (with WB-MRI as an alternative) but needs supplementing with liver-specific MRI, and that liver-specific MRI supplemented with ^{18}F-FDG PET/CT or WB-MRI is best in colorectal cancer. In future, availability of PET/MR may well rationalize the use of multiple imaging modalities.

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Table 1: Currrent Imaging guidelines and imaging recommendations for patients to be included in Oligocare by primary disease site, metastases location and point in disease cycle.

Tumour type	When	Who	Where	Recommendation of current oncological guidelines		Recommendation for Oligocare inclusion
				ESMO	NCCN	
Lung	New Primary	High-risk histology, local nodes positive	Lymph Nodes Liver, Brain, Bone, (Adrenal)	chest and upper abdomen contrast-enhanced CT including liver, kidneys and adrenal glands Brain CT/MRI for patients with neurological symptoms or signs Bone imaging, if bone metastases are clinically suspected ^{18}F-FDG–PET/CT	Brain MRI ^{18}F-FDG-PET/CT Pathological confirmation of the metastatic lesion if possible	Conventional staging imaging per routine practice ^{18}F-FDG-PET/CT at diagnosis ^{18}F-MRI Brain if above positive or patients with neurological symptoms ^{18}F-FDG-PET/CT in presence of suspicious lesion on surveillance imaging WB-MRI if available PET/MRI if available
	Recurrent disease	Suspicious lesion on surveillance imaging at follow up		Close follow up with chest and upper abdomen CT	Follow up with chest CT with or without contrast FDG-PET/CT can be used to differentiate true malignancy	
Breast	New Primary	Node positive at presentation, High risk histology or poor response to neoadjuvant chemotherapy	Lymph Nodes Liver, Bone, Brain,	Chest and abdomen CT Bone scan ^{18}F-FDG-PET/CT, if available (instead of and not on top of CTs and bone scan). Brain imaging should not be routinely performed in asymptomatic patients	Chest, abdomen $\pm$ pelvic CT with contrast Bone scan FDG-PET/CT (optional) If diagnostic CT and ^{18}F-FDG-PET/CT both indicate clearly bone metastases, bone scan and sodium fluoride PET may not be needed. Brain MRI with contrast if	Conventional staging imaging per routine practice ^{18}F-FDG-PET/CT at diagnosis MRI Brain if above positive or patients with neurological symptoms ^{18}F-FDG-PET/CT in presence of suspicious lesion on surveillance

					suspicious neurological symptoms	imaging If the primary clinical question is to detect or exclude liver metastases, MRI with liver-specific contrast agents especially to assess small lesions WB-MRI if available PET/MRI if available
	Recurrent disease	Blood marker increase		Follow up by CT imaging, frequency depends on the dynamics of the disease, the location and extent of metastatic involvement, and type of treatment	Follow-up by CT and response assessment based on RECIST. ^{18}F-FDG-PET/CT when standard imaging results are equivocal Equivocal lesions identified by FDG-PET/CT should be confirmed with biopsy if possible	
Prostate	New Primary	High – Intermediate risk disease	Bones Nodes	Bone scan chest-abdominal CT scan or whole-body MRI or choline PET/CT	Bone scan Pelvic CT/MRI	Conventional staging imaging per routine practice At PSA <5 ng/mm, ^{68}Ga-PSMA outperforms Choline PET/CT for both nodal and bone recurrence Choline PET/CT recommended when PSA >5 ng/ml WB-MRI if available
	Recurrent disease	Biochemical recurrence			Chest X-ray, bone scan, abdomen/pelvic CT/MRI with or without contrast Consider choline PET/CT	
Colon-rectal cancer	New Primary	High risk	Liver Lung	Abdominal/pelvic and thoracic CT, in the case of doubt, a second method such as contrast-enhanced ultrasound, MRI or PET/CT scan depending metastases location. Ultrasound to characterise liver metastases; MRI for liver, peritoneal or pelvic metastases and PET/CT extrahepatic disease. A stepwise imaging approach is recommended in relation to the therapeutic possibilities, rather than the use of all imaging modalities in all patients.	Chest/abdomen/pelvic CT Routine PET/CT for baseline imaging or staging is discouraged. ^{18}F-FDG-PET/CT considered for pre-operative patients, or if anatomic imaging indicates potential curable M1 disease.	Conventional staging imaging per routine practice Liver MRI should include contrast-enhanced imaging and diffusion-weighted imaging for optimal sensitivity and specificity FDG-PET/CT staging for pre-operative patients or when CEA increases. WB-MRI if available
	Recurrent disease	Rising CEA			Chest/abdomen/pelvic CT and consider ^{18}F-FDG-PET/CT If imaging results are normal and CEA is rising, repeat CT 3 monthly until either disease is identified or CEA declines.	

Figures:

Figure 1

Solitary bone metastasis in lung cancer on ^{18}F-FDG PET/CT: 66 year old female with pulmonary adenocarcinoma (cT1b N0), (a= CT; b= ^{18}F-FDG PET; c= fused PET/CT axial images) showing a spiculated, metabolically active mass in the right upper lobe (arrows). There was a single, pathologically proven, distant bone metastasis (M1b) (d= CT; e= ^{18}F-FDG PET; f= fused PET/CT axial images) in the coracoid process of the left scapula identified on ^{18}F-FDG-PET/CT (arrows). The patient received radiation treatment to the bone lesion (30Gy administered in 10 fractions) with complete local response. Subsequently, she was treated with gefitinib 250mg/day (EGFR mutation status positive) until progression in the D12 vertebra. Her progression free survival was 1 year and overall survival was 2 years.

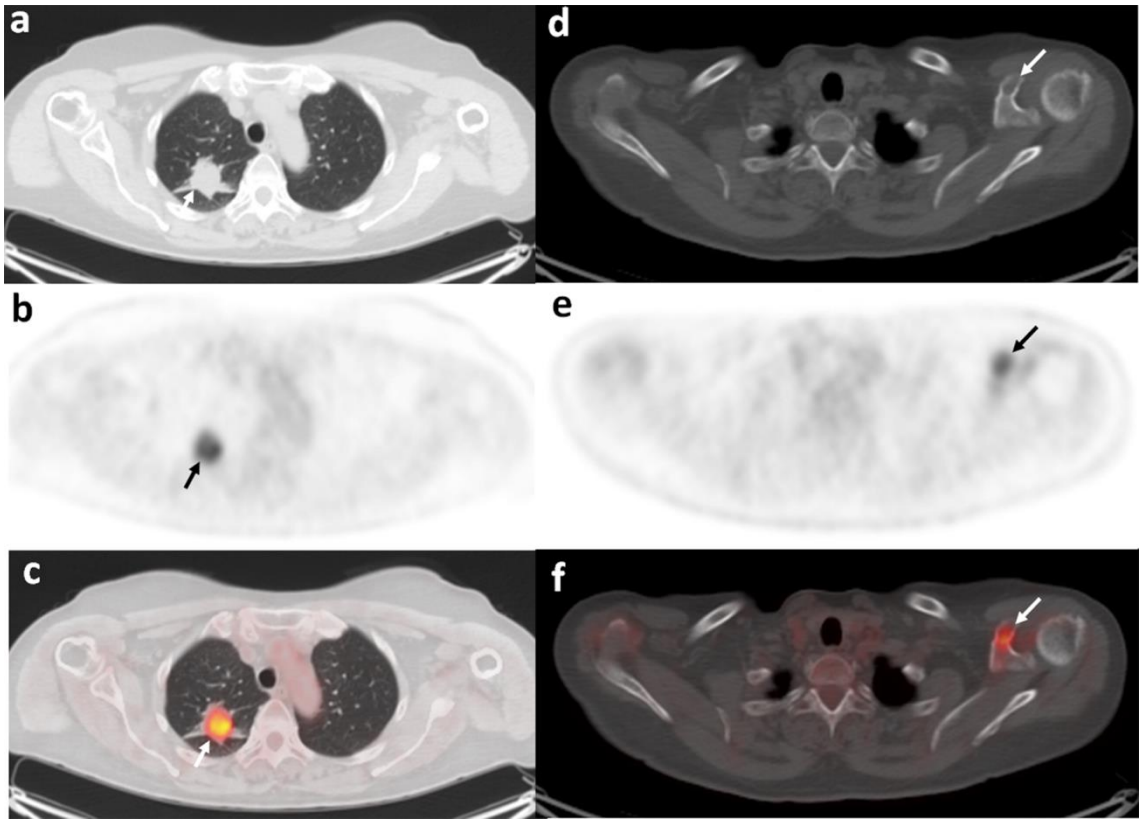


Figure 2

Oligometastatic lymph node metastases in prostate cancer on ^{18}F-Choline PET/CT: 69 year old male with a histologically confirmed adenocarcinoma of the right prostate lobe (pT1c N0M0; Gleason 3+3= 6), presented 3 years after intensity modulated radiation therapy to the prostate with a PSA rise of 10 ng/ml. ^{18}F-Choline PET/CT scan (a – attenuation correction axial PET images, b – CT, c – fused PET/CT axial images) showed a non-enlarged right iliac lymph node with moderate uptake (arrows) suspected to be a solitary lymph node metastasis. It was treated with stereotactic body radiation therapy (d). Following a further PSA rise 2 years later (15 ng/ml), there was a decrease in size and uptake of the previously treated right iliac node (a' - c') but a new suspected non-enlarged right pre-sacral lymph node with high uptake was seen (e- g, arrows). Treatment of this node with stereotactic body radiation therapy (h) resulted in a PSA decrease to 3 ng/ml.

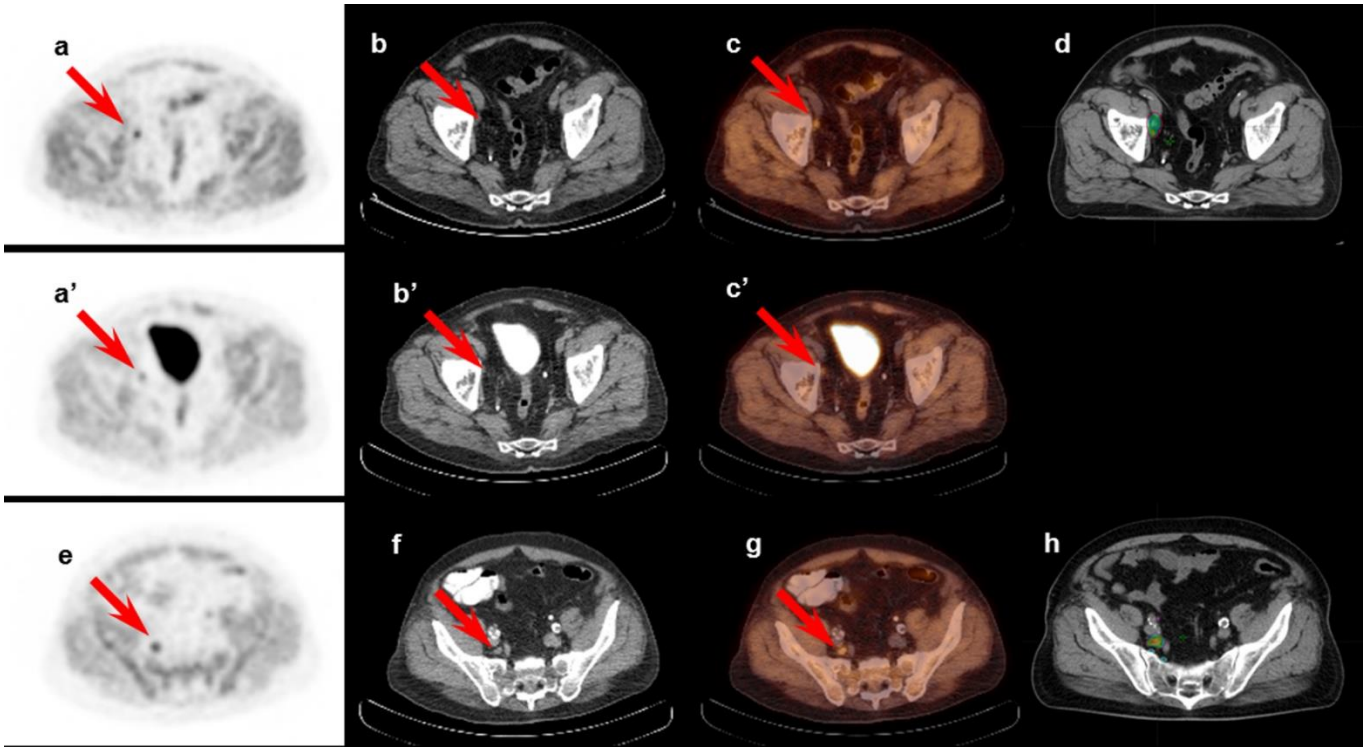
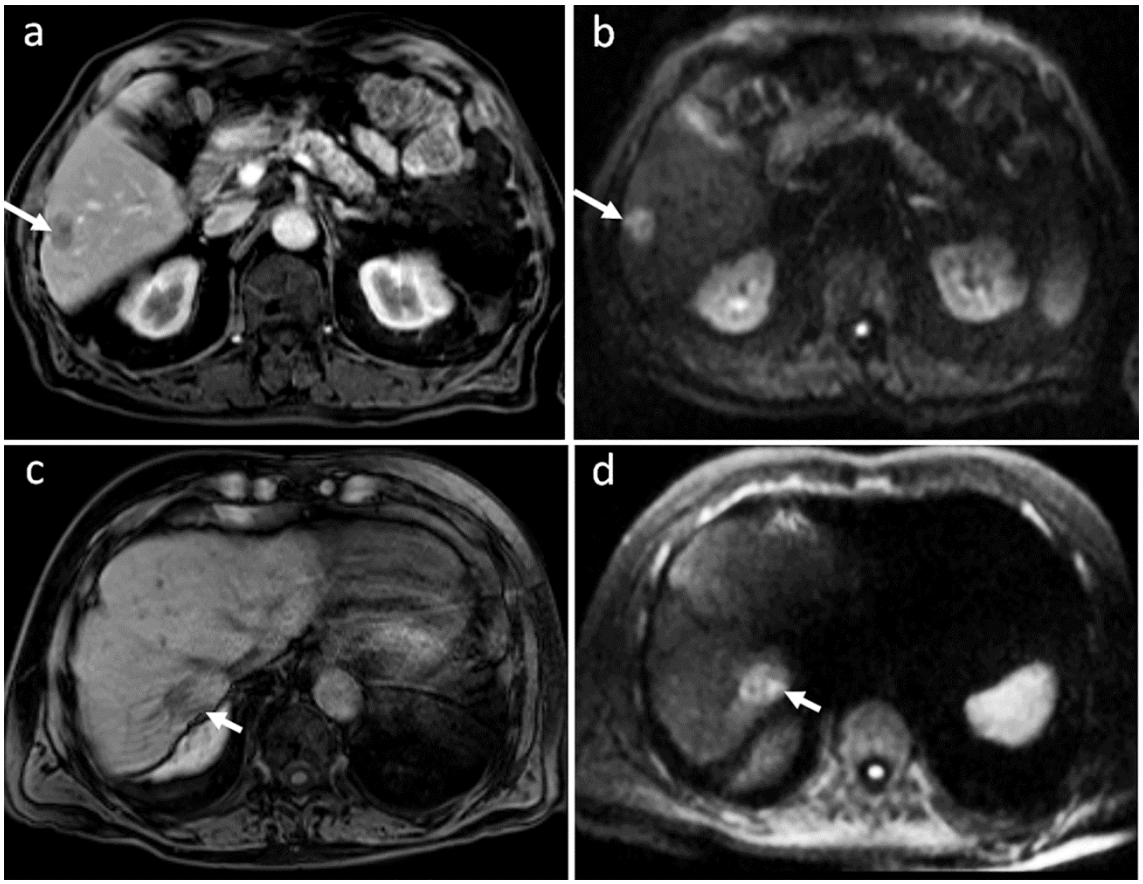


Figure 3

Solitary liver metastasis in colorectal cancer on DW-MRI: 82 year old male with colorectal carcinoma. On T1W contrast-enhanced imaging with a liver-specific agent, a hypovascular area is noted in segment 6 (a, arrows). This shows markedly restricted diffusion (arrow) on DW-MRI (b, TR=7100 ms/TE=62 ms/ b=750 s/mm^2). This solitary lesion was resected. Four years later, the patient presented with a new lesion in segment 7, again seen on the T1W contrast enhanced images as a hypovascular lesion (c, arrow), but more easily identifiable on the DW-MRI (d, arrow). The patient was treated with stereotactic radiation therapy.



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