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PET/MR Part 3: PET/MRI Protocols and Procedures

Elad Nevo[1], Peter Kamvosoulis[2] & Geoff Currie[3,4]

[1]Department of Radiology, Lucille Packard Children's Hospital, Stanford University, Palo Alto, USA

[2]Magnetic Resonance Department, New York-Presbyterian / Weill Cornell Medical Center, New York, USA

[3]School of Dentistry and Health Science, Charles Sturt University, Wagga Wagga, Australia

[4]Department of Radiology, Baylor College of Medicine, Houston, USA

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Corresponding author:

Geoff Currie

gcurrie@csu.edu.au

Learning objectives:

- demonstrate an understanding of MRI sequences and their application in PET/MRI
- demonstrate an understanding of the protocols and procedures associated with PET/MRI
- demonstrate strong conceptual understanding of the protocols and procedures in PET/MRI from the context of application in adult and pediatric procedures
- develop a framework to support decision making regarding PET/MRI protocols
- demonstrate awareness of procedural implications on PET/MRI patients and quality outcomes

Abstract

The emergence of position emission tomography (PET) and magnetic resonance imaging (MRI) as a hybrid modality has demanded new approaches to protocol and procedure. While protocols for MRI and PET individually lend themselves to synergistic and simultaneous approaches, there are a number if unique challenges and patient preparations that require consideration. This manuscript provides an insight into the protocols, procedures and challenges associated with simultaneous PET/MRI in both adult and pediatric populations. While protocols may be specific to applications or pathologies of interest, a richer discussion of the clinical applications of PET/MRI is beyond the scope of this manuscript and will be detailed in part 4 of the series. The foundations of PET/MRI protocols is an understanding of the various MRI sequences which are outlined succinctly. The principles outlined for protocols and procedures are general in nature and specific application will vary among departments. Given the procedures of PET is well established amongst the readership of this journal, the manuscript provides an emphasis on MR factors unless specific variations in standard PET protocol or procedure are driven by the simultaneous MRI. This manuscript is the third in a four-part integrated series sponsored by the SNMMI-TS PET/MR Task Force in conjunction with the SNMMI-TS Publication Committee.

Introduction

The emergence of positron emission tomography (PET) fused with computed tomography (CT) required variations to protocols to accommodate the sequential PET/CT procedure. The more complex and time consuming protocols for magnetic resonance imaging (MRI) simultaneously obtained with PET require more careful consideration of protocols and procedure. While the vast majority of PET/MRI investigations utilize ^{18}F FDG, a number of other ^{18}F tracers and those chelated to radiometals like ^{68}Ga and ^{64}Cu are expected to emerge. There are three main aspects of PET/MRI protocols and procedures:

1. Patient preparation for both MRI and PET procedures.
2. The imaging procedures themselves.
3. Quality assurance procedures.

It should be noted that patient preparation and the imaging protocol need to be considered for both adult and pediatric populations.

PET/MRI combines the high sensitivity and quantification of molecular level tracers of PET with the exquisite soft tissue contrast and some functional imaging parameters of MRI (*1*). Despite these benefits, the major limitation is the complex array of MRI sequences that could be performed and the time cost per bed position. For PET/CT, 2-4 minutes per bed position is typical of a whole body scan but in clinical PET/MRI, as many as five MRI sequences could require 5-10 minutes per bed position (*1*). There are a number of benefits in optimizing the MRI sequence timing to the standardized PET bed position. Firstly, it maintains the consistency associated with quantitation (eg. SUV) to maintain inter- and intra-site consistency. Secondly, extending PET bed position timing has a marginal increase in impact, particularly the latter part of the acquisition) on both radionuclide decay and target to background ratio. Recent developments in ultrafast MRI sequences have shortened the MRI acquisition to 3-5 minutes per bed position (*1*), although 2-4 minutes might be considered optimal. It is possible to adjust protocols for MRI sequences beyond the PET bed position timing to accommodate the extended MRI sequences after the PET acquisition is completed, or alternatively, 15 minutes prior to commencing the PET acquisition.

MRI Sequences

A typical MRI examination consists of imaging the body part of interest multiple times with varying parameters that produce images with different tissue weightings. Each tissue weighting serves to provide a different clinical insight. PET/MRI are generally whole body examinations which for most represents imaging from the base of the skull to the thighs consistent with approaches to PET/CT. The absence of the radiation dose issues for the brain and eyes that CT encountered means that it has become more common in PET/MRI to image vertex through the thighs. For some indications or in a pediatric setting, vertex of the skull to the toes is the norm. PET/MRI acquires the PET and MRI data simultaneously with each bed position having 2-4 different MRI image sequences. Conversely, PET/CT is acquired sequentially with a rapid CT component. Thus, if the MRI sequences selected do not prolong the bed position, PET/MRI could be a faster acquisition by the margin of the CT acquisition (seconds). Nonetheless, PET/MRI also has sequential MRI acquisitions with the localizer prior to PET acquisition and potential for additional sequences without PET at the end that extend the protocol marginally (minutes) but generally negligible in the overall protocol. Both contrast protocols and positioning the patient confound these times. Nonetheless, optimizing the MRI sequences for PET/MRI is critical for patient comfort and compliance, and the diagnostic integrity of the examination. Perhaps the simplest way to consider sequences is to first consider T1 and T2 weighted images and then explore specific sequences. The following sequences are not exhaustive but represent the more common sequences in MRI and the more detailed discussion will be reserved for those sequences relevant specifically to PET/MRI protocols. More detailed treatment of less frequent, less relevant (to PET/MRI), or more novel sequences is beyond the scope of this manuscript and can be explored in the broader literature.

- Spin echo (SE);
    - T1 short repetition time (TR) and echo time (TE)
    - T2 long repetition time (TR) and echo time (TE)
    - Fast spin echo (FSE)
    - Dual echo
    - Proton density (PD) weighted long TR and short TE

- Gradient echo (GRE);
    - Susceptibility weighted (SWI)
    - T1WI volume interpolated spoiled GRE which could be referred to as volumetric interpolated breath hold examination (VIBE) or liver acquisition with volume acquisition (LAVA) depending on manufacturer
    - T2 and T2*
    - Steady state free precession (SSFP)
    - Dual gradient echo
- Inversion recovery;
    - Short tau inversion recovery (STIR) fat suppression
    - Fluid attenuated (long tau) inversion recovery (FLAIR) fluid suppression
        - T1WI or T2WI
- Diffusion weighted (DWI);
    - Apparent diffusion coefficient maps (ADC; post-processed sequence)
- Diffusion tensor imaging (DTI) and tractography of nerves
- Perfusion weighted (PWI);
    - T1 gadolinium contrast enhanced
    - Arterial spin labelling (non-contrast technique)
- Functional MRI (fMRI)
- MR angiography (MRA);
    - Contrast enhanced MRA
    - Time of flight (TOF) angiography (without or with contrast)
    - Phase contrast MRI (non-contrast technique)

In PET images, the shade of grey or color represents count density or counts per pixel/voxel. In CT, the shade of grey represents the degree of attenuation or tissue density (*2*). For MRI, the shade of grey of tissues represents signal intensity, with white typically high signal intensity through to black being low signal intensity. In PET, relative quantitation is undertaken visually or with calculations that compare the count density on the structure of interest to a reference tissue. Examples include a tumor to liver comparison and regional cerebral cortex to contralateral side or cerebellum. For MRI,

intensity is also compared between the tissue of interest and reference tissues with the term hyperintense indicating whiter, brighter, greater intensity than the reference tissue, hypointense indicating darker or lower intensity than the reference tissue, and isointense meaning the same brightness or intensity as the reference tissue. For example, a brain tumor relative to surrounding brain tissue.

The process of image formation and pulse sequences have been explained in the previous article in this series (*3*) but there is a need to briefly define several specific terms. Following RF excitation, the time for the signal to return to equilibrium is called relaxation time and the signal produced is referred to as free induction decay (FID) (*4,5*). The time between each RF pulse is called the repetition time (TR) (*4,5*). The echo signal is termed spin echo (SE), is stronger than the FID signal and it is measured at the peak time of echo (TE) (*4,5*). FID is formed by a single RF pulse (often thought of as 90^o but technically not necessarily). Gradient echo (GRE) is formed by 1 RF pulse with a gradient reversal. Spin echo (SE) is formed with 2 RF pulses (eg. 90^o and 180^o) and stimulated echo is formed with 3 or more RF pulses. Hahn echo is generally used to refer to echo produced by RF pulses other than 90^o and 180^o (but technically could include 90^o and 180^o pulses) (*4,5*).

<u>T1 Images</u>

T1 weighted images are a standard part of any MRI protocol and might also be referred to as T1WI. As these terms suggest, the T1 pulse sequence highlights differences between tissues based on T1 relaxation times or longitudinal relaxation (sometimes referred to as spin lattice relaxation time) (*3-6*). As outlined in figure 1, the proton dipoles align with the magnetic field (B_0) after the radiofrequency (RF) pulse. After this, the proton dipoles revert back (relax) to near their original orientation. The time it takes an individual tissue to relax results in different signal intensities. For example, water content, air, and bone have a slow relaxation which produces lower signal and darker representation on images. Conversely, fat, protein rich fluid and slow flowing blood have a rapid relaxation time that produces a whiter or brighter signal on images. T1W spin echo produce the most “true” T1 signal but generally take longer to acquire, typically anywhere from 2-5 minutes.

An alternative option is to use T1W gradient echo which uses the properties of the gradient coils inside the MR scanner to generate the T1 weighted images faster than conventional spin echo techniques. Clearly this is advantageous for simultaneous PET/MRI where bed position time needs to be optimized but as outlined in the previous article in this series (*3*), the coils themselves can produce artefact in the PET images. Gradient echo images are also more susceptible to artefacts caused by inhomogeneity in the magnetic field as a result of metal or blood products (eg. pixel swap). Pixel swap is an artefact associated with the Dixon technique where the algorithm confuses water and fat pixels and is most typical of extremities or areas with low fat signal. These sequences are also more susceptible to motion artefact and anatomical wrap around artefact. Regardless, T1W gradient echo allows multiple sequences with imaging less than 30 seconds. These phenomena can be further exploited using paramagnetic contrast agents (eg. gadolinium) to produce a number of variations to the T1 pulse sequence.

Gadolinium Enhancement and Fat Suppression

T1 signal intensity is amplified by gadolinium based contrast agents which, compared to non-contrast T1 images, produce brighter (more intense) signals from tissues. In effect, this appears to shorten the T1 relaxation times given that intensity of slow relaxation time tissues have now become brighter. While this helps understand the process, the reality is that the relaxation time is not actually shortened but, instead, the signal itself is increased from tissues. One application of this would be in diseased tissue where increased perfusion or tissue permeability (eg. injury, tumor, inflammation) results in higher concentration of contrast agent and a disproportionate increase in signal intensity compared to normal tissues.

Unfortunately, fat tissues are already very intense and increases in intensity may not be easily distinguished from normally intense tissues. As a result, fat suppression sequences are typically imaged post-contrast administration to reduce the fat signal (eg. phase contrast techniques, and inversion recovery sequences). These might also be referred to as fat attenuated or fat saturation. Nonetheless, both fat saturated and non-fat saturated images provide useful insights but in the context of multiple sequences and time cost, it

is not convenient to run both pulse sequences. An alternative is the Dixon dual echo sequence which uses algorithms and the inherent properties of the signal (chemical shift) generated by fat and water in MRI to generate both fat saturated and non-fat saturated image sets from a single acquisition. In essence, water and fat precess at different rates which means cyclically they will be in-phase and out-of-phase (a little like the seconds hand of a clock being out-of-phase with the minutes hand until each minute approximately they become in-phase). By acquiring in-phase and out-of-phase images, the algorithm can produce 4 separate sequences; in-phase (water plus fat), out-of-phase (water minus fat), fat (in-phase minus out-of-phase), and water or fat-suppressed/fat saturated (in-phase plus out-of-phase). An ultra-fast gradient echo Dixon technique takes about 15-20s per bed position to acquire. In addition, this sequence is a 3D acquisition that can be reformatted into multiple planes in post processing with minimal image resolution loss. This technique is essential for generating the attenuation correction (MRAC) maps for the PET data. (*3*)

T2 Images

As with T1 weighted images, T2 pulse sequences are a standard part of most MRI protocols and might also be referred to as T2WI. As these terms suggest, the T2 pulse sequence highlights differences between tissues based on T2 relaxation times or transverse relaxation (sometimes referred to as spin-spin relaxation) (*4,5*). As outlined in figure 2, the proton dipoles align with the magnetic field (B_0) after the radiofrequency (RF) pulse. After this, the proton dipoles revert back (relax) to near their original orientation for the T1 signal. Each proton dipole also has precession altered in alignment by the RF pulse. The time it takes an individual tissue to relax precession alignment results in different signal intensities. For example, water content and brain grey matter produce high intensity signal while muscle, fat and white brain matter produce intermediate intensities. A minor issue relating to T2 sequences is the influence of inhomogeneous magnetic fields on tissue T2 relaxation times; sometimes referred to at T2*. T2 then is the most “true” T2 signal using a spin-echo sequence. Gadolinium contrast shortens T2 relaxation which suppresses rather than amplifies the signal so is not used which means T2 sequences are run before contrast enhancement. The exception to this is the T2 FLAIR steady state

gradient echo sequence which shows contrast enhancement due to a mixed T1 and T2 signal.

Typically, T2 weighted images are used to visualize a pathological process like edema. Again, there are several ways to achieve this goal. Traditional spin echo techniques to obtain T2 images are time prohibitive, and thus, several methodologies have been developed to decrease the amount of time it takes to acquire them. The fastest of these is ultra-fast spin echo, which has image acquisition times under a minute typically. Another option is the fast relaxation fast spin echo technique; this technique is slower than the ultra-fast spin echo technique but substantially faster than spin echo. Since both fat and water produce bright signal on T2 imaging, obtaining fat saturated T2 images can help better define the nature of what is visualized. Like T1 sequences, fat suppression can be achieved with STIR sequences which are useful from an imaging perspective but limited by the 5 minutes sequence time.

Proton density

Proton density (PD) sequences uses the nature of MRI (proton or hydrogen ion imaging) to image the density of protons (*4*). Tissues with high density or proton intensity include fluid and fat; similar to T2. Since the technique was useful in differentiating high intensity fluid from low intensity fibrocartilage and intermediate intensity hyaline cartilage, it is often used for joint imaging with FLAIR displacing its use in brain imaging.

Spin echo (SE)

SE uses 90º RF excitation pulses (figure 3) to flip longitudinal magnetism (T1) and dephases transverse magnetism (T2). The subsequent 180º RF refocusing pulse rephases the spins to produce coherence (*4,5*). Thus, recovery of transverse magnetism produces a spin echo. FSE is the same principle as SE (figure 3) except it uses a series of rapidly applied 180º RF rephasing pulses to produce multiple echos (echo train length) within the same TR (*4,5*). This allows more rapid data collection but has a limit on echo train length (typically less than 7 for T1). The TE may vary from echo to echo in the train and produce different characteristics

(contrast versus resolution for example). T1 is generated from the initial echos and T2 from the later echos. Longer echo train lengths with short TEs degrade contrast and produce blur but may be useful for enhanced T2 images. Dual echo (figure 3) is the same principle as FSE with an echo train length of two where the first echo is usually PD and the second T2WI.

Gradient echo (GRE)

GRE use bipolar gradient pulses following the 90^{o} excitation RF pulse (*4,5*). For standard GRE there is no 180^{o} refocusing RF pulse as depicted in figure 4. The addition of one or more of the 180^{o} refocusing pulse produces fast GRE sequences. Standard GRE uses a negatively pulsed gradient to dephase the spin which is then rephased with a second positively pulsed gradient. This generates the echo signal independently of the 180^{o} refocusing RF pulse.

Inversion recovery

Short tau inversion recovery (STIR) is a fat suppression sequence (figure 4) that uses an inversion time (TI) for T1 where TI is ln2 (approximately 0.693) multiplied by the T1 for fat. The sequence works because the T1 for fat and water are different (*4,5*). In the same way, water suppression can be accomplished using fluid attenuated inversion recovery (FLAIR) sequences (FLAIR can resemble T2 images). While these approaches produce fairly homogeneous suppression of water or fat, they are not specific for fat and water respectively so can cause decreased demarcation of tissues. Furthermore, they are incompatible with gadolinium contrast administration because the apparent shortening of contrast enhanced tissues will be impacted (suppressed) by short inversion recovery time.

Diffusion weighted (DWI)

Diffusion weighted imaging (DWI) is a type of MRI that shows how fluid is moving through tissues (extracellular space). Using a strong gradient, greater diffusion results in greater de-phasing so signal is reduced. As a result, DWI is effective in identifying restricted diffusion of water molecules as higher signal intensity. DWI can be used to assess tissue

edema, ischemia and cellularity (eg. proliferation of tumor cells). DWI represents one image set with different b values. The b value are values that reflect gradient strength and timing and so the higher the b value the stronger the diffusion. DWI is a combination of true diffusion values and the T2 signal and, therefore, the lower the b value the more T2 weighted the image is (*4*). Different tissues and resultant pathology exhibit different diffusion behavior from random Brownian motion to constrained motion in 1 voxel direction. Injury that changes water diffusion will change the DWI signal. Diffusion tensor imaging (DTI) is a variation on DWI that measures diffusion in multiple directions that allows mapping of nerve fibers and tractography. An apparent diffusion coefficient map (ADC) is literally a map or tensor of the actual diffusion values for tissues without the influence of T2.

Other Sequences

Functional MRI (fMRI) is a cluster of MRI approaches designed to reveal regional or time dependent variations in MR signal and is primarily associated with brain imaging. fMRI target a variety of physiological parameters and utilized numerous MRI sequences discussed above. Perfusion weighted imaging (PWI) is mostly gadolinium T1 images but also arterial spin labelling (ASL) without gadolinium (*4*). Susceptibility weighted sequences (SWI) exploit the T2* sequence susceptibility to small fluctuation in magnetic field and, consequently, can distinguish calcium from blood. This is useful in differentiating blood products in various pathological processes.

MR angiography (MRA) generates images with a high degree of contrast between tissues and blood. The images are generated associated with blood flow rather than vessel structures. Some aspects of flow are predictable and can be used to generate image contrast while other aspects of flow can create procedure difficulties or artefact (eg. turbulence, velocity or direction changes). There are a number of approaches to MRA. The first is contrast enhanced MRA which used gadolinium contrast agents to “shorten” the T1 relaxation time and enhance the brightness of blood signals (*4,5*). Time of flight (TOF) MRA does not use contrast agents but instead captures the unsaturated spins of flowing blood with GRE sequences to produce a bright vascular image (*4,5*). Phase

contrast MRA (PCA) uses amplitude and phase information to image blood flow velocity (*4,5*).

Patient Preparation

Patients need to undergo the preparation associated with both the PET scan and MRI. For PET, this will include fasting and instruction regarding radiation safety. For MRI, the screening questionnaire for magnetic safety and gadolinium contrast needs to be completed. Additionally, PET requires limitations associated with strenuous activity and management of any patients that are diabetic. Patients need to undergo metal screening to ensure there are no unsafe implants or devices going into the MRI environment. A lot of the pre-screening can be accomplished as the exam is being ordered or scheduled with just a few questions that target implants that could contraindicate the exam (e.g. pacemakers, magnetic spinal rods, cochlear implants, palate expanders), or impact image quality (e.g. dental spacers, braces). When patients arrive for their appointment, they are also required to fill out a more comprehensive MRI metal screening form that is then reviewed verbally with trained MRI personnel to ensure safety. Patients should also undergo a final visual inspection prior to entering zone 4 (the PET/MRI scan room) as a final verification that nothing unsafe is going into the magnet.

Patient history can be especially useful in image interpretation and, therefore, a robust patient history is an essential part of patient preparation. In oncology for example, some patients receive bone marrow stimulating medications at the end of a cycle of therapy that may alter biodistribution of the radiopharmaceutical in PET imaging. If delayed scheduling after these peak effects is not ideal, this information will assist with the accurate interpretation of the PET/MRI data.

Protocols vary across clinical sites and radiopharmaceuticals, however, an uptake phase of 45-90 minutes is typical. Patients are usually injected intravenously in an ambient environment to minimize stimulation. Recent investigations have demonstrated higher dose extravasation rates associated with manual injection using a syringe/needle or syringe/butterfly apparatus (*7-9*). Lower extravasation rates are achieved with canula use

with autoinjector infusion. For patients undergoing gadolinium contrast sequences, a single canula could be used for both the PET tracer administration and the later gadolinium administration. Clearly care with line security is crucial throughout the uptake phase and patient positioning.

Patient compliance is an important consideration given the extended time of the PET/MRI procedure. Compared to MRI, PET has the additional requirements of fasting and blood sugar level adjustment, plus the long uptake phase without stimulation. Compared to PET, MRI has the additional time and complexity associated with coil and patient setup, screening for magnetism susceptible objects, and noise. Additionally, the PET/MRI gantry can create issues associated with claustrophobia, even in patients with no previous history of claustrophobia. For some patients, compliance requires the pre-administration of anxiolytics like diazepam. In some cases, sedation or general anesthesia may be required and this adds additional complexity to both the protocol and patient care. Sedation and general anesthesia are generally not initiated until at least 30 minutes after administration of the PET radiopharmaceutical, however, in some circumstances it may be administered immediately after radiopharmaceutical injection.

PET/MRI Protocols

PET acquisition parameters are generally the same for both PET/CT and PET/MRI. Each bed position is acquired in 2-4 minute intervals. In PET/CT the PET portion determines the bulk of the length of the procedure with CT being performed very fast in a sequential model. Contrast CT protocols clearly extend the overall imaging procedure. Conversely, in PET/MRI images are acquired simultaneously and PET cannot progress to the next bed position until all the MRI sequences are completed. PET/MRI procedures commence with a localizer, comparable to the topogram in a PET/CT, to be used for planning both the PET bed positions and the MRI sequences in each bed position. In PET/MRI a specific MR attenuation correction sequence (MRAC) is obtained in each bed position to create the attenuation correction maps for PET reconstruction. In addition, depending on the region being imaged and the pathology of interest, several other sequences will be performed in each bed position. It should be kept in mind that while the Dixon method is

referenced in this manuscript for attenuation correction, there are a number of other approaches to attenuation correction in clinical practice and others emerging from development as detailed in the second article in this series (*3*).

Reducing artefact from respiratory motion is an important consideration. Breath hold techniques can be very effective if the sequence is short enough and the patient is compliant. This works particularly well for the short duration T1 weighted images, but even ultrafast sequences are too long for T2 breath hold approaches. Respiratory triggering or gating acquired images synchronized to the patient's respiratory cycle. Respiratory gating works best with patients breathing at a steady regular rate. The third option performs respiratory motion correction based on liver motion during respiration by tracking a MRI voxel at the apex of the liver.

More recent interest in accelerated protocols with 4, 3, 2 and even 1 minute bed positions have spurred debate about the benefits of reduced time and the image quality, for PET and MRI (*1*). The counter debate is that compromising a full sequence of MRI to minimize the time per bed position undermines the value and insights of MRI. Nonetheless, a hybrid protocol might permit a longer application of a suite of MRI sequences and longer PET acquisition (or potentially dynamic imaging during the uptake phase) for the single bed position of interest followed by reduced sequences and standard PET bed positions for the remainder of the acquisition.

MRI only acquisitions during the radiopharmaceutical uptake time may assist in reducing acquisition time associated with each PET/MRI bed position. For example, MR imaging of the total spine prior to the PET/MRI can be co-registered with the PET/MRI if the patient has not moved with gadolinium contrast spine sequences added after the PET/MRI. This approach could save the patient a considerable amount of time and optimize the PET/MRI sequence; especially when considering the duration of pre-contrast total spine imaging can vary between 30 minutes and 90 minutes depending on patient related factors.

Whole Body Oncology PET/MRI

While protocols will vary substantially from site to site and depending on equipment and clinical indications, for the purpose of a general overview it is useful to consolidate whole body PET/MRI protocols into several scenarios. In each scenario, the MRI sequence commences with a localizer scan followed by attenuation correction, T1, T2 and then special sequences if appropriate. The first approach is a fairly standard set of five MRI sequences per bed position with a total acquisition time of 5-8 minutes per bed position that includes (*1,10*):

- T1 weighted Dixon for attenuation (< 15 seconds),
- DWI with three b values (almost 1.5 minutes),
- T1WI volume interpolated spoiled GRE (VIBE) (< 30 seconds),
- T2 weighted single shot half spin echo (about 30 seconds to 1 minute),
- T2 weighted STIR (2 minutes)
- T1WI volume interpolated spoiled GRE, post-contrast if appropriate (18 seconds).

In this first approach to PET/MRI, following the conclusion of the whole body a more specific region may be added to the standard sequences, for example, prostate bed. For this approach, it would be prudent to perform the whole body PET/MRI first to capitalize on disease localization, enhance PET target-to-background in the targeted region, and to acquire critical data first to avoid non-compliance issues.

To minimize MRI sequence timing to better match each PET bed position without compromising diagnostic quality, some axial MRI images can be replaced with images in the coronal plane. Typically, three axial bed positions are equivalent to one in the coronal plane. For example, high quality T2 and STIR sequences can be run in the coronal plane. Additionally, a coronal VIBE can be imaged in addition to the axial plane VIBE.

A second approach utilizes a wider range of sequences per bed position for the whole body acquisition and these might vary depending on the nature of the investigation. The result is a more comprehensive suite of MRI sequences for the whole body PET/MRI but longer scanning time beyond 10 minutes for key bed positions corresponding to the region

of interest (figure 5). In this scenario, a basic set of sequences (eg. three) might be applied to each bed position while the broader suit is applied to the key bed position (including long PET imaging time). The basic sequences might be Dixon attenuation correction, coronal T1 FSE (or coronal VIBE to include fat saturation) and axial T2WI for example. Advanced sequences are applied to specific bed positions covering regions of specific interest and may include, without being limited to T2 FSE, STIR, DWI, dynamic contrast enhanced (DCE) and pre and post contrast T1. Specifically, PET/MRI with a focus on liver neoplasia might insert the extended suit of sequences as bed position 3 of 5 and include a breath hold technique. The thoracic region might insert the extended suit over two bed positions and including respiratory gating. Head and neck cancer would have the longer sequences in bed position 1 and pelvic pathology would also have the broader suite of sequences in bed position one. This is because for most whole body applications imaging commences from head progressing to thigh. For the pelvis, given bladder excretion of PET tracers, imaging starts at the pelvis and progresses to the head.

This second approach has the advantage of a single imaging session with all data included in one whole body protocol. Unfortunately, this approach can increase the time per bed position and, thus, impact the SUV for each bed position because the uptake time post injection for each bed position is progressively extended. Longer sequences could threaten later bed positions if compliance becomes an issue. Importantly, increased MRI sequence time increases the potential for heating patient tissues and implants, posing a safety issue. In both approaches, the use of dedicated imaging increases the quality of the procedure by combining the attributes of PET with the MRI sequences. Further, the PET/MRI combination enriches, deepens and broadens the anatomical, physiological and biochemical insights in tissues and organs.

Neurological and Cardiac PET/MRI

The value of PET/MRI in the brain and heart arises from the simultaneous acquisition and co-registration of structural information provided by standard MRI sequences, physiological insights provided by advanced MRI sequences, and molecular and metabolic status provided by PET (*11*). While rapid PET protocols have emerged for brain

and cardiac imaging in 5 minutes for a single bed position, 10-15 minutes for the single bed position are more typical. This longer window (compared to whole body oncology bed positions) allows a broader range of MRI sequences without extending the length of the study. It is also possible that a standard PET/MRI of the brain or heart with 10-15 minutes bed position is followed by a whole body PET/MRI with 3-5 minutes per bed position. In this scenario, the sequences are different from that of the whole body; reflecting both the change in time per bed position and the purpose of MRI.

PET/MRI of the brain generally requires the following sequences (figure 6):

- Attenuation correction with T1-weighted Dixon GRE
- Conventional brain MRI with T1WI, T2WI, DWI, SWI and contrast-enhanced T1WI.
- Depending on clinical indication, advanced sequences with PWI, fMRI, DTI, contrast-enhanced T1WI, fast gradient echo, MR spectroscopy and FLAIR.
- Simultaneous PET acquisition could occur with a number of radiotracers including ^{18}F FDG, ^{18}F FLT, ^{18}F FMISO, ^{18}F florbetapir, ^{18}F FET, ^{18}F FDOPA, ^{18}F FLT, and others.

PET/MRI of the heart generally requires the following sequences (figure 6):

- Attenuation correction with T1-weighted Dixon GRE
- Conventional cardiac MRI with T1 FSE, T2 spectral attenuated inversion recovery (SPAIR), and contrast-enhanced T1WI.
- Depending on clinical indication, advanced sequences with late gadolinium enhancement (LGE), rest perfusion (GRE, EPI and SSFP) and wall motion (ECG gating, harmonic phase analysis [HARP] and spatial modulation of magnetization [SPAMM]).
- Simultaneous PET acquisition could occur with a number of radiotracers including ^{18}F FDG for viability, ^{82}Rb, ^{13}N or ^{18}F based perfusion tracers and novel inflammatory or amyloid markers.

Conclusion

PET/MRI is a relatively new imaging modality that, to establish a reliable niche in the imaging market, requires development of universal, practical and reliable protocols. Protocol development should have a foundation of evidence based standards for PET, for MRI, and for PET/MRI combined. Patient compliance and diagnostic integrity are central factors for protocol development. While the complexity of PET/MRI protocols appears onerous, sequence rationalization has produced universally accepted streamlined protocols that fit within the time constraints of standard PET bed positions.

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Figure 1: Schematic representation of the T1 signal produced by longitudinal relaxation. Proton dipoles have a net magnetism in a magnetic field (left) but become aligned following a RF pulse (middle) and produce a T1 signal on relaxation (right).

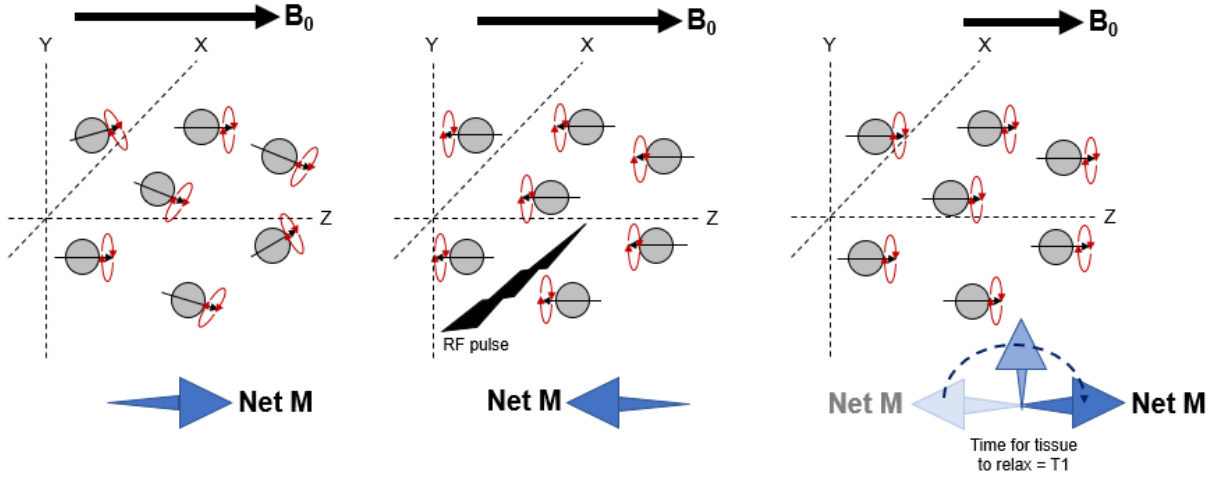
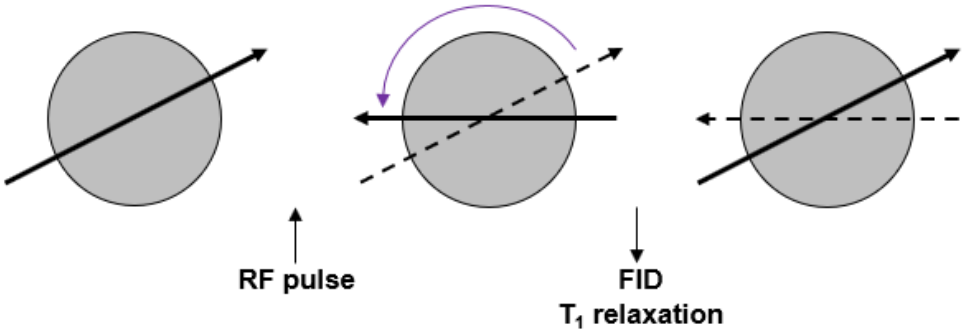


Figure 2: Schematic representation of the difference between T1 (top) and T2 (bottom) signal production. For T1, proton dipoles become aligned following a RF pulse and produce a T1 signal on relaxation. T2 signals relate to precession of the proton dipoles relaxing back to ground state.



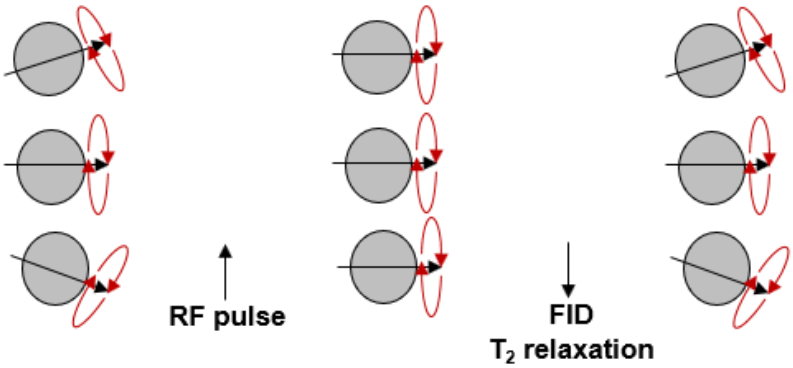


Figure 3: Schematic representation of MR sequences. Spin echo (top) uses a 90° followed by 180° RF pulse to produce an echo. Fast spin echo (middle) uses a 90° followed by multiple 180° RF pulse to produce multiple echos. Dual spin echo (bottom) as the name suggest produced 2 echos from a 90° followed by a repeated 180° RF pulse.

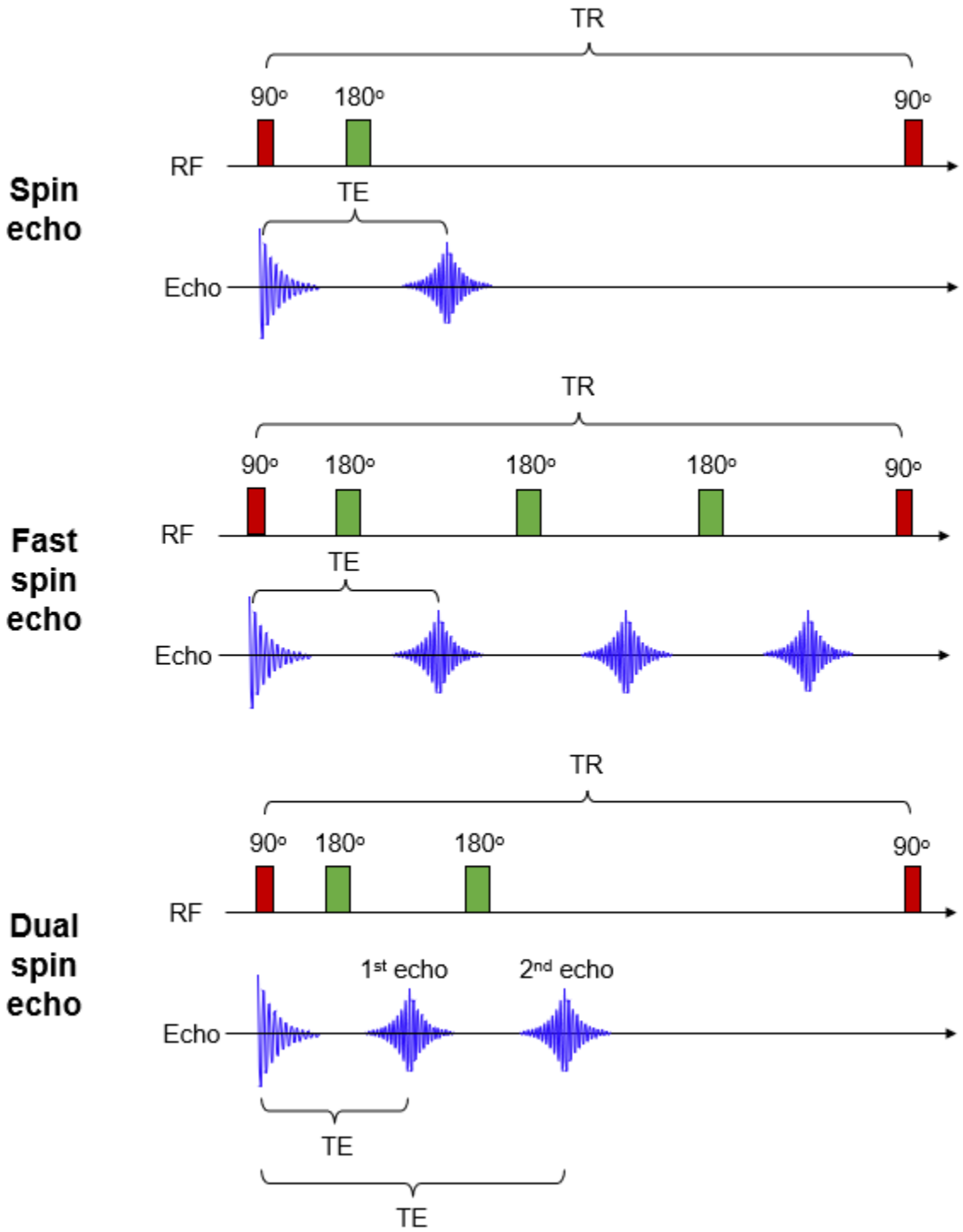


Figure 4: Schematic representation of gradient echo where a 90º RF pulse is followed by bipolar gradients first dephasing the FID and then rephasing the FID (top). Schematic representation of inversion recovery spin echo where a 180º RF pulse is followed by a 90º RF pulse (bottom).

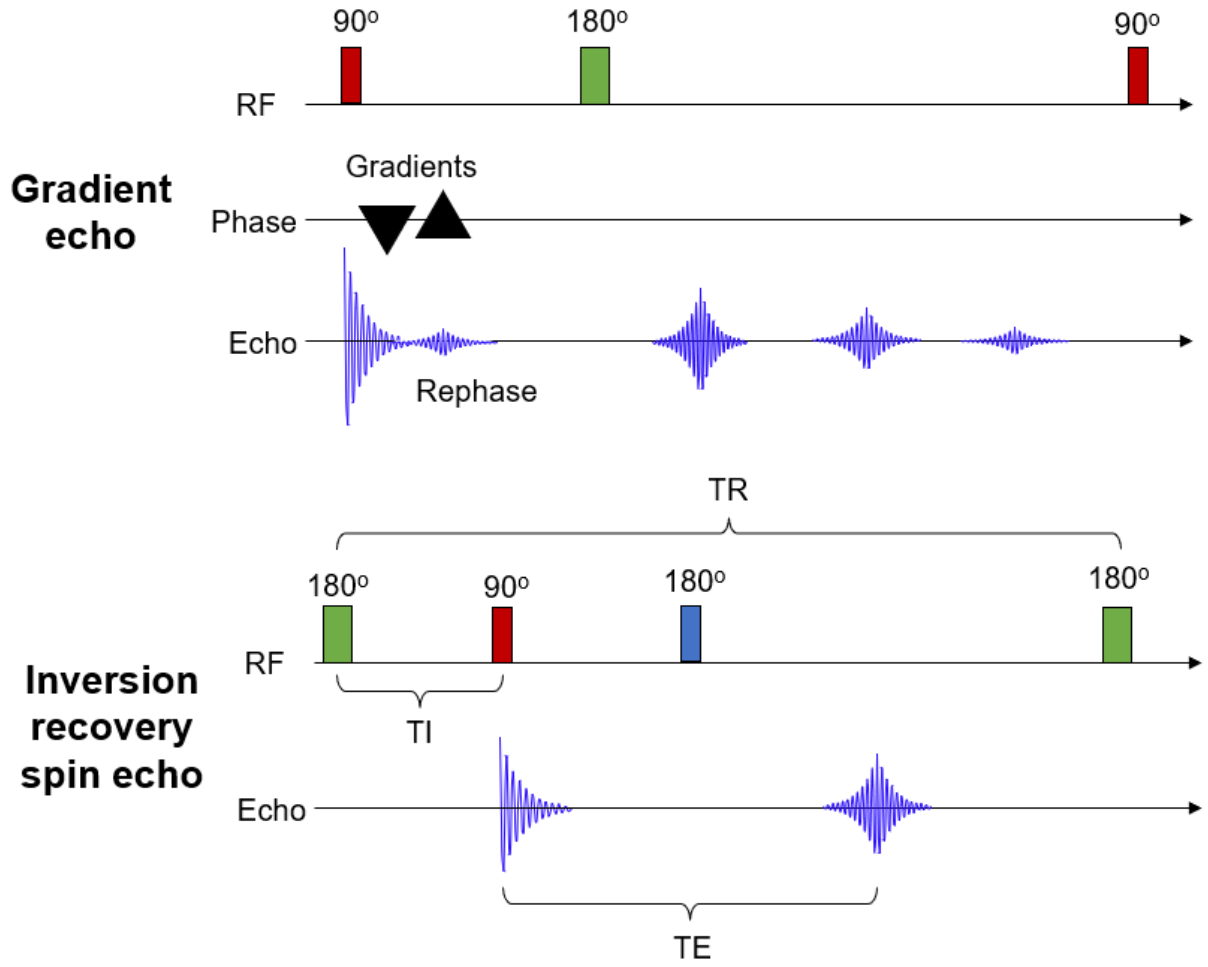


Figure 5: Flow chart of an example of a PET/MRI sequence used for whole body oncology studies.

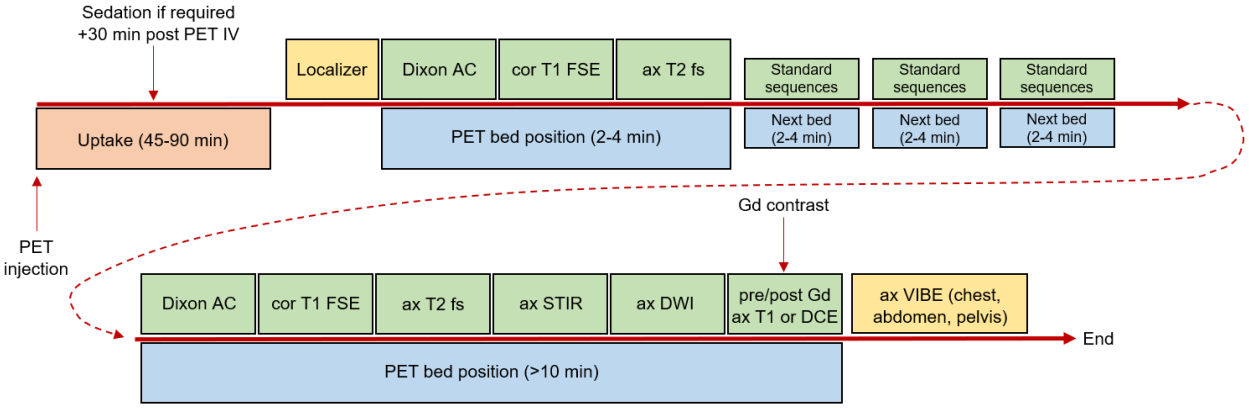


Figure 6: Flow chart of an example of a PET/MRI sequence used for brain studies (top) and cardiac studies (bottom).