Double Inversion Recovery Imaging of the Brain: One Institution's Experience

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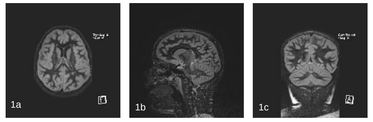
Introduction:
The double inversion recovery (DIR) sequence is a relatively novel imaging sequence which uses two inversion pulses before a turbo spin echo sequence to selectively image grey matter by simultaneously nulling white matter and CSF (1). This allows for optimal evaluation of the cerebral cortex, a portion of the brain which is inherently difficult to image because of the thin and folded structure as well as the close proximity of white matter and CSF, which have markedly different cellular properties. Previous studies have demonstrated usefulness of the DIR sequence for identifying multiple sclerosis lesions, cortical tubers in tuberous sclerosis, and identifying epileptic foci (2-4). We sought to evaluate these and other conditions in which the DIR sequence would be potentially useful by selectively adding the sequence to brain MRI studies of patients that had compelling clinical symptoms. Particular effort was made to image pediatric patients to improve the sensitivity in seizure evaluation. We have compiled several unique cases which demonstrate abnormalities which are apparent on the DIR sequence.

Materials and Methods:
The MR examinations were performed on a 1.5-T or 3-T whole body MR unit (Magnetom; Siemens, Erlangen, Germany) with an 8-channel head coil (Siemens). Routine sequences were performed per institutional protocol. Additionally, a double inversion recovery sequence was performed prior to IV injection of a gadolinium-based contrast agent, if it was indicated.

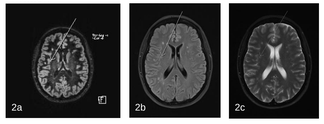
The theory behind the DIR sequence is as follows. Inversion recovery sequences can be used to suppress the signal of a tissue type by appropriately choosing an inversion interval TI (1). A common example of this is the use of the STIR sequence, where the TI is chosen to null the fat tissue signal (5). The double inversion recovery sequence uses 2 consecutive inversion pulses (TI_1 and TI_2) to allow suppression of 2 tissue types, in this case CSF and white matter. The DIR sequence is most successful when the 2 tissue types that are being suppressed have very different relaxation times (T_1)(1). The relaxation times of white matter, grey matter, and CSF at 3-T are assumed to be 830ms, 1250ms, and 4300ms, respectively (6). Following the first 180˚ inversion pulse, the magnetization of the grey and white matter recovers almost completely, while the CSF, with a substantially longer T_1, recovers only a fraction of its equilibrium magnetization. The second 180˚ inversion pulse is chosen to null white matter magnetization and must be timed so that CSF magnetization passes through the null point as the same time as white matter. Grey matter has a longer T_1 than white matter, and thus remains negative and generates a signal when the 90˚ excitation pulse is applied (1).

Findings and Discussion:
Figure 1 depicts the normal appearance of the brain performed with the DIR sequence. There is a high level of contrast between the bright grey matter and the nulled white matter and CSF. Cortical and deep grey matter are both adequately demonstrated with this sequence. Previous literature has described that DIR images show slightly more artifacts in the posterior fossa and choroid plexus relative to FLAIR and T2-weighted TSE sequences (7). These findings are likely due to vessel and CSF pulsation and as previously described are not felt to be detrimental to the diagnostic quality of the study (7).

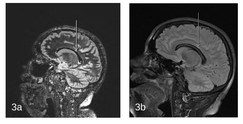
Multiple prior studies have supported the use of the DIR sequence to increase the sensitivity in detecting multiple sclerosis lesions compared with FLAIR and T2-weighted TSE sequences (2, 7, 8). It has been shown previously that the multifocal inflammatory demyelinating lesions of multiple sclerosis affect both white and grey matter and typically occur in juxtacortical, periventricular, and infratentorial locations (9). It is the cortical or juxtacortical lesions which are best depicted on DIR relative to FLAIR or T2-weighted TSE sequences. Figures 2a, 2b, and 2c demonstrate lesions from a patient with known multiple sclerosis detected on DIR, FLAIR, and T2-weighted TSE sequences, respectively. Note that there is a right sided juxtacortical lesion which is much more conspicuous on the DIR image. Figures 3a and 3b demonstrate a pericallosal lesion in a different patient with known multiple sclerosis which is also much more conspicuous on the DIR image relative to the FLAIR image.



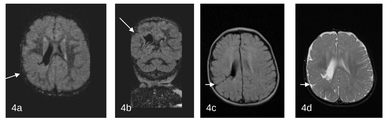
Figures 1a, 1b, and 1c: Axial, sagittal, and coronal DIR brain MR images in a normal young adult subject demonstrates suppression of CSF and white matter. This results in high contrast of grey matter relative to CSF and white matter allowing for accurate delineation of the cerebral cortex and deep grey matter.



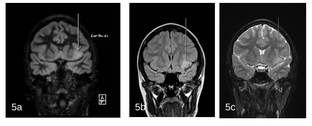
Figures 2a, 2b, 2c: Axial DIR, FLAIR, and T2-weighted TSE brain MR images of a 43-year-old female with a history of multiple sclerosis. Please note the increased conspicuity of a right sided juxtacortical lesion (arrows) on the DIR sequence relative to FLAIR and T2-weighted TSE sequences. There are also multiple bilateral white matter lesions present.



Figures 3a and 3b: Sagittal DIR and FLAIR brain MR images of a 27-year-old female with a history of multiple sclerosis. Please note the increased conspicuity of a pericallosal lesion (arrows) on the DIR sequence relative to the FLAIR sequence.



Figures 4a, 4b, 4c, and 4d: Axial and coronal DIR, axial FLAIR, and axial T2-weighted TSE brain MR images of a 10-month-old male with seizure demonstrate a transmantle cleft in the right parietal lobe (arrows). The DIR images highlight the fact that the cleft is lined by ectopic grey matter. These findings are consistent with a closed lip schizencephaly. Also noted is absence of the septum pellucidum.



Figures 5a, 5b, and 5c: Coronal DIR, FLAIR, and T2-weighted TSE brain MR images of a 15-year-old female with seizure disorder demonstrate a high signal lesion in the left insular cortex (arrows). The findings are non-specific but have been stable over several studies and in conjunction with MR spectroscopy are suggestive of a low grade neoplasm.

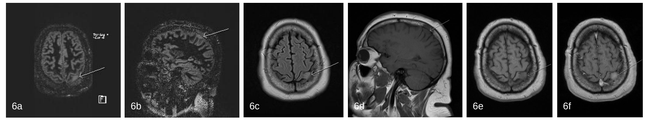
Findings and Discussion (cont.):
A potential area of further research into double inversion recovery imaging is in the arena of malformations of cortical development, specifically focal cortical dysplasias. Focal cortical dysplasias are the most common group of malformations of cortical development in patients presenting with epilepsy and they are the most common cause of epilepsy in childhood (10). MRI is the most useful imaging modality to evaluate the brain for a possible epileptogenic zone. The MRI diagnosis of focal cortical dysplasia relies on the detailed analysis of cortical thickness, the grey/white matter junction, grey matter signal abnormalities, white matter signal abnormalities, abnormal gyral or sulcal patterns, and focal and/or lobar hypoplasia/atrophy (11). DIR imaging has the most potential to aid in the diagnosis of abnormalities which affect the grey matter such as cases in which ectopic grey matter is a possible epileptogenic focus. Alternatively, DIR could also prove helpful by being able to confidently rule out grey matter abnormalities. Figures 4a, 4b, 4c, and 4d demonstrate a unilateral right parietal closed lip schizencephaly in a 10-month old male with seizure. The DIR image highlights the fact that this cleft is lined with ectopic gray matter.

DIR is also potentially useful in identifying other potential causes of epileptogenic foci. Figures 5a, 5b, and 5c demonstrate brain MR images obtained from a 15-year-old female with history of seizure disorder. The DIR, FLAIR, and T2 weighted TSE MR images demonstrate a high signal lesion in the left insular cortex. While the imaging findings are not specific, this is almost certainly the epileptogenic focus.

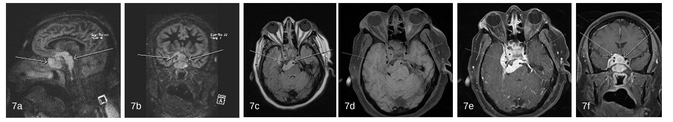
A surprising area in which the DIR sequence proved beneficial was in detecting dural based lesions which were presumed to represent meningiomas. Figures 6a, 6b, 6c, 6d, 6e, and 6f and Figures 7a, 7b, 7c, 7d, 7e, and 7f demonstrate brain MR images obtained from two different patients with presumed meningiomas. Of the sequences obtained before the administration of IV gadolinium based contrast, the meningiomas appear most conspicuous on the DIR sequence, followed by the FLAIR sequence. Once contrast media is administered, the lesion is most evident on the post-contrast MP-RAGE sequence. Increased conspicuity of these lesions on the DIR sequence could potentially allow patients getting routine follow-up of meningiomas to have the study performed without an IV contrast agent. Most importantly, this would eliminate the risk of the patient experiencing an allergic contrast reaction. Additionally, without the need for placing an IV line and obtaining post-contrast images, this could potentially decrease the time of the exam.

MRI plays a very important role in detecting both primary brain malignancies and metastatic disease. The workhorse sequences for detecting brain malignancies are typically pre and post-contrast enhanced T1 weighted sequences and FLAIR sequences, although there are potential roles for other sequences to increase the overall sensitivity of detecting such lesions. Tumors such as oligodendrolioma and gangliogliomа are predominantly located in the cerebral cortex. Gliomatosis cerebri typically presents as an infiltrating mass which enlarges the cerebral cortex. Also, metastatic disease in the brain is frequently found at the corticomedullary junction. As the DIR sequence selectively depicts the grey matter while nulling CSF and white matter, there may be a role for the DIR sequence to increase sensitivity of detecting cortical and juxtacortical malignancy. A recent study demonstrated that the double inversion recovery sequence was superior to the T2 FLAIR sequence for detecting metastases located in the grey matter (66.7% vs. 48.1%) (12). Figures 8a, 8b, 8c, and 8d demonstrate brain MRI images from a 49-year-old man with a history of previously resected left frontoparietal glioblastoma. The images depict increase signal in the cortex of the medial right frontal lobe and right frontal operculum with obscuration of the grey-white junction. The highest signal abnormality is seen on the DIR sequence. MR spectroscopy was performed as part of this study and the findings were most consistent with gliomatosis cerebri.

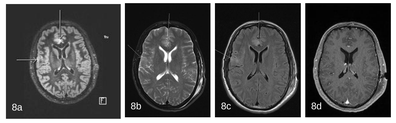
As with all sequences, there are intrinsic weaknesses of the DIR sequence. In addition to the aforementioned vessel and CSF flow related artifacts, previous literature has established that the DIR sequence has an inherently low signal-to-noise ratio and low spatial resolution (13). Our experience was no different. In order to facilitate multi-planar reconstruction, we chose to acquire isotropic data with 1.5mm slices, thus limiting the signal. If we would have chosen a larger slice thickness, such as 3mm, the signal would have improved, but reconstruction of the images in other planes would not have been possible.



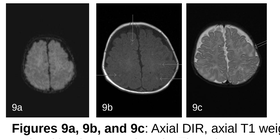
Figures 6a, 6b, 6c, 6d, 6e, and 6f: Axial and sagittal DIR, axial FLAIR, sagittal T1, and axial pre and post-contrast MP-RAGE brain MR images of a 37-year-old male demonstrate a small dural based extra-axial lesion near the left posterior vertex (arrows) which is most suggestive of a meningioma. On pre-contrast imaging, the lesion is most easily identified on the DIR sequence. The lesion demonstrates avid post-contrast enhancement.



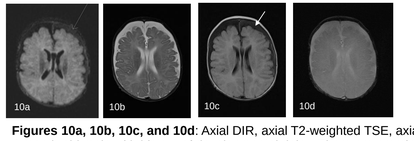
Figures 7a, 7b, 7c, 7d, 7e, and 7f: Sagittal and coronal DIR, axial FLAIR, axial pre and post-contrast MP-RAGE and coronal T1 post-contrast brain MR images of a 65-year-old female with a dural based extra-axial mass (arrows) centered in the cavernous region with encasement of the right internal carotid artery, invasion of the right inferior orbital fissure, and mass effect upon the brainstem. The lesion has been slowly growing over time and is most consistent with a meningioma. Again, on pre-contrast imaging this lesion is most conspicuous on DIR sequences, although the lesion is also visible on the FLAIR sequence. The lesion demonstrates avid post-contrast enhancement.



Figures 8a, 8b, 8c, and 8d: Axial DIR, axial T2-weighted TSE, axial FLAIR and axial post-contrast MP-RAGE brain MR images of a 49-year-old male with history of previously resected left frontoparietal glioblastoma. Imaging demonstrates increased signal on DIR, T2-weighted TSE, and FLAIR sequences within the cortex in the medial right frontal lobe and right frontal operculum (arrows) with obscuration of the grey-white junction. Note there is no appreciable enhancement in these regions. MR spectroscopy was performed as a part of the study, and findings were consistent with gliomatosis cerebri.



Figures 9a, 9b, and 9c: Axial DIR, axial T1 weighted, and axial T2 weighted TSE sequences in a 3-month-old male with tuberous sclerosis. There is poor suppression of the white matter which makes identification of cortical/subcortical tubers (seen as high signal intensity lesions on T1 weighted images) (single arrows) and thickened cerebral cortex (seen best on T2 weighted TSE sequences) (double arrows) essentially impossible on the DIR images.



Figures 10a, 10b, 10c, and 10d: Axial DIR, axial T2-weighted TSE, axial FLAIR and axial T2* brain MR images in a 4-month-old male with history of developmental delay. There are prominent extra-axial fluid collections over the frontal and temporal lobes bilaterally. The DIR and FLAIR sequences demonstrate that the fluid collection on the left (arrows) has asymmetrically slightly increased signal, while on the T2-weighted TSE and T2* sequences the signal is symmetric. There is no evidence of blood products in the fluid collection on the T2* sequence and the vessels coursing through the fluid collection on the T2-weighted TSE sequence confirm that this is within the subarachnoid space. These findings are consistent with benign external hydrocephalus. It is not clear, however, what caused the abnormal signal on the DIR and FLAIR sequences, and may relate to pulsation artifact. Also note there is poor white matter suppression due to incomplete myelination of this 4-month-old brain.

Findings and Discussion (cont.):
An additional possible drawback of DIR imaging which, to our knowledge, has not been previously described is that regarding the suppression of incompletely myelinated white matter in neonates and infants. Myelination of the human brain continues up until 2 years of age, and thus the optimum inversion pulse to null the white matter in a fully myelinated brain will likely differ from that in a partially myelinated brain. Sub-optimal white matter suppression makes it very difficult to detect abnormalities on the DIR sequence. Figures 9a, 9b, and 9c depict the axial DIR, axial T1 weighted, and axial T2 weighted TSE sequences in a 3-month-old male with tuberous sclerosis. Due to incomplete myelination, there is poor suppression of the white matter which makes identification of cortical/subcortical tubers (seen as high signal intensity lesions on T1 weighted images) (single arrows) and thickened cerebral cortex (seen best on T2 weighted TSE sequences) (double arrows) essentially impossible on the DIR images. Continued research into this area including optimization of the inversion pulse for non-myelinated white matter would prove beneficial.

With regard to artifacts, one possible example we encountered related to benign external hydrocephalus. Figures 10a, 10b, 10c, and 10d demonstrate images from a brain MRI in a 4-month-old male with bilateral extra-axial fluid collections over the frontal and temporal lobes. While on the T2-weighted TSE and T2* sequences the signal is symmetric and consistent with CSF, the DIR and FLAIR sequences demonstrate that the fluid collection on the left has asymmetrically slightly increased signal. This increased signal is most prominent on the DIR sequence but is also present on the FLAIR sequence. It is not clear what the cause of the increased signal is related to, but it is possible that the DIR sequence was affected by subtle signal changes from vessel or CSF pulsation. Pulsation artifact is a well described artifact on the FLAIR sequence and as the DIR sequence is an extension of FLAIR which includes suppression of both CSF and white matter, it is reasonable to expect that if there is artifact on the FLAIR sequence there will also likely be artifact on the DIR sequence.

Conclusion:
The use of a double inversion recovery sequence may prove useful when evaluating a number of abnormalities, including lesions of multiple sclerosis, focal cortical dysplasias, malignancies of the cerebral cortex, and even dural based lesions such as meningiomas. The new information gained from this collection of cases should guide further experimental work to determine the most practical way to implement double inversion recovery imaging in clinical practice.

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