Fluorine-18 Fluorocholine (FCH) Positron Emission Tomography/ Computed Tomography Imaging (PET/CT) in differentiating Radionecrosis from viable gliomas: A Pictorial Essay

Poster No.: C-1850  
Congress: ECR 2011  
Type: Educational Exhibit  
Authors: T. Win, A. Tan Eik Hock, S. P. Thang, W. Xie; Singapore/SG  
Keywords: Tissue characterisation, Diagnostic procedure, PET-CT, Nuclear medicine  
DOI: 10.1594/ecr2011/C-1850

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
**Learning objectives**

We present a pictorial essay on the initial experience in utilizing Fluorine-18 Fluorocholine (FCH) Positron Emission Tomography/Computed Tomography (PET/CT) imaging in differentiating radionecrosis from viable glioma post-radiotherapy.
Background

Brain gliomas are the commonest CNS tumours in adults, comprising 45 to 50% of all primary brain tumours. The typical approach for treatment of brain gliomas is surgical resection followed by external beam radiation therapy with or without chemotherapy. Recently, stereotactic radiosurgery is being used as an alternative to conventional radiotherapy or surgery.¹

In regards to external beam radiation therapy (RT) and radiosurgery, radionecrosis becomes a major post-treatment complication. It is often challenging using conventional imaging techniques to differentiate viable tumours from radionecrosis. Although Flourine-18 Fludeoxyglucose (FDG) PET/CT imaging has demonstrated some utility in detecting viable tumour, there are significant incidences of false negatives due to the high background uptake of glucose by normal brain tissue.

Fluorocholine (FCH) is an analogue for choline which is phosphorylated by choline kinase and integrated into phosphatidylcholine, a major membrane phospholipid, and be tagged with positron tracers such as Flourine-18 (18F) or Carbon-11 (11C). Malignant cells commonly over express enzyme choline kinase resulting in increased uptake of choline,² and several papers have already reported that FCH PET/CT is a novel technique which has good sensitivities and specificities in the evaluation of brain gliomas.²,³
Imaging findings OR Procedure details

Method

We retrospectively reviewed 18F-FCH PET/CT scans performed post external beam radiotherapy in patients with histologically proven brain gliomas in our institution and correlated with conventional imaging (MRI or CT) and FDG PET/CT where available.

18F-FCH tracer was synthesized according to the methodology described by DeGrado et al.\textsuperscript{4} Emission scanning was performed for 10 minutes, 45 minutes after intravenous administration of 3 to 5 millicurie (mCi) of 18F-FCH. Non-contrast enhanced CT brain study was performed together with emission scan for anatomical correlation.

Imaging Findings

Case 1

30 year-old-female with biopsy-proven right frontal anaplastic oligodendroglioma, treated with excision and external beam radiation. She presented with seizures. Contrast enhanced MRI revealed a stable lobulated cystic lesion in the right frontal lobe with a new enhancing nodule at inferior medial aspect of the cyst. FDG PET/CT scan showed mildly increased diffuse FDG uptake in the remnant adjacent cortex in the right frontal lobe, which was non-specific. However, there was no focal FDG avidity corresponding to the enhancing nodule seen on prior MRI scan. Subsequent FCH PET/CT scan demonstrated focally increased FCH uptake in the right frontal lobe which corresponded to the enhancing nodule on MRI scan with LNR of 3.8. Recurrent oligodendroglioma was confirmed on biopsy.

Case 2

47 year-old-female with histologically confirmed grade II left frontal astrocytoma, status post radiotherapy. She presented with persistent headache. MRI revealed a left frontal lobe mass involving the body of the corpus callosum. FCH PET/CT showed increased tracer uptake in the corresponding region with LNR of 10.4. Biopsy confirmed that it was recurrence.

Case 3
62 year-old-female with histologically proven glioblastoma multiforme in the left thalamus extending into the corpus callosum, treated with external beam radiotherapy. She developed clinical deterioration and MRI was performed, showing slight morphological change in tumour. It was further evaluated with FDG PET/CT and FCH PET/CT scans. Significant FCH tracer uptake was noted in the lesion with lesion to normal white matter ratio (LNR) of 20.33, similar to FDG. Follow-up MRI scan done after a few weeks revealed increase in size of tumour.

**Case 4**

50 year-old-female diagnosed with WHO grade II oligodendroglioma, status post resection of tumour followed by external beam radiation therapy. MRI scan depicted a stable encephalomalacia with a new area of T2 signal abnormality without contrast enhancement noted adjacent to the original tumour site. FDG PET/CT revealed no evidence of tracer uptake while FCH PET/CT showed low level FCH tracer uptake with LNR of 2.12. No biopsy was performed but there was slight increase in size of the lesion on follow-up MRI at 7 months interval, suggestive of low-grade tumour recurrence.

**Case 5**

62 year-old-male with histologically proven right temporal lobe glioblastoma multiforme status post debulking surgery and external beam radiotherapy. He presented with worsening of GCS. On contrast enhanced MRI brain scan, new rim-enhancing lesions were seen in the right parieto-temporal lobes with possible diagnosis of either brain abscesses or recurrence of the tumour. Subsequently, FDG PET/CT and FCH PET/CT scans were performed. FDG PET/CT scan revealed relatively photopenic hypodense lesions in the right parietal and temporal lobes which corresponded to the regions of enhancing lesions seen on prior MRI scan. On FCH PET/CT, significant FCH tracer uptake ($\text{SUV}_{\text{max}} 2.4$) is noted at periphery of the hypodense lesions with LNR of 5.3. Patient refused to undergo biopsy and follow-up MRI scan done after 4 months showed slight improvement of the lesions with mild reduction in sizes.

**Case 6**

19 year-old-male with biopsy-proven glioblastoma multiforme in the right basal ganglia treated with chemo and radiotherapy. He presented with severe headache associated with vomiting and evaluated with contrast enhanced MRI which showed increase in size of known right basal ganglial irregular rim-enhancing mass. Significant FDG uptake was seen at the periphery of the mass on initial FDG PET/CT scan. FCH PET/CT scan was done on the next day, demonstrating increased tracer uptake ($\text{SUV}_{\text{max}} 1.7$) with similar
peripheral distribution. The lesion to normal white matter ratio was 3.4. Biopsy was not performed and follow-up MRI scan done after 2 months revealed slight interval decrease in size of the mass.
Fig. 0: Case 1: Magnetic resonance T1 post-gadolinium axial and coronal images showing a small enhancing nodule at inferior medial aspect of the surgical bed of the previous right frontal lobe anaplastic oligodendroglioma. (arrow)

© Radiology, Singhealth, KK Women and Children Hospital - Singapore/SG
**Fig. 0:** Case 1: FCH PET/CT (middle row) showed focal increased tracer uptake in the right frontal lobe, which corresponded to the enhancing nodule in prior MRI. FDG PET/CT (bottom row) also revealed increased tracer uptake in the corresponding region as well as in the adjacent remnant cortex. Absent FCH uptake in the normal brain parenchyma was noted in contrast to background FDG uptake in normal cortex and deep grey nuclei.
Fig. 0: Case 2: Magnetic resonance imaging: axial (a), coronal (b) and sagittal (c) T1 post-gadolinium images demonstrating WHO grade II astrocytoma in the left frontal lobe, extending into the body of the corpus callosum. (arrow)

© Radiology, Singhealth, KK Women and Children Hospital - Singapore/SG
Fig. 0: Case 2: FCH PET/CT showed intense tracer uptake in the left frontal lobe

© Radiology, Singhealth, KK Women and Children Hospital - Singapore/SG
**Fig. 0:** Case 3: Magnetic resonance imaging: axial (a), coronal (b) and sagittal (c) T1 post-gadolinium images showing a heterogeneously enhancing left thalamic glioblastoma multiforme.

© Radiology, Singhealth, KK Women and Children Hospital - Singapore/SG
**Fig. 0:** Case 3: FCH. PET/CT image (b) revealed intense tracer uptake in the left thalamic tumour. FDGPET/CT image (c) showed corresponding hypermetabolic activity. Background FDG uptake is again seen in normal cortex.

© Radiology, Singhealth, KK Women and Children Hospital - Singapore/SG
**Fig. 0:** Case 4: Magnetic resonance imaging: axial FLAIR (a) image demonstrated increased T2 signal intensity in the left frontal lobe adjacent to the site of previous left frontal oligodendroglioma. T1 post-gadolinium axial image (b) showed no enhancement post-contrast.

© Radiology, Singhealth, KK Women and Childen Hospital - Singapore/SG

**Fig. 0:** Case 4: FCH. PET/CT image (b) revealed (very) low level FCH uptake in the region deep to the left sylvian fissure with no corresponding FDG uptake (c). Areas of hypometabolism are noted in left frontal lobe corresponding to the area of encephalomalacia on prior MRI, where previous resection of the left frontal oligodendroglioma was performed.
**Fig. 0:** Case 5: Magnetic resonance T1 post-gadolinium axial images showed rim enhancing lesions in the right parieto-temporal lobes.
Fig. 0: Case 5: FCH. PET/CT image (b) revealed increased FCH tracer uptake at the periphery of the hypodense lesions in the right parieto-temporal lobes which corresponded to the rim-enhancing lesions seen on earlier MRI. FDG PET/CT images (c) showed focal areas of relatively decreased tracer uptake in the corresponding regions.

© Radiology, Singhealth, KK Women and Children Hospital - Singapore/SG
**Fig. 0:** Case 6: Magnetic resonance T1 post-gadolinium axial images showed irregular rim enhancing lesions in the right basal ganglia.

© Radiology, Singhealth, KK Women and Children Hospital - Singapore/SG
**Fig. 0:** Case 6: FCH. PET/CT image (b) revealed intense nodular FCH tracer uptake at the periphery of the hypodense lesions in the right basal ganglia with similar pattern of increased FDG uptake noted on FDG PET/CT images (c).

© Radiology, Singhealth, KK Women and Children Hospital - Singapore/SG
Conclusion

Discussion

Non-invasive imaging plays a crucial role in the management of patients with glioma. During the course of treatment or follow-up, it is important to differentiate radionecrosis from viable tumours, since the management and prognosis are different. Conventional imaging techniques such as CT and MRI scans are frequently found to be challenging in discriminating the radionecrosis from viable tumour due to overlapping imaging features.

Radionecrosis is a well known post-treatment complication in the patients with glioma. Radiation induced injury to the brain are classified into three types: 5,6

1. Acute injury occurs during radiation therapy or just after completion of it. It commonly present with transient worsening of symptoms and signs of increased intracranial pressure. Symptoms are usually transient and reversible.
2. Subacute injury usually occurs within the first 12 weeks post-radiation. Patients may present with worsening of pre-existing neurological focal deficits, or remain asymptomatic. It is usually improved within a few weeks or months treating with corticosteroids or sometimes spontaneous improvement is seen.
3. Late injury occurs months to years after completion of RT, and it is usually progressive and irreversible. Radionecrosis is one of the most frequently presenting types of late injuries which may result in diagnostic dilemma in patients post-radiation therapy.

Radiation induced necrosis is attributed by endothelial cell damage. Fibrinoid necrosis in the walls of the blood vessels results in vessel wall thickening, hyalinization and telangiectasia, which will eventually leads to damage of the blood-brain barrier. An influx of leukocytes to the damaged area causes over production of cytokines and oligodendrocyte apoptosis. Leakage of the serum into the brain parenchyma through the damaged capillaries contributes to glial injury and extensive fibrinoid coagulative degeneration of the white matter which ultimately forms a hard mass with ill-defined contours. 6,7

Radionecrosis can mimic a viable tumour since both frequently occur in the same area or close to the original tumour site, and share similar imaging features and enhancement pattern on conventional imaging techniques (CT and MRI). Usually, viable tumours are more metabolically active than the radionecrosis and FDG PET/CT imaging has been
proved to be a better technique to differentiate the radionecrosis from viable tumour. However, standard FDG PET/CT has some limitations in brain imaging due to avid uptake of FDG by normal cortex, basal ganglia, thalami, caudate nuclei and other deep grey matter. Occasionally, increased FDG uptake is seen in the region of the original tumour after RT due to migration of the macrophages to radiation site, which may pose difficulty in distinguishing radionecrosis from viable tumour.  

Several studies showed that FCH PET/CT has better sensitivity and specificity in the evaluation of brain gliomas compared to the FDG PET/CT due to absence of normal cortical metabolic uptake and inflammatory uptake. Higher concentration of FCH in the viable tumour in contrast to low tracer concentration in normal cortex results in good delineation of the viable tumour from normal brain.

There are 6 cases included in our study and all cases have MRI study immediately done before the PET/CT scan. FCH PET/CT was performed together with FDG PET/CT in 5 out of 6 cases, providing direct comparison between two tracers. MRI scans of three patients revealed new enhancing lesions at the site of original tumour while the existing enhancing tumour showed slight morphological changes in two patients and the remaining patient has a new focal non-enhancing area of T2/FLAIR signal abnormality adjacent to the encephalomalacia related to previous treatment. All 6 cases showed increased FCH uptake in the areas which corresponded to the lesional areas delineated on prior MRI scans. The lesion to normal cortex ratio ranged from 2.1 to 20.33 in our study. FDG PET/CT was performed in 5 cases with variable degree of FDG avidity in 3 cases while no significant tracer uptake was seen in 2 other patients. No FCH uptake is noted in normal grey matter in contrast to FDG.

Two out of 6 cases underwent biopsy and histology confirmed presence of viable tumour. Follow up MRI scans in 2 other patients revealed slight progression of the lesions, consistent with that of low-grade glioma. Remaining 2 patients showed slight interval improvement on follow-up MRI scan.

PET/CT with other tracers, such as methionine, fluoro-DOPA (F-DOPA) and fluorothymidine (FLT) are also used in evaluation of the brain glioma. FDG and FLT, which are highly dependent on cellular proliferation, are found to be more helpful in evaluation of the high-grade gliomas. Radiolabeled aminoacid tracers such as (11C) methionine and F-DOPA as well as radiolabeled substrate FCH are better at imaging of low-grade tumours.
Other modalities like MR spectroscopy (MRS) is used in evaluation of brain glioma. The brain metabolites such as N-acetylaspartate (NAA), choline (Cho) creatinine (Cr), lactate and lipids are commonly seen on the MR spectrum. MRS may allow characterization of metabolic changes associated with tumor growth, degree of malignancy, grading of tumors, response to treatment, and the sequelae of treatment.

Generally, NAA and creatine decrease and choline, lactate and lipids increase in malignant tumours. These spectral patterns are usually reliable in cases of either pure tumor or pure radionecrosis, however, where both tumor cells and radiation-injury are present and the spectral patterns are often less clear.  

Conclusion

Brain gliomas are the commonest CNS tumours in adults. External beam radiation therapy and stereotactic radiosurgery are commonly used in management of brain glioma and radionecrosis becomes a major post-treatment complication. Conventional imaging technique such as MRI has limitation in differentiation of radionecrosis from viable tumour due to overlapping features. FDG PET/CT has been widely used in evaluation of brain tumour but high tracer uptake in normal grey matter may result in false negative. Increased FCH tracer uptake is noted in most of the brain gliomas with absent uptake in normal cortex, resulting in better delineation of the viable tumour. Based on our initial experience, FCH PET/CT has strong potential clinical utility in differentiating viable gliomas from radionecrosis.
Fluorine-18 Fluorocholine (FCH) Positron Emission Tomography/ Computed Tomography Imaging (PET/CT) in differentiating Radionecrosis from viable gliomas: A Pictorial Essay

Thida Win, Andrew Tan Eik Hock, Sue Ping Thang, Wanying Xie

Department of Nuclear Medicine and PET imaging, Singapore General Hospital, Singapore

Corresponding author:

Dr Thida Win

Department of Nuclear Medicine and PET, Singapore General Hospital, Outram Road, 169608 Singapore

Tel: (65) 63266041; Fax: (65) 62240938.

E-mail: thidawin.myintkyu@gmail.com
References