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^{18}Fluoromethylcholine PET/CT: a new tool for CNS lymphoma

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BACKGROUND

- Primary central nervous system lymphoma (PCNSL) accounts for approximately 4% of newly diagnosed central nervous system (CNS) tumours and 1-2% of all lymphomas.
- Secondary CNS involvement occurs in 2.3-10% of patients with systemic diffuse large B cell lymphoma (DLBCL).
- The gold standard for CNS imaging in primary and secondary CNS lymphoma is with gadolinium-enhanced magnetic resonance imaging (MRI). However MRI does have limitations:
  - Some patients will have small persistent abnormalities from scarring due to focal haemorrhage or from a previous biopsy, which can be difficult to distinguish from residual tumour.
  - There have also been recent safety concerns over exposure to gadolinium-based contrast agents with case reports of the development of nephrogenic systemic fibrosis and gadolinium deposits in other organs, leading to the European Medicines Agency restricting or suspending the use of linear gadolinium products in 2017.

FCH-PET/CT

- Choline positron emission tomography computed tomography (PET/CT) uses analogues of choline as a radiotracer. Choline can be labelled with either ^{18}Fluoromethyl (FCH) or ^{11}Carbon ($^{11}CH_3$).
- Choline is a precursor of phospholipids, which upon entry to the cell is phosphorylated by the enzyme choline kinase. The expression of choline kinase is upregulated in tumour cells and allows increased uptake of the Choline tracer.
- As there is minimal background grey matter uptake of the tracer, FCH-PET/CT can be used to detect tumours with a high lesion-to-CNS background ratio, and has been used in diagnosis and follow up imaging in brain tumours, particularly high-grade gliomas. This contrasts with the lack of utility of the 2-deoxy-2-[^{18}F]fluoro-D-glucose (FDG) PET/CT metabolic for CNS lymphoma analysis, due to high FDG physiological activity levels within the grey-white matter.

Our centre has been using FCH radiotracer-PET/CT alongside MRI for CNS lymphoma assessment since 2011 following approval by the Administration of Radioactive Substances Advisory Committee (ARSAC).

AIMS

- To assess concordance rate between MRI and FCH-PET/CT.
- To assess whether FCH-PET/CT would give additional prognostic information.

METHODS

Our centre conducted a retrospective study of patients who underwent both a MRI and a FCH-PET/CT for response assessment at end of treatment (EOT) between 1st November 2011 and 10th October 2019.

Patients with a histopathological or specialist neuroradiological (where biopsy was not feasible) diagnosis of primary or secondary CNS lymphoma who had an EOT MRI and FCH-PET/CT were identified from a radiology database. Patients who did not complete treatment due to death or toxicity, or had the imaging performed after consolidative therapy were excluded.

To assess whether CMR on a FCH-PET/CT would add further information to the MRI results, those who achieved an overall response were then sub-classified into 3 response levels; response level 1 achieved CR/CMR on both modalities, response level 2 achieved PR on MRI and CMR on FCH-PET/CT (2a) or CR on MRI and PR on FCH-PET/CT (2b), and response level 3 achieved PR on both modalities.

RESULTS

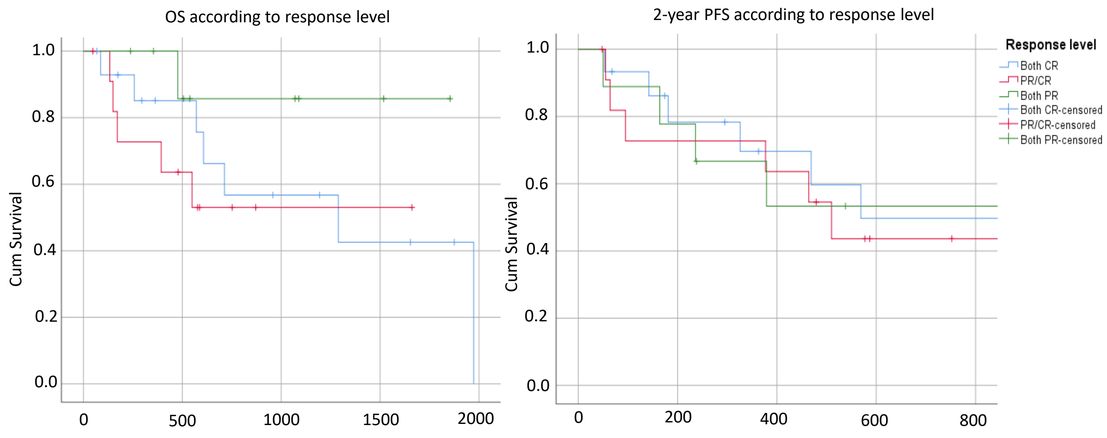
PATIENT CHARACTERISTICS

Forty patients met the inclusion criteria. The median age was 59 (range 19 to 77). 30 patients (75%) had a diagnosis of PCNSL and MATRix was the most common type of chemotherapy. 16 patients (40%) went on to have consolidation therapy following the EOT scans.

SURVIVAL DATA

For the whole cohort PFS was 78% at 100-days and 51.2% at 2-years, OS was 61%. The survival data for the cohort who achieved a response on both imaging modalities is shown in figure 2. The assigned response level did not predict relapse at 100-days (p=0.38) or at 2-years (p=0.92). There was no difference in overall survival (p=0.29) between the groups.

Figure 2. Kaplan-Meier survival curves for the 36 patients who achieved an overall response on both MRI and FCH-PET/CT. PFS was 86.1% at 100 days and 55.6% at 2 years, and OS was 63.9%. The assigned response level did not predict relapse at 100-days (p=0.38) or at 2-years (p=0.92). There was no difference in overall survival (p=0.29) between the groups.



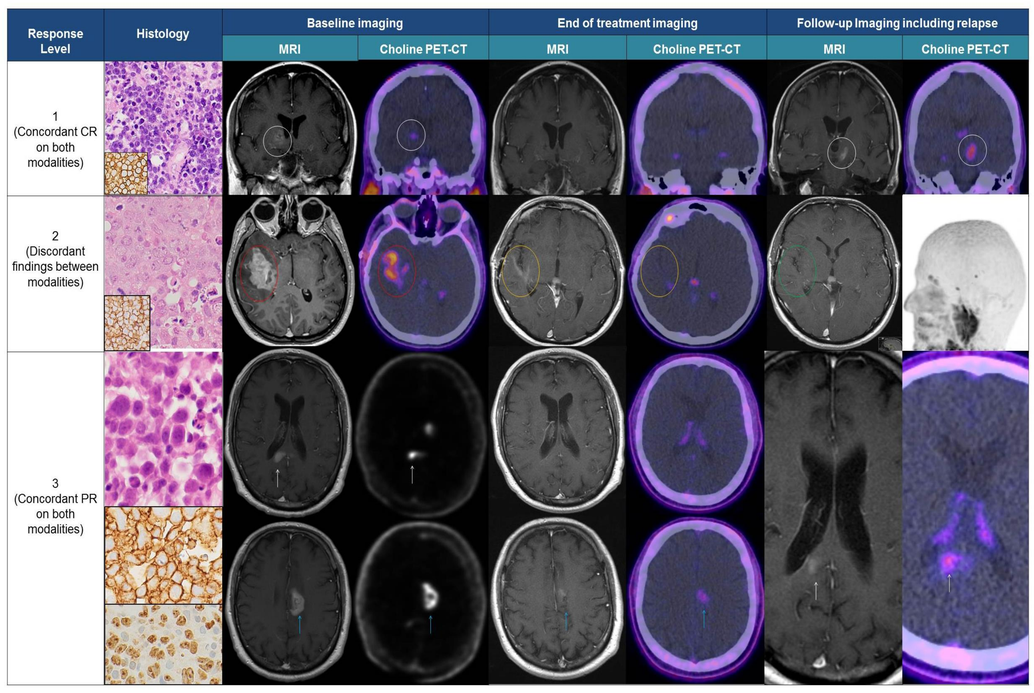


Figure 1. Response assessment in large B-cell lymphoma of the central nervous system: contrast enhanced MRI and FCH-PET/CT.
Top row – response level 1. Histology - large B-cell lymphoma, composed of sheets of large atypical lymphoid cells, (haemtoxylin and eosin [H&E] stain) that are CD20 positive (inset). This patient had concordant MRI and FCH-PET/CT imaging findings throughout treatment. The baseline coronal CE T1W MRI demonstrates an enhancing lesion within the right thalamus and a focus of increased tracer uptake in the same region on the contemporaneous coronal FCH-PET/CT image (white circles). These areas of enhancement and tracer uptake had both resolved on the EOT imaging, consistent with radiological CR. Follow up imaging demonstrates a new focus of enhancement and corresponding tracer uptake within the left thalamus and cerebral peduncle on the coronal CE T1W MRI and FCH-PET/CT images, respectively (white circles).
Middle row – response level 2. Histology - large B-cell lymphoma, composed of sheets of large atypical lymphoid cells (H&E stain) that are CD20 positive (inset). This patient had discordant findings between imaging modalities. The baseline axial CE T1W MRI shows an enhancing mass within the right medial temporal lobe and posterior insula (red circle). The contemporaneous choline PET-CT is concordant, demonstrating increased uptake in the same anatomical location (red circle). Partial response is achieved on the EOT CE T1W MRI as illustrated by interval reduction in size of the mass although some pathological enhancement remains (amber circle, this area was not hyperintense on the pre-contrast T1W imaging - not shown). The EOT choline PET-CT is discordant, showing complete metabolic response (amber circle). Follow up imaging shows resolution of the mesial temporal and insular enhancement (green circle) and ongoing normal physiological FCH tracer uptake in the cranium on the maximum intensity projection FCH-PET/CT reconstruction, consistent with radiological CR.
Bottom- rows – response level 3. Histology - large B-cell lymphoma, composed of sheets of large atypical lymphoid cells, (H&E stain, top panel) that are CD20 positive (middle panel) and display a high Ki 67 proliferation index (lower panel). This patient had a partial response which was concordant between modalities throughout treatment. The baseline axial CE T1W MRIs depict an enhancing lesion within the right side of the splenium of the corpus callosum (top, white arrows) and the left cingulate gyrus (bottom, blue arrows) with corresponding increased uptake on the axial FCH-PET/CT in the same regions. The splenial lesion has resolved on both the EOT MRI and FCH-PET/CT (top) but the left-sided lesion is still present on both modalities (bottom, blue arrows).

RESPONSE LEVELS

A total of 36 patients (90%) achieved a response on both MRI and FCH-PET/CT. Of these, 15 were assigned to response level 1, 11 to response level 2a, 1 to response level 2b, and 9 to response level 3. Figure 1 depicts 3 examples of the histology and MRI and FCH-PET/CT results for each of the three response levels.

CONCORDANCE

Fourteen patients (35%) had discordant results on EOT imaging. The majority of discordant cases (11 out of 14) were patients who had PR on MRI but showed a CMR on FCH-PET/CT. In the remaining discordant 3 cases , 2 had PD on MRI with PR on FCT-PET/CT and one had CR on MRI and PR on FCH-PET/CT.

CONCLUSIONS

Our results showed a concordance rate of 65% between FCH-PET and MRI. Eleven out of 14 discordant cases were in patients who achieved a PR by MRI, but were in CMR on FCT-PET/CT. This group had a clinic course similar to the patients who achieved a CR/CMR on both, with similar PFS and OS rates. This may suggest that the residual enhancement seen on MRI was scarring or post treatment changes and may have been better classified as CRu. However patients who only achieved a PR on both modalities also had similar outcomes. The matter is further complicated as 3 patients in the response level 3 cohort achieved a CR or CMR following consolidation therapy. Although, of the 6 patients who did not go on to have consolidation, 3 have not required further treatment. Based on these results the depth of response doesn't appear to predict long term outcomes.

KEY FINDINGS

We conclude that FCH-PET/CT is a reasonable alternative or additional mode of imaging to gadolinium-enhanced MRI brain, providing a new tool for assessment of CNS lymphoma. Further studies are warranted evaluating the potential role for FCH-PET/CT in CNS lymphoma, including-assessment of whether FCH PET/CT is-superior to MRI in predicting persistent disease or identifying patients that need consolidation therapy.

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