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Cancer Imaging With Fluorine-18–Labeled Choline Derivatives

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The choline transporter and choline kinase enzyme frequently are overexpressed in malignancy. Therefore, positron-emitter-labeled compounds derived from choline have the potential to serve as oncologic probes for positron emission tomography. The fluorine-18 (^{18}F)–labeled choline derivative fluorocholine (FCH) in particular has demonstrated potential utility for imaging of a variety of neoplasms, including those of the breast, prostate, liver, and brain. The pharmacokinetics of FCH and other choline tracers allow for whole-body imaging within minutes of injection while still achieving high tumor-to-background contrast in most organs, including the brain. These features, along with the possibility of imaging malignancies that have proved elusive with the use of ^{18}F-fluorodeoxyglucose positron emission tomography support further clinical investigations of ^{18}F-labeled choline tracers.
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In mammals, choline is an essential nutrient that serves as an extrinsic substrate for the synthesis of phosphatidylcholine (PC), a major constituent of the cell membrane. Phosphorylation by choline kinase (CK) constitutes the first intermediate step in the incorporation of choline into phospholipids via the Kennedy pathway. The importance of this metabolic pathway for cell viability is underscored by the fact that there are no known inherited diseases in humans affecting this pathway. However, in cancer, there is often an increase in the cellular transport and phosphorylation of choline, as well as an increase in the expression of the CK enzyme.[1–3] These observations have fueled interest in developing imaging and therapeutic agents out of compounds metabolized by CK. With this in mind, this article will summarize the development of fluorine-18 (^{18}F)-labeled choline

radiopharmaceuticals as oncologic probes for positron emission tomography (PET).

Development of Choline Tracers Labeled With Fluorine-18

Tumor imaging with choline-based tracers was introduced by Hara and coworkers using carbon-11 (^{11}C) choline PET to successfully visualize brain tumors and prostate cancer.[4,5] As a true tracer, ^{11}C choline is biochemically indistinguishable from natural choline. This compound has shown particular promise for imaging tumors of the genitourinary tract because of its limited urinary clearance and avidity for bladder and prostate cancers.[6–11] However, the short decay half-life of the carbon-11 (20 minutes) has limited its use to centers equipped with an on-site cyclotron.

The practical need for longer-lived agents has led subsequently to the development of ^{18}F-labeled choline derivatives. The first of these, fluoroethylcholine (FeCH) and ^{18}F fluorocholine (FCH), were introduced by Hara and coworkers and DeGrado and coworkers, respectively.[12,13] Contrary to initial observations, these compounds, which are phosphorylated by CK, do appear to participate further in the synthesis of membrane phospholipids as substrates for cytidylyltransferase, although the rate of their incorporation into phospholipids may be slower than that of choline.[14] In addition to compounds that serve as specific substrates of CK, there are choline transporter-specific ligands which can be

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used to specifically image the choline transporter system. These include deshydroxy-^{18}F fluorocholine as well as analogs of hemicholinium-3, an inhibitor of membrane choline transporter.[15,16] Of these agents, FCH has undergone the most study to date.

FCH is a fluoromethylated analog of choline consisting of fluoromethyl-dimethyl-2-hydroxyethylammonium labeled with fluorine-18. Several synthesis methods are available for producing this compound in commercially acceptable yields.[17–20] At the present time, it is not known which choline derivative is most advantageous for clinical use. There have been no direct in vivo comparisons between individual compounds, and previous in vitro comparisons have not controlled for potentially confounding factors, including the presence of synthetic contaminants such as dimethylethanolamine, which may modulate the phosphorylation and transport of these compounds in vitro.[21] In vitro experiments suggest that the rate of FCH phosphorylation by yeast CK, as well as the rate of FCH uptake by PC-3 cancer cells, does approach that of natural choline.[18] Thus, for now, it may be sufficient to consider FCH as a prototypical ^{18}F choline until the optimal formulation is known.

Given the role of extrinsic choline in eukaryotic phospholipid synthesis, tracers derived from choline were proposed as imaging agents for measuring proliferative or mitogenic activity. The observation that phosphorylcholine can trigger DNA synthesis in quiescent NIH3T3 fibroblasts, along with the observation that inhibition of CK (by hemicholinium-3) can block proliferation activity unless bypassed by extrinsic phosphorylcholine, supports CK as a regulator of mitogenic activity.[22] However, to date, few studies have shown a strong correlation between markers of proliferation in malignant tumors and choline radiopharmaceutical uptake in vivo. A study that compared tumor uptake of ^{11}C choline and ki-67 labeling in malignant prostate tissues did not support the presence of a direct correlation between ^{11}C choline uptake and cellular proliferation rate.[23] One possibility is that transformation reduces the efficiency of choline metabolism, resulting in a disassociation of choline uptake rate and cell membrane synthesis rate. The general finding of high levels of phosphorylcholine in a variety of tumor types is consistent with the argument that these rates are not well-coupled. Despite the apparent avidity of choline tracers in a variety of malignancies, further research will be needed to determine whether clinically relevant markers of tumor growth can be derived from the measured uptake of these compounds.

The choline metabolite peak on magnetic resonance spectroscopy (MRS) also has been proposed as an indicator of malignancy or proliferation.[24] However, correlations between ^{18}F-FCH or ^{11}C choline uptake on PET and choline metabolite concentrations on MRS have not always been observed, alluding to the possibility that increased choline spectral peaks on MRS may not specifically reflect free choline or the active accumulation of choline metabolites by cells.[25,26] For example, in the case of a tumefactive demyelinating lesion, where increases in choline metabolite concentrations are frequently observed with MRS (presumably due to demy-elination), there may not be corresponding increases in the uptake of ^{11}C choline or ^{18}F- FCH.[26,27] In malignant glial tumors, where mitogenic activity would be expected to result in the active utilization of choline, a direct regional correlation has been observed between ^{18}F-FCH uptake and choline metabolite peaks on spectroscopy.[26] Without a better understanding of the biochemical basis of what is measured by both MRS and choline-based PET imaging, it will be difficult to integrate this information for clinical purposes.[24] Because there is occasional discordance, there will most likely be complementary value to both measures.

Because the authors of several in vitro studies have suggested the cellular uptake of FCH is dependent on choline transporter and CK activity, we explored the expression of these proteins in an array of 30 distinct tumor types. Abnormal expression of one or both proteins was observed in most malignancies, including prostate carcinoma, glial tumors, breast carcinoma, lymphoma, sarcoma, esophageal carcinoma, melanoma, and lung carcinoma. In the case of glial tumors and breast cancer, the degree of CK expression was found to correspond to tumor grade (Fig. 1). Pilot investigations with FCH-PET in a limited number of patients with these diseases have produced analogous results supporting the potential of radiolabeled choline metabolic substrates for imaging a broad variety of neoplasms (Fig. 2).

DeGrado and coworkers pursued further work to develop FCH as a clinical imaging probe. These investigators performed the first human dosimetry study of ^{18}F-FCH to determine the dose-critical organ and radiation dose limit for research studies. While the favorable dosimetry of FCH and ability to perform scans shortly after injection allows for excellent image quality at commonly administered doses, newer PET instruments with very high count-rate performance will likely be capable of optimal image quality at a lower dose.[28]

Prostate Cancer Imaging With Fluorocholine

Prostate cancer is the second-leading cause of cancer death in American men older than 50 years of age. Clinically, there has been a long-standing need for better imaging methods that can be applied to diagnose, risk stratify, stage, and direct treatments for prostate cancer. Conventional ^{18}F-fluorodeoxyglucose (FDG)-PET has proven to be of limited usefulness for diagnosing prostate cancer, although it does appear possible to detect advanced or metastatic prostate cancer with this technique.[29,30] To compare the avidity of FCH and FDG for prostate cancer, Price and coworkers performed both FCH-PET and FDG-PET in 18 patients with prostate cancer.[31] They found that more lesions were identifiable with FCH-PET, including lesions of the prostate, bone, and soft tissues. In addition, an in vitro component to this study revealed significantly greater uptake of FCH compared with FDG in cell cultures of androgen-dependent (LnCAP) and -independent (PC-3) prostate cancer. These results favor the use of FCH rather than FDG for prostate cancer imaging.
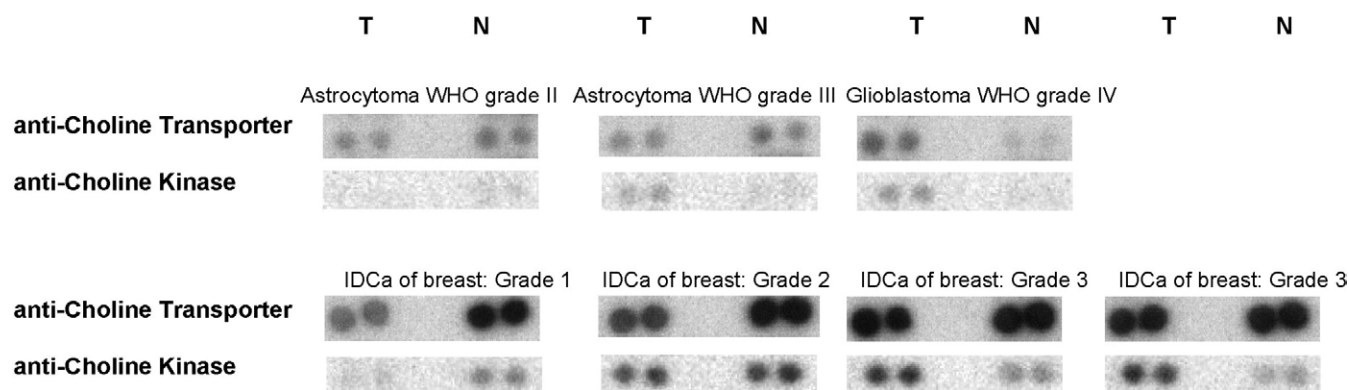
Figure 1 Dot blot analysis of choline transporter and choline kinase (CK) expression in tumor lysates (T) of glial tumors and breast carcinomas and their corresponding normal (N) tissue controls. Washing conditions were optimized for CK expression by use of Western blot standards. Top row: CK expression (and, to a less-appreciable extent, choline transporter expression) increases with increasing World Health Organization tumor grade in malignant glial tumors. Bottom Row: Both choline transporter and CK expression increases with increasing breast cancer grade. Malignant expression of CK exceeds that of normal breast tissue, but normal tissue expression of choline transporter exceeds that of malignancy. IDCa, infiltrating ductal carcinoma.

Subsequently, a number of early clinical studies have investigated the potential usefulness of FCH-PET for diagnosing or localizing primary prostate cancer. Currently, ultrasound-guided prostate biopsy is the most common method for diagnosing this disease. However, conventional prostate biopsy using standard 6 or 12 needle templates is susceptible to sampling error, with a false-negative rate as high as 20% regardless of the number of needles used.[32,33] A few studies have preliminarily investigated FCH-PET as a method for improving cancer localization in the prostate. In a study by Kwee and coworkers,[34] prostate sextants harboring malignancy were found to demonstrate significantly higher FCH uptake than biopsy-negative sextants, with the cancer-affected side in 6 of 6 patients with unilaterally positive prostate biopsies demonstrating the highest uptake on FCH-PET. By identifying areas within the prostate that have the highest likelihood of malignancy, FCH-PET could potentially serve to identify areas for additional biopsy, thus potentially reducing the false-negative rate of the procedure.

It is worth noting that, with FCH-PET, delayed imaging may be required for adequate tracer uptake and distribution in the prostate. In a study by Kwee and coworkers, delayed FCH-PET imaging up to 1-hour after injection led to both a significant increase in measured uptake by malignant tumors in the prostate, as well as a significant decrease in uptake in benign areas.[35] In contrast, FCH-PET imaging of the prostate at 2 minutes after injection was not found to be useful for differentiating between benign hyperplasia and malignancy in the prostate.[36] Additional studies using whole-prostate specimen analysis for histopathologic correlations are underway to better estimate the accuracy of intraprostatic cancer localization with FCH-PET.

The advent of hybrid PET/computed tomography (CT) has led to a number of studies using FCH for whole-body staging of prostate cancer.[36–39] Because of its ability to provide structural/anatomical correlation, PET/CT is advantageous for localizing disease in lymph nodes, a common route of spread in prostate cancer. In a study by Schmid and coworkers,[36] FCH PET/CT was able to identify local and distant sites of disease in both patients with newly diagnosed prostate cancer and patients suspected of having recurrent cancer. Lesions that were identified included local recurrent tumors, nodal metastases, and skeletal metastases. Thus, FCH PET/CT may have the potential to provide information that can be used for deciding between regional and systemic treatment in both patients with newly diagnosed and recurrent prostate cancer.
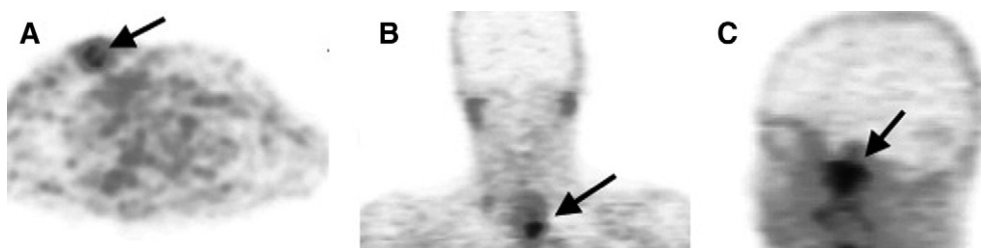

Figure 2 FCH-PET scans in patients with malignant breast, esophageal, and nasopharyngeal cancers. (A) Transaxial PET image: increased FCH uptake in right breast carcinoma (arrow). (B) Coronal PET image: increased FCH uptake in esophageal carcinoma. (C) Saggital PET image: increased FCH uptake in recurrent metastatic nasopharyngeal carcinoma.
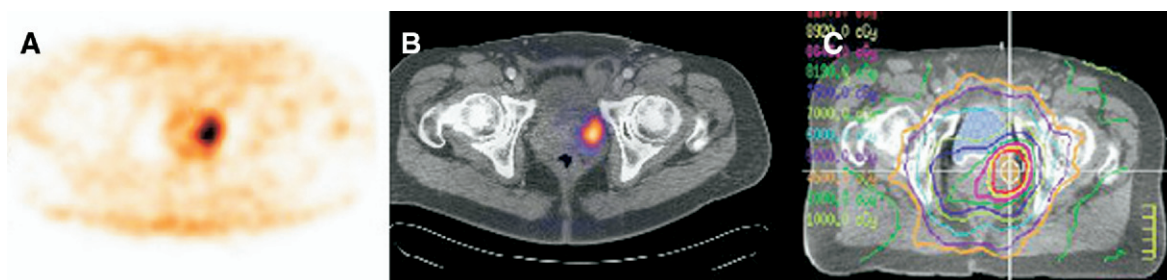
Figure 3 FCH-PET-guided radiotherapy. (A) The black area on this transaxial PET image corresponds to increased FCH uptake in a malignant tumor situated in the left lobe of the prostate gland. In an experimental treatment plan, this PET-defined biological target volume (BTV) will be prescribed a radiation dose of at least 90 Gy. (B) A "fused" PET/CT image is used to plan the radiation treatment. In this patient, the prostate volume was 62 mL and the BTV volume was 14 mL. (C) The experimental treatment plan is summarized by colored lines corresponding to prescribed iso-doses of radiation. Doses of 91 Gy and 76 Gy were prescribed to the BTV and prostate, respectively, without significantly increasing radiation exposure to un-involved organs (rectum and bladder).

With regard to recurrent prostate cancer, several other studies using FCH-PET/CT have explored the relationship between prostate-specific antigen (PSA) level and lesion detection in patients with posttreatment increases in PSA. A study by Heinisch and coworkers found that FCH PET/CT detected tumor recurrences in only half of patients suspected of having recurrent prostate cancer with a PSA level <5 ng/dL.[38] In another study of 100 patients by Cimitan and coworkers, use of FCH-PET/CT led to the identification of prostate cancer recurrence in 53 of the patients.[39] In this study, 89% of the patients with presumably false-negative FCH-PET/CT scans had a serum PSA level <4 ng/dL. Thus, FCH-PET/CT does appear to be less sensitive for recurrent prostate cancer if the PSA level is low. However, it is worth noting that the use of FCH-PET in these studies had value for distinguishing between local and distant metastatic recurrence. Such a distinction is clinically relevant since it helps determine the appropriateness of local salvage therapy.

With regard to clinical decision making and treatment planning, FCH-PET/CT may also have value for newly diagnosed patients with prostate cancer.[34,36,40] Recently, Langsteger and coworkers[40] reported that FCH-PET/CT performed during initial preoperative staging for prostate cancer patients who were at high risk for metastases (eg, Gleason score >7 or PSA >10 ng/mL or doubling time <3months) led to downstaging in 4% of cases and upstaging in 12% with potential consequential changes in clinical management. In addition to staging, FCH PET/CT could also prove useful for planning treatments for patients with newly diagnosed prostate cancer. For example, with intensity-modulated radiation therapy, or a combination of brachytherapy and external radiation therapy, it may be possible to apply very high radiation doses to specific targets in the prostate identified with FCH PET, while still treating the remainder of the prostate with a conventional therapeutic radiation dose in addition to maintaining acceptable levels of radiation exposure to uninvolved organs. The current conventional approach is to treat the prostate uniformly with a radiation dose that is usually limited by toxicity concerns rather than the radiation sensitivity of the tumors. By targeting tumor areas specifically, it becomes possible to apply higher doses to the most critical targets while still maintaining a reasonably safe level of radiation exposure to uninvolved areas. We examined the feasibility and safety of this concept by applying FCH-PET to guide the augmentation of radiation dose to prostate tumors. An experimental intensity-modulated radiation therapy protocol was developed to deliver the highest radiation dose (at least 90 Gy) to a biological target volume (BTV) that corresponds to the area of highest ¹⁸F-FCH uptake in the prostate. This protocol was based on the premise that the area of highest tracer uptake on prostate PET images represents the dominant area of malignancy in the prostate.[34,35,41] While treating the BTV with supra-conventional radiation doses, the experimental treatment protocol was still designed to maintain a tolerable dose to surrounding normal tissues while achieving a conventional therapeutic dose of 76 Gy to the remainder of the prostate gland. In this manner, the experimental treatment would be expected to be at least equivalent to conventional treatments with regards to potential efficacy. Using standard dose volume histograms to estimate the radiation exposure to uninvolved organs (rectum and bladder), we were able to preliminarily assess the potential safety of both experimental and conventional treatment plans.

Figure 3 illustrates the experimental treatment approach. In this plan, a dose of 91 Gy could be delivered to the BTV while attaining a minimum dose of 76 Gy to the remainder of the prostate. This experimental plan also met desired safety constraints, with less than 20% of the rectal wall receiving 70 Gy or higher dose and less than 25% of the bladder volume receiving 75 Gy or higher dose. Although not actually used, this plan demonstrates the feasibility of selective radiation dose escalation using FCH-PET as a means to target high-risk intraprostatic regions, while still achieving therapeutic goals for the remainder of the prostate and meeting the safety constraints of other organs. Given that the likelihood of local tumor control after external beam radiotherapy for organ-confined prostate cancer is directly related to radiation dose, this approach may potentially improve the therapeutic efficacy of radiation therapy, while maintaining an acceptable safety profile. A clinical trial will ultimately be required to

evaluate the clinical benefit of this approach in a suitable number of patients.

Brain Imaging

DeGrado and coworkers first reported brain tumor imaging with ^{18}F-FCH in a patient with biopsy proven recurrent anaplastic astrocytoma.[18] These investigators noted that the low concentration of FCH in normal cerebral cortex allowed for excellent delineation of the tumor from normal brain. They observed that a ~10:1 tumor-to-cortex ratio was achievable within 5-minutes of tracer injection. FDG-PET revealed a corresponding area of increased FDG uptake; however, the tumor boundaries were difficult to assess with FDG because of high uptake by normal cortex. Although overall there is very little uptake of FCH in the brain, it is worth noting that physiologic uptake does occur in the pituitary gland and choroids plexus. Physiologic uptake in these areas should not be difficult to recognized, especially if the FCH-PET images are interpreted in conjunction with brain magnetic resonance imaging (MRI).

The use of FCH-PET to evaluate primary and metastatic brain tumors was investigated subsequently by Kwee and coworkers in 30 patients with solitary brain lesions.[42] This study found that high-grade gliomas, brain metastases, and benign lesions could be distinguished on the basis of measured FCH uptake, with metastases demonstrating significantly greater uptake than high-grade gliomas. Furthermore, high-grade gliomas were distinguished in this study by a characteristic pattern of FCH uptake consisting of increased FCH uptake beyond the areas of contrast enhancement on MRI (Fig. 4). This pattern of "peritumoral uptake" is hypothesized to be due to infiltration of the white-matter tracts by malignant cells. Such a process of occult tumor spread is known to occur frequently in high-grade gliomas but seldom in metastases.[43–46] This study also found that lesions with low FCH uptake were likely to remain stable radiographically at 1-year of follow-up. However, because this study did not include low-grade tumors, further investigations in a broader spectrum of patients are warranted to evaluate the diagnostic and prognostic value of this technique in patients presenting with an intracranial mass.

Liver Imaging

Hepatocellular carcinoma (HCC) is the fifth most frequent cancer worldwide and the most frequent cause of death in cirrhotic patients.[1] The sensitivity of FDG-PET for the detection of HCC is suboptimal, ranging between 50% and 70%.[3,4] Given that the use of MRS demonstrates high choline content in HCC, it may be possible to detect this disease using FCH,[7] despite the fact that the liver demonstrates significant physiologic uptake of FCH. A proof of concept study was performed by Talbot and coworkers, comparing FDG PET/CT with FCH PET/CT in 9 patients known to have HCC.[8] All 9 patients were positive with FCH (100%) in contrast to 5 with FDG (56%). Despite significant FCH uptake by unaffected portions of the liver, HCC lesions as small as 9-mm in size
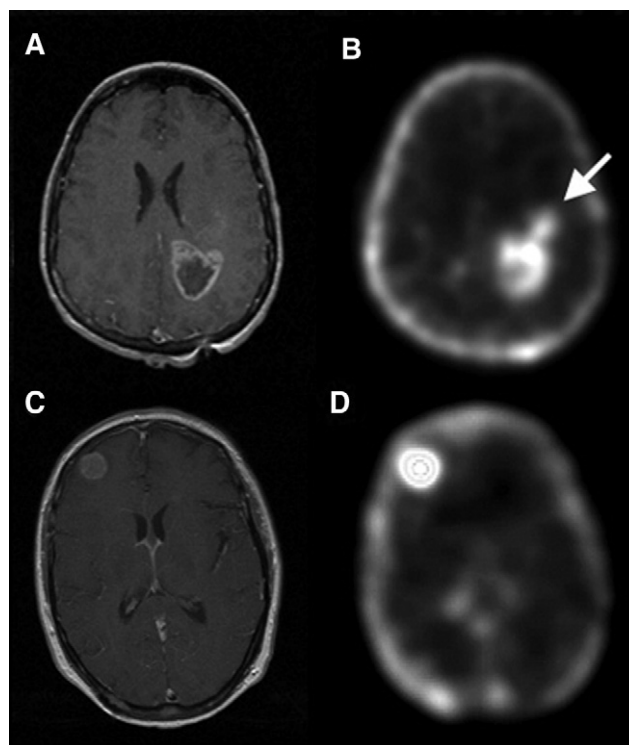

Figure 4 MRI and FCH-PET in primary (A and B) and metastatic (C and D) brain tumors. (A) Glioblastoma multiforme observed as a ring-enhancing lesion in the left occipital lobe on T1-weighted MRI. (B) The corresponding area on PET shows increased FCH uptake. However, abnormal uptake (arrow) was also noted anteriorly beyond the area of enhancement. This characteristic ("peritumoral uptake") appears specific to high-grade gliomas. C) Metastatic ovarian carcinoma seen as a ring-enhancing lesion in the right frontal lobe on T1-weighted MRI. (B) In contrast to the previous case, increased FCH uptake on PET corresponds only to the region of contrast enhancement on MRI.

could be distinguished visually, and by semiquantitative uptake measurement, on FCH PET/CT (Fig 5 and 6). A trend for greater uptake of FCH in well-differentiated HCC compared with moderate and poorly differentiated HCC also was observed in this study. In 2 cases of metastatic HCC, FCH was also taken-up by distant metastases to the lungs and bone. In contrast, colorectal carcinoma metastatic to the liver was found to demonstrate low uptake of FCH relative to the liver, thus potentially distinguishing these lesions from those of HCC (Fig. 7). However, the lack of uptake by metastatic colorectal carcinoma does suggest that FCH PET may be insensitive for colorectal carcinoma and possibly other types of metastases. A subsequent study is currently underway in patients with liver masses to prospectively compare the relative accuracies of FCH PET/CT and FDG PET/CT for the diagnosis, staging, and localization of liver tumors.

Practical Issues and Potential Pitfalls in FCH-PET Imaging

FCH is effectively cleared from the blood within minutes after its intravenous administration. During this brief period
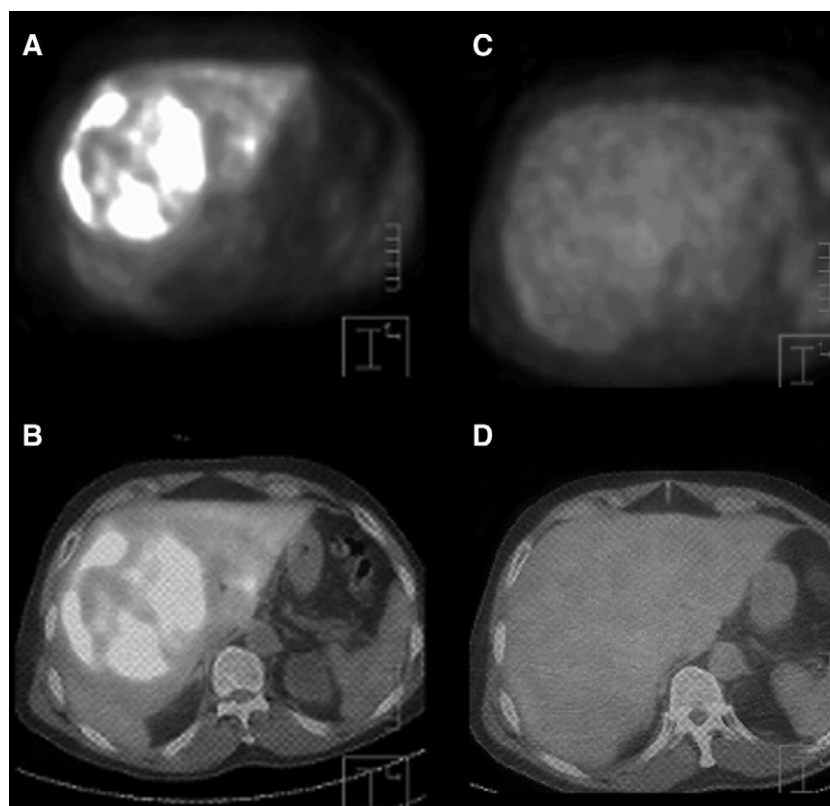
Figure 5 Large liver mass in a patient with hepatitis C virus infection. A liver lesion with intense FCH uptake (maximum standardized uptake value = 20) was noted on PET (A). The lesion measures 12.5 cm and involves Couinaud segments VI and VIII on FCH PET/CT (B). No abnormal uptake is noted on FDG PET (C) and PET/CT (D). Grade 2 well-differentiated hepatocellular carcinoma was confirmed after surgery.

of rapid clearance, FCH is capable of significant uptake and retention by malignant tumors, while achieving minimal retention in organs such as the heart and brain. These features of FCH are advantageous, because they allow for very efficient scanning of the entire body. However, as a consequence of rapid blood clearance, the tissue distribution of FCH is likely to be dependent on delivery (ie, blood flow). Although a study has not been done to correlate blood flow and choline uptake in a tumor model, the correlation is believed to be high since there is little redistribution from other organs after clearance from the blood, and the metabolism of FCH to noncholine metabolites leaves no alternative mechanism for accumulation in tumors. Thus, the influence of blood flow on FCH distribution should be carefully considered in image interpretations, particularly if FCH PET is used to monitor an intervention that modulates blood flow.

A practical end result of the rapid in vivo kinetics of FCH is a whole-body PET scan that can be completed shortly after tracer injection. However, rapid clearance of background activity necessitates the existence of a normal process by which the tracer is eliminated from circulation. In the case of ^{18}F-FCH, this process depends on physiologic tracer uptake by the kidneys. Thus, like with FDG, there can be significant accumulation of radioactivity in the urine over time. This activity has the potential to obscure malignant lesions near the genitourinary tract. However, based on collective experiences in patients with prostate cancer, the urinary excretion of FCH has seldom caused problems with image interpretation.[31,34,35,38,39] This may be caused in part by the effects of urodynamic alterations, which are common in men with prostate disease. Conditions such as urinary retention may serve inadvertently to reduce the concentration of radioactivity in the bladder through dilution effects. In addition, PET imaging protocols with FCH have the flexibility to acquire images during a time when bladder radioactivity is not high.[34,36] For example, using a dynamic scan acquisition, it is possible to retrospectively sum the frames acquired just before the appearance of urinary radioactivity to provide a pelvic image of early FCH distribution. Although hydration or fluid restriction have been proposed as a means to influence urinary excretion, we have not been able to observe a certain effect of these interventions on the appearance of urinary radioactivity. The influence of diet or fasting on the biological distribution of FCH is also not known. Although bladder catheterization and irrigation can effectively eliminate artifacts from bladder radioactivity,[47] we have not routinely used this technique in studying patients with prostate cancer because these patients may be at increased risk of complications after bladder catheterization. Finally, with regards to avoiding potential interpretive pitfalls, the use of PET/CT has helped tremendously by providing anatomical references for findings in the retroperitoneum and pelvis.
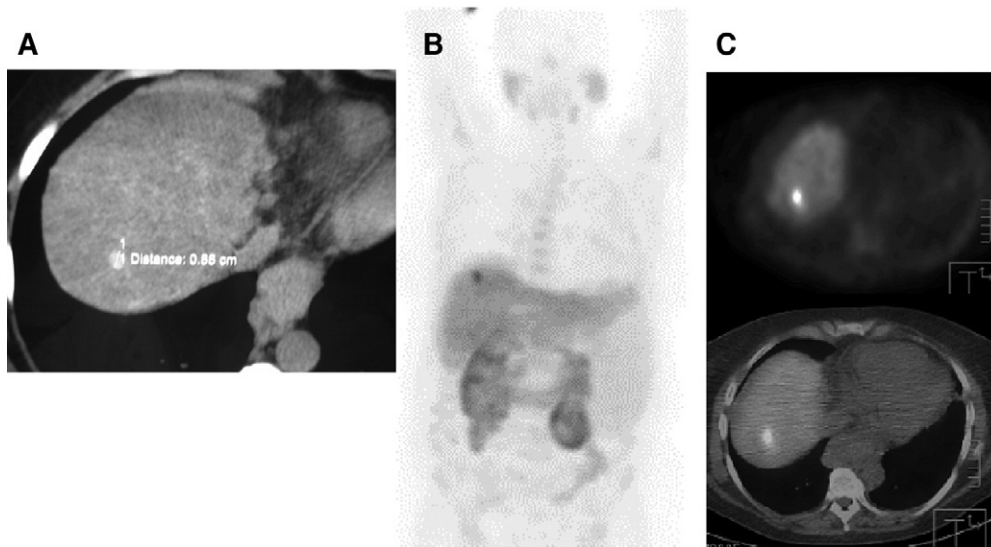
Figure 6 Recurrent hepatocellular carcinoma in a patient with alcoholic cirrhosis. Serum alpha-foeto protein levels were elevated at 1,250 ng/mL. On CT, a 9-mm nodule was found in the segment VII of the liver (A). The lesion demonstrated significant FCH uptake relative to surrounding liver, as shown on maximum intensity projection image (B) and corresponding FCH PET (C, top) and PET/CT images (C, bottom).

Uptake in benign conditions such as infection is known to limit the specificity of FDG-PET for malignancy. It remains plausible that inflammation or benign proliferative processes can lead to an increase in FCH uptake, thus also reducing the specificity FCH-PET for malignancy. It is already known that some benign conditions can cause a transient increase in FCH uptake. Price and coworkers has reported that benign inguinal lymph nodes can demonstrate transiently increased FCH uptake during the first 5 minutes of injection, but that uptake within these benign lymph nodes diminishes rapidly to background levels by 20 minutes.[31] We have also observed this "washout" phenomenon in other lymphatic regions, including cervical lymph nodes. Thus, as with the prostate,[35] delayed or dynamic imaging may be required to resolve issues of transient increases in uptake in benign tissues.

It remains possible that benign proliferative conditions can lead to a persistent increase in choline tracer uptake. With ^{11}C choline, persistent increases in uptake have been observed in cases of liver regeneration posthepatectomy, proliferative synovitis, and inflammatory lung nodules.[48-50] Whether the same holds true for ^{18}F-FCH is not known at this time. In one animal model, FCH uptake in a sterile inflammatory lesion was much less than uptake in an implanted tumor, whereas the uptake of tritium-labeled deoxyglucose was relatively increased in both types of lesions.[51] Other experimental models suggest tissue inflammation (caused by infection or acute radiation injury) can lead to measurable increases in FCH uptake,[17,52] whereas blood–brain barrier disruption alone in the absence of inflammation (as modeled by cryolesions) does not.[17] In lesions caused by radiation injury, the uptake of FCH is lower than uptake in malignant tumors, supporting FCH as potentially useful for distinguishing tumor recurrence from necrosis after radiation therapy.[17] Further in vivo studies in a wider spectrum of diseases are needed ascertain the diagnostic specificity of
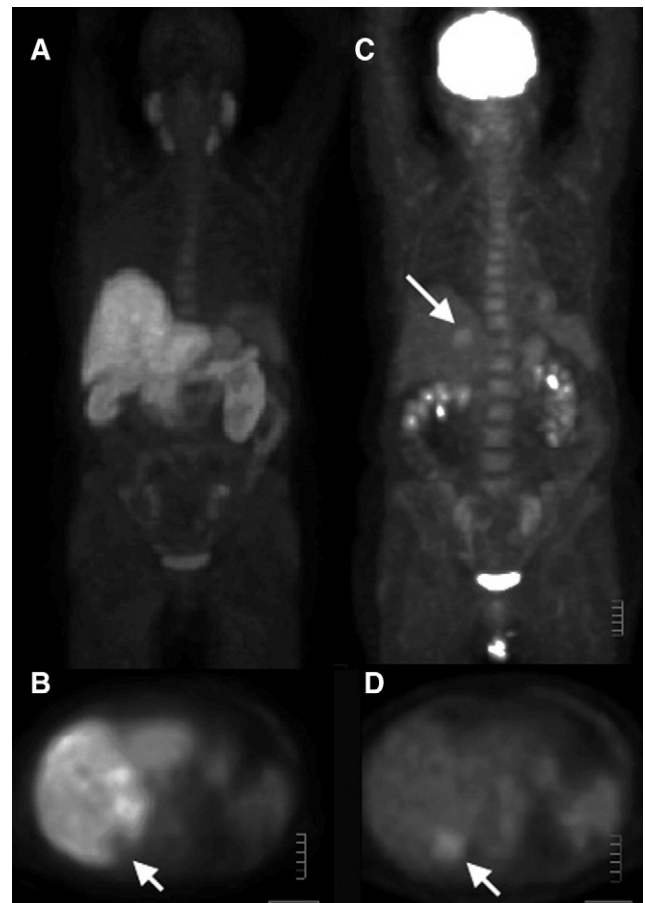

Figure 7 FCH PET (A and B) and FDG PET (C and D) images of a hepatic mass in a patient with a previous history of rectal adenocarcinoma. The mass (arrow) took up FDG and not FCH, appearing photopenic on FCH PET as compared with the surrounding healthy liver tissue. The lesion was confirmed to be metastatic rectal adenocarcinoma at surgery.

FCH PET when applied to the evaluation of tumors and tumor recurrences.

Conclusion

The ¹⁸F-labeled choline analogs, and in particular FCH, are currently under investigation as oncologic probes for the detection and monitoring of malignancies. These probes may be viewed as in vivo biomarkers of choline transporter and CK activity, although their uptake may also reflect a component of tissue perfusion. To date, the majority of studies have focused on the use of the FCH PET to evaluate prostate cancer, with preliminary studies having provided encouraging results for detecting primary and metastatic cancer. Experience in other tumor types is growing, including work involving brain and liver tumors. In most organs, high tumor-to-background contrast is achieved with FCH within minutes of injection. Excellent discrimination can be achieved in the brain, where there is very little physiologic uptake of FCH. In other organs such as the liver, malignant discrimination appears still possible despite a moderate degree of physiologic uptake. The rapid circulatory clearance of FCH is advantageous from a practical point of view since it allows completion of a PET scan within minutes of tracer injection. Although the renal excretion of FCH is not ideal for evaluations of the urinary tract, it has not proven intractable in actual practice. Therefore, FCH and other choline derivatives may possess the features of efficiency and ease of use that is important for successful clinical application.

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