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INTRODUCTION: Mammography has proven effective for reducing mortality from breast cancer, however detection of some lesions is limited by dense breast tissue that obscures the tumor, and the specificity of mammography is low. Functional imaging with positron emission tomography (PET) may help improve detection and diagnosis of breast cancer, although, the diagnostic accuracy of primary breast tumors has been found to be hindered by low glycolytic rates, and nonspecific uptake by nonmalignant breast tissue. Imaging with fluorocholine (FCH) may help to overcome these limitations. An efficient and practical synthesis of FCH has been developed at our institution. The purpose of the study is to evaluate the potential utility of F-18 labeled choline (FCH) as a positron emission tomography (PET) radiotracer for detection and diagnosis of breast cancer in women with highly suspicious breast lesions. Our goals are to determine: 1) the correlation between FCH uptake in primary breast cancer tumors and the histologic tumor type from subsequent pathology; 2) how FCH uptake in breast cancer tumors compares to F-18 2-fluoro-2-deoxy-glucose (FDG) (which is the current standard cancer imaging agent for PET) uptake in breast cancer tumors; and 3) if FCH can improve local staging of the breast in patients with recently diagnosed breast cancer (invasive or *in situ*).

BODY: To date, no subjects have been recruited or enrolled into this study, and the project has received a second 12-month no cost time extension. In order to satisfy all the requirements of the Human Subjects Protection Scientist for Human Subjects Approval prior to beginning the study, it has been required that we apply for an IND from the FDA for the experimental drug fluorocholine. The radiotracer FCH is an investigational radiotracer imaging agent currently produced under the sanction of the Radioactive Drug Research Committee (RDRC) and IRB at Duke University. To date, no adverse events have occurred in our experience with PET imaging using flurocholine analogs in

approximately 25 patients. Regarding the IND status, we are developing an automated synthesis system for making the FCH, and information on this process was requested and is pending for the IND. We are currently still working on the synthesis modules for the fluorocholine, and the hardware has been completed. Programming and optimization of the system is underway. Following completion of the automated synthesis process, and approval of use of the fluorocholine by the FDA, phase 1 studies will be underway. When we have approval for phase 2 studies, we will then finalize the Human Subjects Approval and our Institutional Review Board approval, and should then be able to recruit patients into the study as previously outlined.

KEY RESEARCH ACCOMPLISHMENTS: Progress toward IND final approval has occurred, including development of the automated synthesis system for the fluorocholine, with completion of the hardware components. Programming and optimization of the system is underway, and we have completed the standard operating procedure manual for this process. Phase 1 studies should be underway soon, with anticipated completion in spring 2004.

REPORTABLE OUTCOMES: Not applicable, pending IND approval as above

CONCLUSIONS: Following FDA approval of the fluorocholine as an investigational new drug, Human Subjects and IRB final approval for the study, 20 patients will be recruited into the study. Patients will be imaged on an experimental dedicated PET mammography unit recently developed for Duke University Medical Center, which has been successfully used to image and identify breast carcinomas seen at mammography. Each subject will be scanned with FCH-PET and FDG-PET on different days within a period of 2 weeks, at least one day apart. Imaging will proceed after the radiotracer is administered and an uptake period of approximately 5 minutes for FCH and 45 minutes for FDG has elapsed. Data acquisition will last up to 5 minutes per imaging position. The corresponding mammographic films obtained for routine clinical evaluation will be subsequently digitized and transferred to and displayed on the same computer as the digital PEM images. Findings at PEM imaging with FCH and FDG will be reviewed and compared, and correlated with the mammograms and histology of the known breast cancer.

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