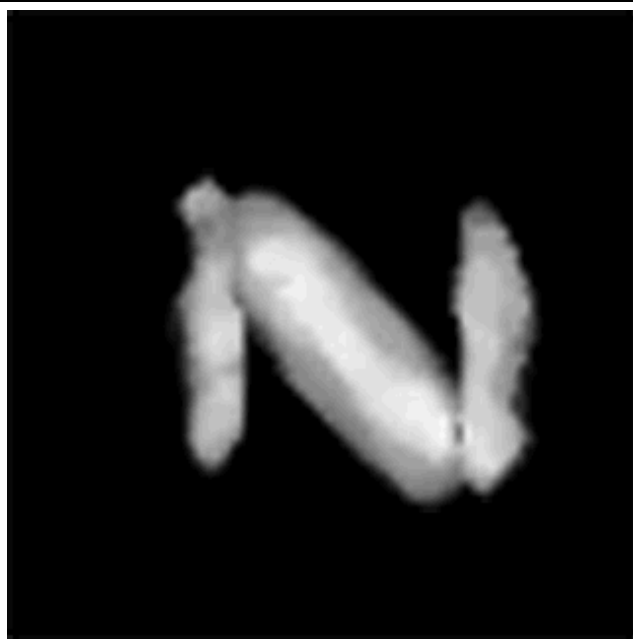


Neutron-Based Imaging May Lead to Earlier Breast Cancer Diagnosis

Carey Floyd (carey.floyd@duke.edu)^{1,2}, C Howell², A Kapadia², B Harrawood¹, J Xia², G Tourassi¹, (1)Duke University Medical Center, Durham,NC, (2)Duke University, Durham,NC

Lay-language Version of WE-D-315-6
Wednesday, July 28, 2:45 PM
2004 AAPM Annual Meeting, Pittsburgh, PA



Neutron Image of an Iron-Copper Sample

INTRODUCTION

In an active collaboration between the radiology and physics departments, Duke University researchers are developing a new approach to molecular imaging called Neutron Stimulated Emission Computed Tomography (NSECT). The long-term goal is to develop technology for non-invasively mapping the concentration of any isotope, stable or radioactive, in any selected 3-D volume of the body. A practical application will be to diagnose breast cancer earlier than previously possible by imaging the relative concentrations of trace elements in breast tissue and looking for subtle differences in chemical composition that are known to exist between benign and malignant tissue. While drawing upon the strengths of existing analysis and imaging techniques, NSECT represents a unique approach to 3D imaging that previously has not been developed for human imaging or for quantitative biological measurement.

NEUTRON IMAGING: THE BASIC APPROACH

NSECT is implemented by illuminating the body with fast neutrons (possessing energies between 1 and 10 MeV). As the neutrons collide with the body, they deposit excess energy in the nuclei (positively charged cores) of atoms and molecules. To release this excess energy, the nuclei release gamma-ray photons. The energies of the photons depend on the type of atom or molecule to which the nuclei belongs. The gamma ray energies range from about 100 keV to 6 MeV for all natural elements except helium (which emits gammas at 25MeV) and hydrogen (which has no excited states and thus is not stimulated to emit gammas). A detector then records these gamma rays at various angles. By reconstructing the locations and energies of the gamma rays, one can create detailed 3D maps that show the concentration of specific chemical isotopes throughout the body.

THE ADVANTAGES OF NEUTRON IMAGING

Compared to other existing and emerging spectroscopic imaging techniques, NSECT offers several potential advantages for *in vivo* applications. Magnetic resonance spectroscopy (MRS) has proven successful for a limited set of isotopes and the response of these isotopes can be strongly influenced by

their molecular binding. Compared to XRF (x-ray fluorescence) which is limited to thin samples or shallow depths in tissue. NSECT can image over the full thickness of the body.

NSECT has several unique advantages: 1) Any isotope, stable or radioactive, can be imaged (with the exception of hydrogen or helium). 2) Neutrons are highly penetrating particles and they can image structures deep within the body that cannot be reached using most other probes. 3) NSECT can obtain true 3D maps of chemical isotopes, by using detector geometries that yield 3D information.

EARLY DIAGNOSIS OF CANCER

Several different investigators have reported statistically significant differences in the concentration of trace elements in benign and malignant human tissue. The biochemical basis for this difference is not well understood but has been demonstrated experimentally. These differences have been observed in every cancer for which these measurements have been made and include breast, colon, lung, and prostate. While a variety of techniques have been used to measure these differences in elemental composition, none of the techniques can be adapted to provide an *in vivo* diagnostic test. The main difficulties include either a highly destructive procedure or the requirement of a very thin isolated tissue sample.

NSECT is designed as a non-invasive technique to provide three-dimensional images in which the concentration of elemental isotopes is measured in each region of the reconstructed 3D image. Cancer would then be diagnosed from the relative concentrations of certain elements following the earlier work that used highly invasive techniques.

Compared to existing imaging techniques for identifying breast cancer NSECT can identify cancer by its change in elemental concentration of the tissues long before the cancer has begun to cause the anatomical changes (such as the formation of dense tumors or microcalcifications) that are detected by mammography, CT, ultrasound, or MRI.

The range of applications could extend from routine screening for breast cancer at very early and potentially at precancerous stages, to fundamental research in molecular biology, genomic phenotyping (the study of how genes are expressed in their environment), metallo-protein transport (the movement of compounds such as hemoglobin through the body). Given sufficient sensitivity, NSECT could image stable isotope tracers and molecular labels. Not only could this dramatically expand the number and diagnostic capability of metabolic tracers, but could allow these tracers to be followed for the full extent of their biological life. The ability to follow the transport of stable isotopes would provide a new tool to shorten the time required for pharmaceutical development. This approach would rely upon being able to perform stoichiometry: determining the relative amounts of C, H, N, O and figuring out what macromolecules are in an image voxel (volume element). Another potential approach would be to use stable isotopes as tracers and tag the pharmaceuticals to determine where they go.

THE AAPM TALK

At the 2004 AAPM meeting, the Duke team will present the first 3D images ever reconstructed from the emission of characteristic gamma rays stimulated by fast neutrons. The images, of an iron-copper sample, demonstrate NSECT's ability to completely distinguish between the iron and copper that made up the sample.

3D image reconstruction for a metal sample made of two elements

An iron-copper sample was scanned by moving it through a 7 MeV neutron beam. The neutron beam enters from the top and 11 beam locations are shown. The neutrons scatter from the sample and its metal constituents release the excess energy from the collision by emitting gamma-ray photons. The photons are

acquired in the detector shown on the left. After the neutron beam is scanned over the 11 positions (actually the metal sample is moved), the sample is rotated to the next angle. The sample was rotated through 22.5 degrees seven times for eight angular samples at 0, 22.5, 45, 57.5, 90, 112.5, 135, and 157.5 degrees.

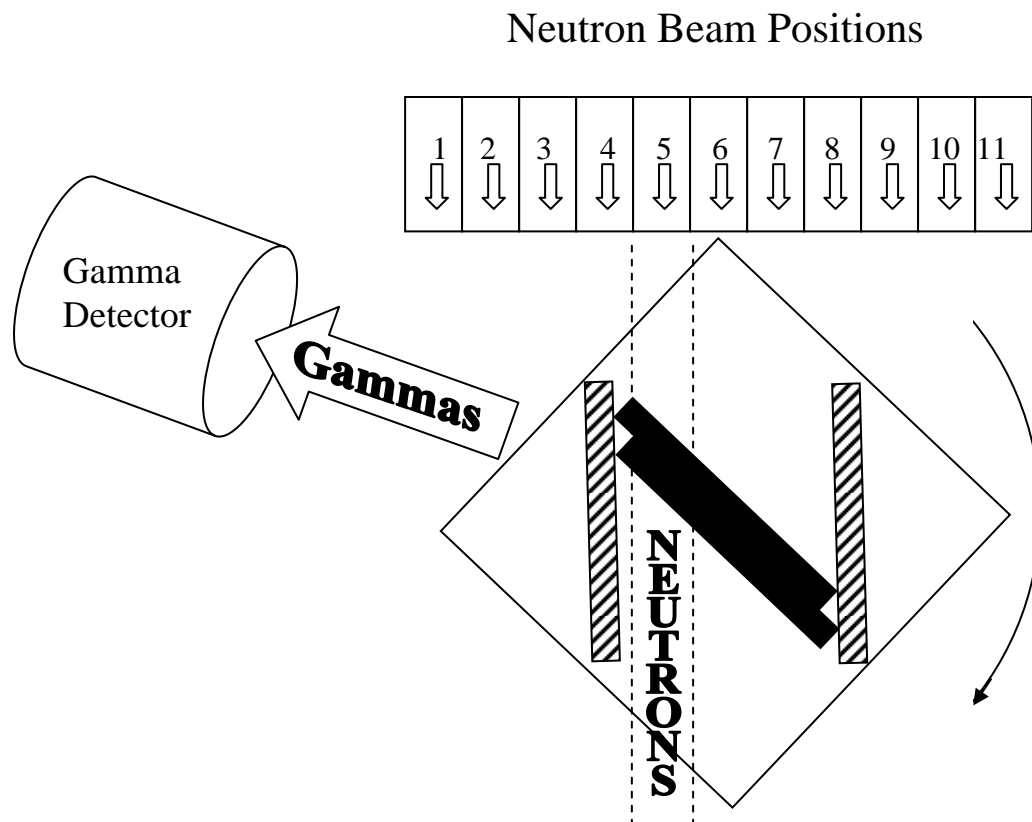
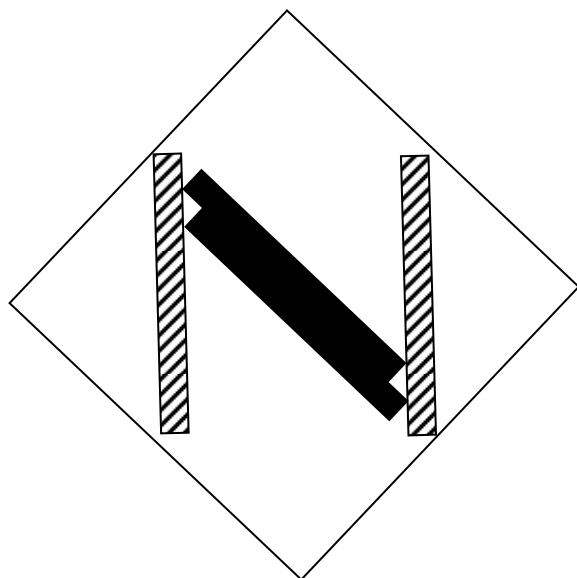
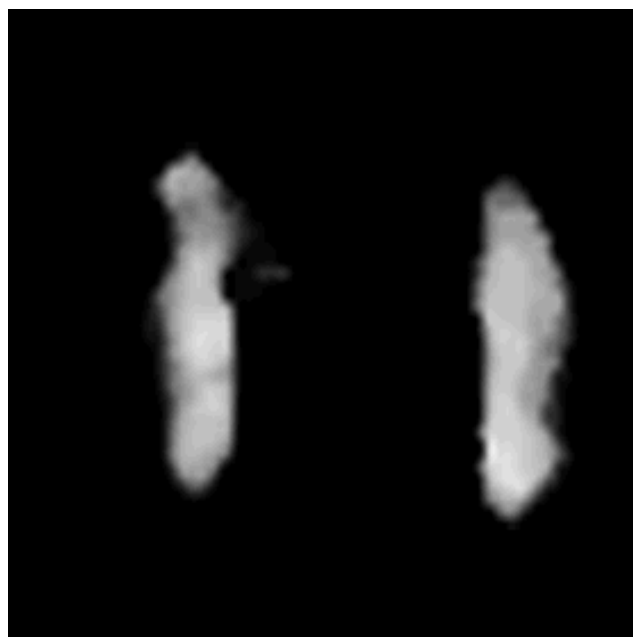


Fig. 1 Top view of sample and 3-D acquisition geometry. Striped bars are copper with length 6 cm, height 3 cm, and thickness 0.7 cm. Solid bars are iron with the same dimensions. The maximum dimension of the metal sample is 9 cm.



Top view of sample. Striped bars are copper with length 6 cm, height 3 cm, and thickness 0.7 cm. Solid bars are iron with the same dimensions. The maximum dimension of the sample is 9 cm.



The image reconstructed from only those photons whose energies were characteristic of copper.

NEXT STEPS

While the physical principles behind this technique have been known for many years and a number of similar techniques have been proposed or simulated by different investigators over the past fifteen years, these images represent the first successful and practical demonstration. As the technique is refined to detect more subtle concentrations of isotopes, the next steps are focused on designing and constructing a prototype system that can image the distribution of iron in the liver in order to diagnose hemochromatosis (iron overload in the liver) without the need for a biopsy. The technology developed will not be restricted to imaging iron but will have a broad applicability for molecular metabolic imaging.

THE FEASIBILITY OF NEUTRON IMAGING

Practically, one of the more exciting aspects of this early stage of developing NSECT is that all of the essential instrumental components are commercially available. As a further encouraging factor, the cost of assembling a prototype scanner for medical imaging will be less than a quarter the cost of a typical clinical CT system. Shielding requirements would be greater than those required for x-rays but the total square footage required for installation in a radiology department would be comparable to that of an MRI system.

RADIATION DOSE FROM NEUTRONS

A key issue in the development of NSECT will be the relationship between diagnostic accuracy and dose to the patient. Preliminary calculations indicate that an accurate test for breast cancer could be performed at a dose similar to that of a current mammography examination. While an improvement in the signal-to-noise of the current technique will be required to achieve this performance, the recent experiments that are described in the presentation at AAPM demonstrate the feasibility of the NSECT approach. The required improvement in signal-to-noise is considered practical as a refinement of current techniques and will not require the invention of new technology.

One of the specific goals in this research is to minimize the number of incident neutrons that are required since an individual neutron is more damaging to the body than a single x-ray of equal energy. This goal is being approached in three ways: by optimizing the design of the equipment to increase the efficiency of gamma detection; 2) by refining the image reconstruction algorithms to maximize the information extracted from the measurements; and 3) by using advanced artificial intelligence to aid the diagnostic classification as benign or malignant.

TWO APPROACHES TO NEUTRON IMAGING

3D images are acquired by either illuminating the entire body with neutrons and collecting the emitted photons with an instrument known as a "collimated position-sensitive spectrometer" which measures the energy of the photon and can detect where from the body it is being emitted; or by scanning a narrow neutron beam over the body and collecting all gammas that are emitted from all nuclei along the path of neutron illumination.

Either approach has both advantages and disadvantages at these neutron and gamma energies. An advantage of the first approach is that it is conceptually simple. It consists of illuminating the body with neutrons which stimulate the emission of gamma photons and then recording them with a detector that has a narrow opening, or "collimator." Then one performs a series of complex calculations to reconstruct the location of the emitted photons and build up a 3D image. A disadvantage is that gammas of this energy are very difficult to collimate and that conventional gamma cameras do not have good spatial or energy resolution at these photon energies. An advantage of the second approach is that it is practical with current gamma spectrometers (which have a third of the cost of current gamma cameras). A disadvantage is that scanning the neutron beam across the whole body can be a time-consuming process.

THE FUTURE

As promising as our preliminary experiments have been, there is still considerable development ahead before NSECT will be routinely available in a clinic. A stand-alone system is expected to be ready for clinical trials within 5 years. This initial research is funded by the National Cancer Institute.

THE NSECT TEAM

NSECT is being developed by Dr. Carey Floyd Ph.D., professor of Radiology and Biomedical Engineering at Duke University in collaboration with Dr. Calvin Howell Ph.D., professor of Physics at Duke and Deputy Director of the Triangle Universities Nuclear Laboratory (TUNL) where the initial development of NSECT is being conducted. Since 1968, TUNL has enjoyed an international reputation as a premier nuclear structure laboratory. With a complete assortment of particle sources, accelerators, detectors, signal processing electronics, data acquisition computers, analysis software, and most significantly, a staff and faculty with unique expertise, TUNL provides an ideal environment for the initial development and evaluation of NSECT. The collaboration with Dr. Floyd's labs of the Digital Imaging Research Division in the department of Radiology brings their imaging expertise into the collaborative effort. As graduate students in physics, these two investigators worked together at TUNL investigating the physics of nuclear structure. Now, after twenty years of pursuing independent research topics, they have combined the different skills to develop NSECT as a practical technique for medical diagnosis and research. In a scientific presentation at the 2004 meeting of the AAPM, Dr. Floyd describes the potential application of NSECT to breast cancer diagnosis and the technological developments that are still required for this application.