Computed Tomographic Mammography in the Diagnosis of Breast Diseases

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INTRODUCTION

Mammary cancer is a significant health problem which will affect one in every 16 women in the United States of America at some time in her life. Cancer of the breast accounts for 26 percent of all malignancies in American women and for 20 percent of all deaths due to cancer in females. In 1977, the American Cancer Society anticipated that 8,000 new cases of breast cancer would be diagnosed, and that 33,700 deaths would have been attributed to the disease.

The introduction of computed tomography (CT) has revolutionized radiological practice. CT mammography is a new method for the study of breast disease.

It has been well-documented that diseased mammary tissue contains increased amounts of iodine and iodide (Chang et al. 1977; Chang et al. 1978a; Chang et al. 1979; Eskin et al. 1974; Gisvold et al. 1977; Gisvold et al. 1979; Lyttle et al. 1979; Palmer 1972). Due to an inadequate detector system, however, this metabolic abnormality has never become a practical clinical method for detecting breast carcinoma.

CT examination using contrast medium enhancement technique can demonstrate both the static morphological changes in the breast as well as any altered iodide concentration in mammary tissues. This unique capability of CT mammography provides many advantages compared to conventional mammography.

CT MAMMOGRAPHY UNIT

Initially, Reese and his coworkers at the Mayo Clinic (24) demonstrated the feasibility of imaging breast cancer by an EMI scanner using pathological specimens, and construction of a CT mammography unit was suggested to the General Electric (G.E.) Company in May 1974. In January 1975, G.E. began construction of a prototype dedicated breast scanner (CT/M). In October 1975, a CT/M unit installed in the Mayo Clinic for purposes of clinical evaluation. In October 1976, a second CT/M unit was installed at the University of Kansas College of Health Sciences and Hospital for further clinical evaluation. These two units remained in operation, conducting clinical evaluations, until G.E. decided not to market the CT/M scanner. The CT/M unit at the Mayo Clinic was removed in August 1979, and the unit at the University of Kansas was withdrawn in January 1980.

The G.E. CT/M system was a prototype CT fan-beam scanner that was especially designed for breast scanning only. The system included a three phase x-ray generator, G.E. Maxiary 75 tube, and array of 127 high-pressure xenon gas detectors, a Data General S/200 Eclipse computer with magnetic tape drive, a Control Data Corp disc, a RAMTEC display console, a Versatic printer and Dunn camera. It has canvas table with a central opening and a horizontal gantry with a central water container. Scanning was performed with the patient prone. The breast was completely immersed in the water container which was filled with continuously flowing body-temperature water. The CT/M scan showed coronal sections of the breast. The scanning field was 20 cm in diameter, and it scanned a 1 cm slice of the breast in 10 seconds. The resolution volume for each picture point was 1.56×1.56×10 mm. Reconstruction time per slice was 90 seconds. Images from the 127×127 matrix were displaced on a scale of −127 to +128 CT number with water calibrated to zero. Each CT number was equal to 2 Hounsfield units (HU) and indicated 0.2 percent density difference.

In February 1980, a technique for CT examination of the breast using a conventional body scanner was established at the University of Kansas Medical Center.
and since then over 500 patients have been scanned with this technique. Breast scans are performed on a modified G.E. CT/T 7800 unit. This device uses a grid-controlled x-ray tube operating in a pulsed mode and a high-pressured xenon ionization detector to generate CT profile information in a fan-beam format. The detector, which contains 12 reference and 511 measurement chambers, is connected to an on-line image analysis computer for data collection and reconstruction. The computer portion of the CT/T is a Data General Eclipse S/200. It simultaneously controls three tasks: data collection, image reconstruction and image analysis. Data collection and image reconstruction are controlled at the operator console by a radiologic technologist who is able to select either a 0.5 cm or 1.0 cm slice thickness and any one of four reconstruction formats. This gives the capability of choosing 0.8, 1.1 or 1.3 mm² pixel formats for reconstruction, depending on the body part to be imaged. For the most frequently used combination of 1.0 cm slice thickness and 1.1 mm pixel size, the volume of each individual CT element (voxel) is 12.1 mm³ or .012 cm³. Reconstruction is accomplished in 35 seconds using G.E.'s Fast Reconstruction Unit, a built-in array processor. After reconstruction, the image is saved on the CT/T's 96 megabyte magnetic disc, where it is accessible to the physician's viewing console. This console, which runs its programs independently of the operator console, allows the physician to adjust the contrast and CT level of the CRT display image, create film images on a multifomat camera and make a variety of geometric and statistical measurements on the displayed image. Images are displaced on a scale of 500 to +500 CT numbers with calibrated to zero. Each CT number of CT/T is equal to 2 HU and represents 0.2 percent difference in density, which is the same as the CT value of CT/M. Since July 1983, a G.E. CT/T 8800 unit or occasionally a G.E. CT/T 9800 unit has been used for CT mammography.

CT TECHNIQUE

Patients are scanned in supine positions with arms flexed above their heads, as a surgeon sees patients on the operating table. Transverse scans for the breasts are obtained at 1 cm intervals before and after the rapid intravenous infusion of 300 cc of diatrizoate meglumine (RenO-M-Dip, Squibb) within 10 minutes. Our study clearly demonstrate that the maximum contrast enhancement of breast cancer is achieved by this method.

The total number of slices is predetermined by measuring each breast from the inferior margin to the axilla. A breast is referenced with respect to the nipple which is marked with a small amount of barium paste and indexed as O. Slices made superior to the nipple are labeled positive and numbered by the distance from the nipple. Slices made inferior to the nipple are labeled with negative numbers accordingly. To facilitate that precontrast and postcontrast scans are identical in position, scans are taken at the end of expiration following the taking of a deep breath, with breath holding. Also, intravenous infusion of contrast is given without removing the patient from the gantry. It is convenient to obtain both pre- and postcontrast studies in the same run but mark only the postinjection slices. All premenopausal patients are examined seven through fourteen days following the onset of the last menstruation.

All CT slices are photographed. Pre- and postcontrast slices are carefully matched by identifying anatomical landmarks in the breasts. All breast tissues are thoroughly measured in the pre- and postinjection slices, and the difference (Δ CT values) is recorded. For every measurement of the area, the highest CT value has been used instead of an average CT number value. The slice containing the lesion is magnified, usually two times, and the lesion is marked by using the smallest ROI box. The magnified slice is then photographed to the same size and also photographed with grid line spacing on the image. The nipple line is drawn through the center of the nipple and perpendicular to its base. The nipple and nipple lines are marked on the CT slice containing the lesion by using the same coordinate points of grid line spacing on the image. All lesions have been localized by fixing the position of the lesion in relation to the nipple line. The horizontal coordinate (X) is obtained by measuring the distance medially or laterally from the nipple line to the center of the lesion. The vertical coordinate (Y) is obtained by subtracting the slice containing the lesion from the scan containing the nipple shadow. A positive number indicates a

Table 1. Comparative detection rate in 18 breast cancers diagnosed by a body scanner

<table>
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<tr>
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<th>Negative</th>
<th>Positive</th>
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<tr>
<td>Film Mammography</td>
<td>5</td>
<td>13</td>
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<tr>
<td>Physical Examination</td>
<td>9</td>
<td>9</td>
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<tr>
<td>CT</td>
<td>1*</td>
<td>17</td>
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* A 47-year-old patient who had a hysterectomy 10 years previously and functioning ovaries. There was diffuse increased contrast enhancement throughout her breasts.
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superior location and a negative number means that the lesion is inferior to the nipple. The depth (Z) of a lesion is directly measured parallel to the nipple line from the skin to the center of the lesion.

Since exposure rate to the patient is higher when a body scanner is used, many efforts are made to reduce the radiation dose. Our phantom studies using different mAs's revealed that an image made with 80 mA and 4.8 second exposure revealed a good quality of imaging at the least dose. The technique of imaging is done at 120 kVP, 80 mA, 2.2 ms pulse width, and 4.8 seconds per 360°C rotation. The skin dose for an average-sized breast with 11 scans is 0.75 rads (7.5 mGy); thus, a total skin exposure rate is 1.5 rads (15 mGy) for both pre- and postcontrast studies.

CT FINDINGS

Breast Carcinomas: In a fatty breast, breast carcinoma can be seen as an irregular mass, and the CT number is markedly increased, 50 HU or above, on the postcontrast scans (Chang et al. 1977; Chang et al. 1978a; Chang et al. 1979; Chang et al. 1980; Gisvold et al. 1979; Sibala et al. 1980) (Fig. 1). In moderately to markedly dense fibrocystic breasts, and occasionally even in minimally dense breasts, the lack of tissue contrast prevents the tumor mass from being distinguished from the surrounding benign tissue on the preinjection scan. The carcinoma, however, becomes obvious on a postcontrast scan because of preferential high iodide concentration by the cancer cells. Malignant microcalcification without an associated mass cannot be identified on a preinjection scan due to the averaging effect with the CT computer matrix but can be shown as areas of marked contrast enhancement on postcontrast scans.

During the period of 1980-1981, 18 breast carcinomas were detected by our new technique using a body scanner. Contrast enhancement in the 18 cancers ranged from 46 to 106 HU. One cancer exhibited 46 HU, and all of the other 17 tumors showed a contrast increase of at least 50 HU.

The smallest cancer diagnosed by CT examination was a 2 mm lesion. The size of a tumor mass appeared larger on the postcontrast scan, probably due to extravascular pooling of contrast medium (Dean et al. 1978; Newhouse 1981). For this reason, a CT study is able to demonstrate lesion as small as 2 mm in diameter which approximates the volume of one pixel. The CT study is of particular value in the detection of cancer in dense dysplastic breasts. Unless calcifications are present, a conventional mammogram is of very little value due to a lack of tissue contrast. An exciting contribution of the CT study is the detection of mammographically and physically totally un-

Fig. 1. Breast Cancer

A. Precontrast scan of the right breast showing an irregular mass. An initial CT value of the is 85 HU (cursor). Contrast medium enhancement (Δ CT number) of the mass is 82 HU. Mass is 3 HU (cursor).

B. Postcontrast scan now showing marked enhancement in the mass. The maximum CT number

Number 4
suspected very small breast cancers. The CT study of the breast is also very useful in the diagnosis of recurrent or residual cancers when diffuse fibrosis is present by either postirradiation or postsurgical changes. When an axillary lymph node biopsy is positive and mammograms fail to demonstrate the primary lesion, the CT examination is of great value. The detection of an unsuspected lesion in the ipsilateral or contralateral breast is possible by CT study.

The detection rate of the dedicated CT/M unit of the 92 cancers and one malignant cystosarcoma phyllodes was 94 percent, while film mammography had only a 77 percent rate and physical examination only 62 percent. Film mammography missed 11 cancers in dense dysplastic breasts and two recurrent cancers in postcobalt therapy breasts with marked fibrosis. All these cancers were preoperatively diagnosed by CT/M study. All 93 malignancies were correctly detected by using both CT/M and mammography. The detection rate of our new CT technique using a body scanner for 18 cancers is compared to low dose film mammography and physical examination in Table 1. Seventeen cancers (94%) were diagnosed by the CT study, 13 cancer (72%) were detected by mammography, and physical examination picked up only nine (50%). The detection rate for breast cancer by a body scanner appears equal to the results obtained by a dedicated CT/M unit.

**Benign Lesions:** Diffuse fibrocystic disease is characterized by increased density and obliteration of the normal architecture by dilated ducts, fibrotic reaction and multiple masses. The initial precontrast CT number for fibrocystic disease is similar to cancer. However, the contrast medium enhancement is less than that for breast carcinoma (Fig. 2).

Bland fibrocystic disease demonstrated contrast medium enhancements of less than 30 HU (Chang et al. 1977; Chang et al. 1978a; Chang et al. 1979; Chang et al. 1980). The differential diagnosis of malignant and benign microcalcifications is not always easy on a mammogram. Many benign but suspicious microcalcifications can mimic malignant calcification, and many unnecessary surgical biopsies were performed. The CT study can differentiate benign calcifications from malignant lesions by identifying lower iodide concentration.

Contrast enhancement of above 50 HU has been found in non- or focally-calcified fibroadenoma, breast abscess, comedonecrosis, angiolipoma, and reactive hyperplasia of lymph nodes (Chang et al. 1978a; Chang et al. 1979; Chang et al. 1980; Sibala et al. 1980). However, fibroadenomas and reactive hyperplasia of lymph nodes demonstrate smooth margins. Additionally, the roentgen findings are characteristic.

**Fig. 2. Benign Fibrocystic Disease**

* A. Precontrast scan of the left breast showing an irregular area of increased density. An initial CT value of the lesion is 4 HU (cursor), which is similar to cancer.
  
 B. Postcontrast scan, however, shows only minimal enhancement in the lesion. The maximum CT number is 21 HU (cursor). Contrast medium enhancement (∆ CT number) is only 17 HU.
Breast abscess may simulate a carcinoma, but it has been located close to the skin. Higher iodide concentration in mammary tissue was also observed in hyperprolactinemia and high progesterone level (Chang et al. 1978a). Hence, the CT examination should not be performed until one week after the end of menstruation in premenopausal patients. Posthysterectomy patients with functioning ovaries may exhibit higher iodide concentration in their breasts. This can be a cause of error in the diagnosis of breast cancer.

Potentially Precancerous Breast Lesions: Proliferative disorders of the breast, including atypical terminal duct epithelium hyperplasia and atypical lobular hyperplasia have been considered possible precancerous lesions by many knowledgeable investigators (Black et al. 1972; Chang et al. 1978; Chang et al. 1979; Chang et al. 1980; Dawson 1933; Foote and Stewart 1945; Humphrey and Swerdloow 1962; Kern and Brooks 1969; Moskowitz et al. 1980; Mui 1941; Page et al. 1978; Ryan and Coady 1952; Wellings and Jenson 1975). Abnormal xeromammographic patterns (Wellings and Wolfe 1978; Wolfe 1976) and microcalcifications (Price and Gibis 1978) have been used to predict risk of developing breast cancer. However abnormal breast parenchymal patterns cannot always indicate the presence of atypical epithelial or lobular hyperplasia. The mammographic changes are often due to marked fibrosis, which is not considered to be a premalignant lesion. Microcalcifications are related to past activities, but they cannot always specify present active pathology or identify the exact location of abnormal cellular activity. The CT study, however, can provide the exact location of abnormal cellular activity in the lobuloductal complex of the breasts (Chang et al. 1978; Chang et al. 1979; Chang et al. 1980). All CT scans showed two or more tiny areas, often bilateral and along the duct of markedly increased contrast enhancement, usually over 50 HU. Our experiences suggest that CT study can differentiate potentially precancerous epithelial proliferative lesions from non-precancerous bland fibrocystic lesions in even dense dysplastic breasts by identifying tiny areas of increased iodide uptake.

SUMMARY

The CT study of the breast is a new method of detecting breast cancers using dynamic measurements of abnormal iodide concentration. Breast carcinomas have demonstrated that an elevation of iodide uptake is detectable on CT. A lesion with contrast medium enhancement (Δ CT numbers) of over 50 HU strongly supports a diagnosis of malignancy, and a contrast enhancement above 40 HU supports a suspicion of cancer. In the absence of intravenous contrast material, it appears that the attenuation coefficient of cancers is not significantly different from benign fibrocystic disease. Marked contrast medium enhancement is noted in atypical terminal duct epithelial hyperplasia (possible pre-cancerous lesions). Contrast enhancement above 50 HU has also been found in non- or focally-calcified fibroadenomas, breast abscesses, comedomastitis, angiolipoma, reactive hyperplasia of lymph nodes, hyperprolactinemia and high progesterone level. These can be causes of error in the diagnosis of breast cancer.

The necessity of intravenous infusion of contrast medium, high cost of the examination, lengthy procedure and high radiation dose make CT mammography inappropriate as a screening tool for the general population. CT study of the breast, however, can yield both anatomical changes and increased iodide concentration in the mammagry tissues. This unique capability or CT mammography provides many advantages over conventional mammography in the diagnosis of breast cancer. CT examination appears to be especially superior to mammography for detecting cancers in dense, dysplastic breasts. The CT study can detect totally unsuspected, very small cancers which were occult by conventional mammography or physical examination. A CT scan may also be a valid test for recognizing pre-cancerous high risk lesions.

Although CT study cannot replace conventional mammography in routine breast examinations, it can overcome limitations of mammography. Indications for CT mammography are:

1. clinically suspected breast carcinoma but mammographically occult lesion;
2. questionable distortion and uncertain lesion location;
3. evaluation of postbiopsy or post lumpectomy breast cancers when primary radiation therapy is contemplated;
4. searching for a second primary breast cancer;
5. follow-up study of postirradiation of breast cancer;
6. follow-up postmastectomy patients; and
7. screening procedure for genetically high risk patients, especially those with dense breasts.

REFERENCES


Gisvold JJ, Karsell PR, Reese DF: Computerized tomographic mammography (CT/M). *AJR* 133:1143-1149, 1979


