Exhibit 1

BCS 2100

Radiological Devices Panel Review Material

Panel Review
October 16, 2002

FORWARD

CTI is pleased to provide this packet of information to members of the Radiological Devices Panel for your review prior to the Radiological Device Panel meeting on October 16, 2002.

CTI submitted the final module of our modular PMA application on June 15, 2001, and the final amendment on May 24, 2002. In our PMA application, we presented results from the analyses of two sets of patients, both enrolled under the same clinical protocol. The patients presented in the first set of analyses were enrolled between October 1997 and November 1, 2000. The patients presented in the second set were enrolled from November 2000 through April 2001. Data from the second set of patients were used to confirm the results obtained from analysis of the first set of patients.

Based on the FDA's favorable review of these results, CTI has been invited to attend the panel meeting for which this material is prepared.

PACKET ORGANIZATION

1. GENERAL INFORMATION

1.1 Device Generic Name:

Dynamic thermal imaging system

1.2 Device Trade Name:

CTI Breast Cancer System 2100 (BCS 2100)

1.3 Sponsor Name and Address:

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1.4 Sponsor Correspondent:

John Brenna
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1.5 Device Description:

The CTI BCS 2100 is a dynamic computerized infrared (IR)-based image acquisition device intended for use as an adjunct to mammography in patients with suspicious breast masses that are being considered for biopsy. It is not intended for use in lesions with clear indications for biopsy. The CTI BCS 2100 provides additional information to guide a breast biopsy recommendation.

2. PROTOCOL

2.1 Protocol Title:

"Clinical Study of the Examination of Breasts for Identification of Suspicious Tissue Using Clinical Examination and Mammography with and without the CTI Thermal Imaging System"

2.2 Introduction

Breast cancer affects one out of eight American women and is ranked second only to lung cancer in female cancer-related deaths. Randomized, controlled trials and large-scale screening programs have demonstrated that periodic screening leads to earlier detection as well as a reduction in breast cancer mortality [1-4]. Currently, self-breast examination and regular mammograms are the most effective techniques for detection of breast cancer, and it is recommended that women begin regular screening mammography at age 40 [5-6]. Mammography, the gold-standard screening modality, detects occult malignant lesions in asymptomatic women at an earlier stage and in smaller-size lesions, generally producing a more favorable prognosis than is possible by self-breast examination.

Despite the value of mammography in detection of breast malignancies, the majority of radiographically identified lesions are ultimately found to be benign upon histologic assessment following biopsy. National statistics indicate that between two-thirds and four-fifths of all breast biopsies have a benign outcome [7-9]. Although women are willing to undergo biopsy to ensure that they do not have cancer, biopsies nonetheless cause anxiety and discomfort and introduce disruption into already busy lives. Additionally, breast biopsies are costly, with the expenses ranging from many hundreds to several thousands of dollars [10-12].

As radiologists seek enhancements to the current methods used to distinguish benign from malignant suspicious lesions, increasing interest is being focused on the physiological aspect of the disease. Current diagnostic modalities for breast cancer that rely, at least in part, on physiological processes include sestamibi scintimammography, doppler sonography, gadolinium-enhanced MR imaging, and positron emission tomography. Unfortunately, these procedures are often expensive and invasive. A less invasive and more cost-effective method to aid in distinguishing benign from malignant breast tissue would benefit both patient and physician.

One promising modality is infrared, or IR, imaging, a noninvasive method of detecting IR radiation from the body's physiological processes, rather than evaluating the body's anatomical features. Heat is released from the body in the form of IR radiation. The BCS 2100 system was designed to collect and assess the infrared data. This is accomplished by acquiring a series of breast images, over one hundred, during an imaging session that lasts approximately three minutes per breast. During the three minute imaging session, there is a precise time period during which cooling of the breast tissue is accomplished using refrigerated air. The IR information collected contains over 8 million temperature data points per breast that is rapidly stored and processed by computer, and then immediately available for physician analysis.

There are several physiologic processes related to malignant tissue that may contribute to an altered pattern of IR radiation. One feature is increased blood flow in the area surrounding a malignancy. Studies using ultrasound have reported increased blood flow in breast carcinomas compared to benign lesions (13, 14). A likely contributing factor to this phenomenon is angiogenesis, the formation of new capillaries from existing blood vessels, which supplies the nutrients required by a malignant neoplasm. Although angiogenesis is important to normal physiologic processes such as wound healing, it has only recently become accepted that it also plays a key role in tumor growth (15). Angiogenesis is linked to both the growth of breast cancer as well as to its metastatic potential, (16, 17). Current clinical trials are ongoing to determine whether pharmaceutical inhibition of angiogenic factors such as growth factors are successful in the treatment of breast cancer (18). Another likely factor contributing to the characteristic IR pattern of malignant tissue is the smooth muscle relaxant, nitric oxide (NO). NO induces vasodilation, detectable as increased regional heat

production and the alteration of local thermoregulatory responses (19, 20). Malignant human breast cancer cells have been shown to produce this mediator, and the increased NO release may also contribute to the probability of metastasis (21). Another feature of malignant tumors that may contribute to their IR pattern is enhanced metabolic activity (22).

The BCS2100 IR imaging system is intended for use in clinical practice as an adjunct to mammography for further evaluation of an already identified mammographically apparent breast abnormality. It is not designed to be a screening tool for identifying or localizing lesions. Therefore, the BCS2100 clinical investigation focused on determining the device's specific benefit to subjects with breast lesions already identified as suspicious and warranting a biopsy. Enrolled subjects were patients proceeding to biopsy based on the standard clinical work-up by the physician. This established a study baseline with a sensitivity of 100%, as all malignant lesions were biopsied, and a specificity of 0% as all benign lesions were also biopsied.

The endpoint chosen to determine device effectiveness was whether or not the BCS2100 could correctly identify a portion of those lesions in which biopsy might have safely been avoided. The results of this trial that are subsequently presented in detail show that in fact, there was a 19% improvement over the baseline value of 0%. Thus, approximately one-fifth of biopsies of benign masses would have potentially been avoided by use of the BCS 2100 imaging results. At the same time, a very high sensitivity of 99% was maintained in the clinical investigation. Thus, the IR imaging system was found to be both effective and safe.

2.3 Study Overview:

CTI began to gather clinical data in support of this Premarket Application (PMA) in October 1997. Five clinical sites throughout the United States, one of which encompassed two enrolling centers, enrolled 2,407 subjects into the study. The clinical investigation was conducted in compliance with Institutional Review Board (IRB) regulations, 21CFR56, informed consent regulations, 21CFR50, and the abbreviated requirements of 21CFR812.2(b). The investigation was approved as a non-significant risk study by all reviewing IRBs and in consultation with the FDA.

Investigators invited patients who were recommended for breast biopsy based on abnormal findings on clinical physical examination and/or mammography to participate in the study.

2.4 Study Hypothesis:

The prospective study hypothesis was that the CTI BCS 2100 could safely differentiate benign breast masses from malignant breast masses based on the relatively lower strength of the IR signal in benign tissue.

2.5. Study Objectives:

The overall objectives of the study were to provide evidence to confirm the study hypothesis and to demonstrate that the BCS2100 is a safe and effective device when used adjunctively to mammography to avoid biopsy of benign masses that would have otherwise undergone biopsy.

The specific efficacy objective was to demonstrate that the BCS 2100 could be used to avoid a large number of biopsies of benign masses, without significantly affecting the outcomes of subjects with malignant masses. This objective was demonstrated in all masses that could be localized with mammographic films and that had evaluable IR images.

The study's safety objective was to demonstrate that the BCS 2100 is a safe device. All subjects who enrolled in the study were analyzed for safety.

Other study objectives included determination of the relationship of the IR imaging Indices of Suspicion (IOS) to mass size and to breast density. The relationship of IOS to mass size was demonstrated in all evaluable masses that could be localized with mammographic films, that had evaluable IR images, and that had recorded mass sizes that were determined by the enrolling investigator. The relationship of breast density to IOS was analyzed in all evaluable masses that could be localized with mammographic films, that had evaluable IR images, and that could be assigned a breast density.

2.6 Study Design

The study design incorporated a prospective, blinded, multi-center study that compared the levels of suspicion of malignancy of suspicious breast lesions before and after IR imaging, using the pathology findings from biopsies of the identified lesions as the "gold standard" references.

CTI and all radiologist evaluators who determined the IR test outcome, or Index of Suspicion (IOS), were blinded to the pathology results of biopsied lesions during the IOS assignment procedures. CTI archived a controlled and dated CD copy of the finalized subject data before the lesion pathology results were unblinded.

2.7 Protocol Summary:

Briefly, investigators screened and enrolled subjects into the trial who had suspicious breast lesions that had already been recommended for biopsy based on physical and / or mammographic findings. Subjects underwent IR imaging with the BCS2100, and were released from the study prior to lesion biopsy. Lesion biopsy information was later collected and used to determine if the IR imaging procedure yielded a true or false result.

Specific protocol inclusion / exclusion criteria were as follows.

- Inclusion criteria:
  - Subject underwent a mammogram, results were interpretable and a surgical or core biopsy within sixty days had been recommended, or
  - Subject underwent a clinical examination, results were available and a surgical or core biopsy had been recommended, and
  - Subject signed an Informed Consent Form
- Exclusion criteria:
  - Subject had previous surgery in breast of interest within last year
  - Subject had breast implants
  - Subject had breast reduction
  - Subject had previous radiation therapy in breast of interest
  - Subject's body weight was over three hundred pounds (table limit)
  - Subject was pregnant
  - Subject had histologically proven cancer in breast of interest

Protocol procedures were as follows.

- Subjects who agreed to participate provided signed, IRB-approved written informed consent.
- Information regarding previous mammographic procedures, if applicable, was collected.
- A subject history was taken that included breast cancer risk factors, nicotine, alcohol and caffeine use, and demographic data.
- A physical examination was performed of the subjects' breasts.
- Subjects underwent IR imaging of their breasts with the CTI BCS 2100.
- Safety data regarding the investigational device and procedure were collected.
- The subjects were released and underwent biopsy as previously planned.
- Infrared imaging data, appropriate case report forms (CRFs), and mammographic films and reports were transferred from the sites to CTI.

- Infrared imaging data were correlated with case report form data and mammographic information.
- Infrared imaging files were reviewed for evaluability
- Infrared imaging files were prepared for physician analysis by independent blinded radiological technologists.
- Index of Suspicion (IOS) scores were assessed for each lesion by an independent panel of physician evaluators who were blinded to lesion pathology results.

The protocol was amended twice. Summaries of these amendments are as follows.

- Amendment One:
  The original protocol required the site investigators to assess initial levels of suspicion of malignancy for breast lesions based on physical and / or mammographic findings before the IR imaging procedure, and then to reassess the levels of suspicion incorporating the IR imaging procedure outcomes.

  CTI subsequently became aware that the study design introduced a potential source of study bias. A biopsy recommendation was required in order for a subject to participate in the study, and most subjects were already on a biopsy schedule when they were recruited for the study. In order to reduce subject inconvenience and avoid prolongation of subject anxiety by delaying an already scheduled biopsy, many subjects underwent IR imaging immediately before their breast biopsies.

  The immediate transfer of the subject from IR imaging to biopsy meant that the physicians involved in the patient's care, including, in many cases, the study investigator, became almost immediately aware of the pathology results of the lesion biopsy. This did not provide sufficient time for study investigators to complete the assessment phase of the IR procedure before finding out whether the lesion was benign or malignant.

  Note that this difficulty resulted from the study requirement that all lesions undergo biopsy, and the site investigators' attempts to minimize subject inconvenience by scheduling the IR imaging immediately before already scheduled biopsies. In order to assist the site investigators in providing the best standard of care for all study subjects while ensuring that IR test results were not biased by prior knowledge of lesion pathology outcome, CTI amended the protocol and delegated the responsibility for assigning an index of suspicion to independent, blinded radiologists.

- Amendment Two:
  The second amendment revised the inclusion / exclusion criteria. Specifically, the requirement that a subject could not have undergone surgery in the breast of interest within the last three years was revised to exclude only subjects who had undergone surgery in the breast of interest within the last one year. The exclusion criterion is based on the assumption that inflammation in recently biopsied tissue might interfere with IR test results. However, investigators indicated that three years was an excessive period, as they anticipated that inflammation associated with surgery would be expected to subside within three to six months, and healing would be complete within one post-operative year. Thus, the criterion was revised to exclude only subjects who had undergone breast biopsy within the last one year.

2.8 Patient Population:

Investigators enrolled a total of 2,407 subjects during the clinical trial.

- Algorithm Patient Set
  Of the 2,407 subjects, 700 subjects were used to develop the algorithm incorporated into the BCS2100. Thus, CTI was not blinded to the pathology results for these subjects, and they were not included in any efficacy analyses. They were, however, included in all analyses of device safety.

- Remaining Subject Sets
  The remaining 1,707 subjects can be divided into two groups, one consisting of 1,432 subjects and a second group of 275 subjects. The first group includes those subjects who were enrolled on or before October 31, 2000, and whose lesion pathology data were unblinded in May 2001 for analyses. Results of these analyses were included in Module 5 of the original BCS2100 PMA that was submitted to the FDA on June 15, 2001. This group of subjects is referred to as the "PMA" patient set. In this group of subjects there were 769 evaluable patients who had 875 lesions biopsied, and a manuscript of the study results will be published in the American Journal of Roentgenology in January 2003 (23).

  The second subject group consists of 275 subjects who were enrolled from November 2000 through April 2001, and whose lesion pathology data were unblinded in May 2002. As this group of subjects was unblinded after submission of the original PMA Module 5, this group of subjects is referred to as the "PPMA" patient set. The results from a portion of this group of subjects provided confirmatory information to supplement the original dataset (PMA patient set) and was submitted in an amendment to the FDA on May 24, 2002.

  In both of these groups, there are many subjects who are not included in the final Efficacy Analyses datasets. The major reasons for exclusion are: that the biopsied lesion was not described as a mass; that adequate lesion localization on the IR image was not possible due to incomplete or unavailable copies of the mammography films; that the IR image was not of sufficient quality for evaluation; or that a biopsy was not performed.

  Although not included in the efficacy analyses, all of these subjects (1707) were included in the analyses of device safety.

- PMA and PPMA Patient Sets for Efficacy Analyses
  A subset of the PMA patient group is included in the final efficacy group. This subset is restricted to those where the lesion was described as a mass by the original, enrolling physician. Results of these analyses were included in an amendment that was submitted to the FDA on February 28, 2002.

  The second subject group consisted of 275 subjects who were enrolled after October 31, 2000, and whose lesion pathology data were unblinded separately from the earlier subjects. CTI and the independent radiologists who assigned IR IOS scores remained blinded to the pathology results for these subjects' lesions until May 2002, when the data were unblinded for analyses and the results submitted to the FDA in an amendment that was submitted to the FDA on May 24, 2002. Final efficacy data is drawn from the combination of the PMA and PPMA dataset.

The following table tabulates all subjects enrolled at each site, and categorizes them into the following subject sets – algorithm, PMA subjects, and PPMA subjects. As previously explained, all 2,407 subjects were included in subject complaint and safety analyses.

Table 1: Subject Sets by Site

Site	Algorithm	PMA	PPMA	Total
Site 1a	96	108	0	204
Site 1b	125	40	0	165
Site 3	206	369	51	626
Site 4	145	255	28	428
Site 5	80	538	196	814
Site 6	48	122	0	170
Total	700	1432	275	2407

- Efficacy Data Set
  Efficacy data was drawn from the combination of the PMA and PPMA data sets. In order for a subject to be included in the efficacy analyses, certain evaluability conditions were applied to the subject data. These included, but were not limited to, meeting the inclusion/exclusion criteria, completing the clinical study, absence of any significant protocol deviation, and subsequent biopsy of the identified suspicious lesion. In addition, the IR image had to meet rigid pre-established acceptability criteria, appropriate mammography films were required for evaluator localization, localization had to be consistent with the information contained within the case report form, and the descriptor for the lesion had to include the term "mass". All exclusions due to these various criteria were made prospectively, prior to receiving biopsy results, and were thus not influenced by the pathology outcome.

2.9 Clinical Sites and Investigators

Five investigative clinical sites enrolled 2,407 subjects into the protocol entitled "Clinical Study of the Examination of Breasts for Identification of Suspicious Tissue Using Clinical Examination and Mammography with and without the CTI Thermal Imaging System" beginning October 1997 through April 2001. The principal investigators, sub-investigators, institution names and addresses, and study enrollment periods for each clinical site are specified below. Subjects for the PMA results were collected from all sites. Subjects for the PPMA results were collected from sites 3, 4 and 5.

No foreign clinical data were collected.

- Site 1 (incorporating Site 2):
  Site 1 had two enrolling centers with a device in each center, and maintained separate screening and enrollment logs at each center. Although it was the original intent of CTI to consider the enrolling centers to be two separate sites under separate principal investigators, the IRB that covered both enrolling centers eventually ruled that the two centers were actually one site. Although considered one site, for purposes of data clarity, the data for each enrolling center were analyzed separately as Site 1a and Site 1b. Site 1b was originally designated as Site 2.

  Principal investigator
  Yuri Parisky, MD

  Subinvestigators
  William Dougherty, MD (originally designated as principal investigator for Site 2)
  Peter S. Conti, MD
  Kristin Skinner, MD
  Howard Silberman, MD
  Melvin J. Silverstein, MD
  Linda Hovanessian, MD

  Institution name and address

1a Enrolling Location
Norris Cancer Center
1441 Eastlake Ave.
Los Angeles, CA 90033

1b Enrolling Location
Los Angeles County Hospital
1175 Cummings Avenue OPD-3P7
Los Angeles, CA 90033

Study duration
1a Enrolling location
First IRB protocol approval 7/17/97
Last subject imaged 3/1/00

1b Enrolling Location
First IRB protocol approval 8/4/97 (same approval as enrolling location 1a)
Last subject imaged 2/25/99

Institutional Review Board
Institutional Review Board Health Research Association
Institutional Review Board University of Southern California School of Medicine
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- Site 3:

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Study duration
First IRB protocol approval 12/9/98
Last subject imaged 4/26/01
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  Study duration
  First IRB protocol approval 5/18/98
  Last subject imaged 3/2/01
  Institutional Review Board
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  Yvonne Ortiz, Coordinator

- Site 5:

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  Deepak P. Merchant, MD
  G. Michael Meyer, MD
  Kiran J. Parikh, MD
  Viney Setya, MD
  U. Shah, MD
  William E. Signor, MD
  John Singer, MD
  Hardeep Rosy Singh, MD
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  First IRB protocol approval 2/1/99
  Last subject imaged 4/27/01
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- Site 6:

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Study duration
First IRB protocol approval 2/10/99
Last subject imaged 10/11/00
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3. INFRARED ANALYTICAL AND STATISTICAL METHODS

3.1 Overview:

Below are brief descriptions of study statistical methods. As the purpose of the PPMA study was to provide confirmation of PMA study results, the statistical methods used to analyze data were essentially the same.

CTI contracted with Battelle Memorial Institute to perform the statistical analyses of the PMA, the PPMA, and the combined PMA and PPMA clinical data.

3.2 Sample Size:

Each suspicious lesion was assessed and accounted for individually. Therefore, sample size was calculated on a lesion basis, not on a subject basis. Some subjects presented with more than one suspicious lesion. All suspicious lesions that met evaluability criteria were included in the efficacy analyses.

3.3 Randomization Scheme for IR Evaluation:

All subjects in the PMA study for whom IR imaging indices of suspicion were determined were evaluated as part of a unified scheme involving seven independent radiologists. Subjects were assigned to radiologists according to a balanced incomplete block design with each subject serving as a block. Each evaluable lesion was assessed by three of the seven radiologists.

Lesions in the PPMA study were evaluated as part of a unified scheme involving three independent radiologists, each of whom was one of the original seven radiologists. Because of scheduling difficulties, four of the seven original PMA radiologists did not participate in the second PPMA phase. Subjects were assigned to radiologists according to a balanced complete block design with each subject serving as a block. All three PPMA radiologists read each PPMA lesion.

3.4 Evaluator Determination of IR Index of Suspicion (IOS):

Site personnel performed IR imaging of each subject's two breasts, collecting sequential information over time in a series of IR breast images. Following IR imaging, site personnel saved each subject's IR imaging data onto electronic media. Site personnel forwarded IR imaging data, and copies of corresponding mammographic films and radiological reports to CTI.

For every subject, a composite IR image was created for each breast from the serial images taken of the breast over time during IR imaging. An imaging technologist outlined breast tissue on each composite image.

Each evaluating radiologist reviewed the imaging technologist-defined breast outlines, and modified these outlines if deemed necessary, either to better define breast tissue, or to ensure that the outline included all possible regions of interest (ROI). Following breast outline verification, each radiologist used mammographic films to place a specific region of interest (ROI) on the composite image of the affected breast. Following placement of the ROI, the BCS2100 calculated a discrete numerical Index of Suspicion (IOS) based on propriety algorithm processing. Each IOS numerical score was also translated into a negative or positive IR result based on a predetermined threshold.

3.5 Determination of Density:

The evaluating radiologists also assessed breast density while reviewing the mammographic films during the determination of IOS. They used standard density assessment categories of almost entirely fat, scattered fibroglandular density, heterogeneous density, and extremely dense.

In order to resolve possible disagreements between the three evaluators regarding breast density, each lesion was assigned a value of one, and each evaluator's density assessment was assigned a value of one divided by the number of evaluations. For example, one evaluator may have assessed a lesion as "Almost entirely fat", and the other two evaluators may have assessed the same lesion as "Scattered fibroglandular density". If so, the lesion would have been assigned a value of one, with the "Almost entirely fat" evaluation receiving a weighting of 1/3, and the two "Scattered fibroglandular density" evaluations receiving a weighting of 1/3 each, for a collective weighting of 2/3 (1/3 + 1/3). Alternatively, if only one radiologist had been able to successfully complete an evaluation of a lesion, that one evaluation would have received a weighting of one (one lesion divided by one successful IR evaluation).

3.6 Original Investigator Recommendation:

Because the original investigators recommended all lesions in the original dataset for biopsy, the original investigator recommendation for biopsy was 100%, and the recommendation to delay biopsy was 0%. Thus the original investigator impression was assumed to have a sensitivity of 100%, as all malignant lesions in this subject population were correctly recommended for biopsy, with a specificity of 0%, as all benign lesions were incorrectly recommended for biopsy.

3.7 Algorithm Determination of Index of Suspicion (IOS):

The IOS was calculated from the information obtained in the sequential imaging procedure using a proprietary algorithm developed by CTI. IOS scores range from 0 to 100 with a higher score indicating a greater suspicion of malignancy.

3.8 Determination of Index of Suspicion (IOS) Threshold:

An IOS threshold was used to differentiate a positive from a negative IR test outcome. This threshold was established prior to unblinding both the PMA and the PPMA datasets, and was the same for both datasets. Values less than this threshold were considered negative results, and those above it were considered positive results. Predefinition of this threshold removed a source of possible bias from the final efficacy results of the BCS2100 clinical trial.

3.9 Determination of Sensitivity, Specificity, Negative Predictive Value and Positive Predictive Value:

Sensitivity (SENS), specificity (SPEC), negative predictive value (NPV) and positive predictive value (PPV) were estimated nonparametrically by taking simple ratios of true positive (TP) IR test results, true negative (TN) test results, false positive (FP) test results and false negative (FN) test results as follows.

$$SENS = TP / TP+FN$$

SPEC =Methods based on the binomial and multinomial distributions were used to construct 95% upper and lower confidence bounds.

3.10 Tests of Association:

Regression analysis was used to determine if mass size was associated with IOS. Regression analysis was also performed to determine if breast density was related to IOS. The statistical models used to test these hypotheses properly took into account the incomplete block design nature of the PMA clinical data with multiple readers associated with each patient and the complete block design of the PPMA clinical data.

3.11 Trend Patterns:

Certain cohorts lacked an adequate population to allow identification of trends between sensitivity or specificity, and mass size or breast density. Cohorts in which the range between the upper confidence bound (UCB) and the lower confidence bound (LCB) exceeded 50 points were considered to be insufficient for trend pattern identification. Values for cohorts with over 50 points between LCB and UCB appear in parentheses in tables in this document.

4. EFFECTIVENESS DATA

4.1 Introduction:

This section contains conclusions regarding device effectiveness drawn from both the PMA and PPMA subject datasets. Each dataset was evaluated separately, and also as a single combined dataset. The data demonstrates that the CTI BCS2100 is a safe and effective device when used adjunctively to mammography to avoid biopsies of benign masses that would otherwise have undergone biopsy.

4.2 Effectiveness in Masses:

The primary objective was to demonstrate that the CTI BCS 2100 could be used to lower the large number of biopsies that are performed every year on benign masses. This was demonstrated by assessing the performance of the BCS2100 when used to further assess suspicious masses that had been identified through mammography and / or clinical examination. Results were calculated for PMA masses, PPMA masses, and combined PMA and PPMA masses as discussed below.

- **PMA subject results**

  PMA results showed that the BCS2100 is effective in differentiating benign from malignant masses. The BCS2100 correctly assigned a positive test result to all ninety malignant masses, achieving a sensitivity of 100% and specificity of 18.0% for this dataset. The BCS2100 achieved a negative predictive value (NPV) of 100% and a positive predictive value (PPV) of 25.4%. These results are shown in Tables 2 and 3 below.

Table 2. PMA subjects: Sensitivity and specificity

	Number of masses			Sensitivity			Specificity		
Lesion type	Malig.	Benign	Total	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Mass	90	322	412	100.0%	96.7%	100.0%	18.0%	14.6%	21.9%

Table 3. PMA subjects: Negative and positive predictive values

	Positive predictive value			Negative predictive value		
Lesion type	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Mass	25.4%	24.6%	26.2%	100.0%	*	100.0%

** Method employed for calculation of lower confidence bound (LCB) for negative predictive value does not produce accurate values for point estimates of 100%.*

- **PPMA subject results**

  PPMA analysis confirmed that the BCS2100 is effective in differentiating benign from malignant masses. The BCS2100 correctly assigned a positive test result to fourteen of the fifteen malignant PPMA masses, achieving sensitivity in this dataset of 93.3%, and a specificity of 25.4% as shown in Table 4. The NPV and PPV are shown below in Table 5.

  The results in the PPMA dataset when compared to the PMA dataset showed a higher point value for specificity and a lower point value for sensitivity. It is noted that the lower point value for sensitivity in the PPMA dataset resulted from the test values assigned to a single lesion. All three evaluators assigned to this lesion a negative test value that was slightly below the positive / negative testing threshold.

Table 4. PPMA subjects: Sensitivity and specificity

Lesion type	Number of masses			Sensitivity			Specificity		
	Malig.	Benign	Total	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Mass	15	63	78	93.3%	72.1%	99.7%	25.4%	16.6%	36.0%

Table 5. PPMA subjects: Negative and positive predictive values

Lesion type	Positive predictive value			Negative predictive value		
	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Mass	23.0%	20.0%	25.9%	94.1%	85.1%	100.0%

- **Combined PMA and PPMA subject results**

The ability of the device to theoretically avoid biopsies of masses which turned out to be benign was confirmed with the combined PMA and PPMA data sets, as specificity increased from 18% in the PMA dataset to 19.2% for the combined PMA and PPMA dataset. In the combined dataset, data for the 63 benign PPMA masses data were added to data for 322 benign PMA masses, with a narrowing of the confidence interval length from 7.3% (Table 2) to 6.8% (Table 6). Sixteen biopsies of PPMA masses that turned out to be benign would have been avoided. Combining these results with the 58 delayed biopsies of PMA masses that turned out to be benign would have resulted in sparing a total of 74 biopsies of masses that were benign (described further under Section 5. Clinical Utility).

The ability of the device to correctly assign positive IR test results to masses that turned out to be malignant was also confirmed. A positive IR test result was assigned to 14 of the 15 malignant PPMA masses. When combined with PMA results, this resulted in a correct assignment of a positive result to 104 of the 105 malignant masses, resulting in an overall sensitivity of 99% (Table 6) and NPV of 98.7% (Table 7).

The following tables show the result of combining the PMA data and the PPMA data.

Table 6. Combined PMA and PPMA subjects: Sensitivity and specificity

Lesion type	Number of masses			Sensitivity			Specificity		
	Malig.	Benign	Total	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Mass	105	385	490	99.0%	95.6%	100.0%	19.2%	16.0%	22.8%

Table 7. Combined PMA and PPMA subjects: Negative and positive predictive values

Lesion type	Positive predictive value			Negative predictive value		
	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Mass	25.1%	24.2%	25.9%	98.7%	96.5%	100.0%

4.3 Effectiveness Related to Mass Size:

- **PMA subjects (mass size)**

  It was demonstrated that malignant mass size was associated with IOS in the PMA dataset (Tables 8, 9) with regression analysis (Table 10) showing a statistically significant relationship ($p<0.0001$). In contrast, the IOS value did not correlate to benign mass size (Table 9). Regression analyses relating IOS to benign mass size (Table 11) also did not produce statistical evidence of a relationship for the PMA dataset ($p=0.27$).

Table 8. PMA subjects: Sensitivity and specificity by mass size

Size	Number of masses			Sensitivity			Specificity		
	Malig.	Benign	Total	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
0 < size < .5cm	2	10	12	(100.0%)	(22.4%)	(100.0%)	0.0%	0.0%	25.9%
.5cm < =size < =1cm	39	154	193	100.0%	92.6%	100.0%	12.3%	8.2%	17.6%
size > 1cm	49	158	207	100.0%	94.1%	100.0%	24.7%	19.1%	31.0%
Total	**90**	**322**	**412**	**100.0%**	**96.7%**	**100.0%**	**18.0%**	**14.6%**	**21.9%**

* Cohorts in which the range between UCB and LCB exceeded 50 points were omitted from trend pattern consideration. Values for these cohorts appear in parentheses.

Table 9. PMA subjects: IOS by mass size

Size	IOS					
	Malig.	LCB	UCB	Benign	LCB	UCB
0 < size < .5cm	45.1	18.0	72.1	46.7	39.5	54.0
.5cm < =size < =1cm	48.3	46.0	50.7	43.2	40.8	45.5
size > 1cm	58.5	54.8	62.2	41.1	38.0	44.2
Total	**53.8**	**51.4**	**56.2**	**42.3**	**40.4**	**44.2**

Table 10. PMA subjects: Malignant masses – regression analysis of IOS on mass size

Source	Degrees of Freedom	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	4984.95792	4984.95792	37.04	<0.0001
Error	88	11844.57553	134.59745		
Total	89	16829.53345			

Table 11. PMA subjects: Benign masses – regression analysis of IOS on mass size

Source	Degrees of Freedom	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	527.58922	527.58922	1.24	0.2666
Error	320	136297.53306	425.92979		
Total	321	136825.12228			

- **PPMA subjects (mass size)**

  Probably due to the small number of malignant masses (15) in the PPMA data, a statistically significant relationship between malignant mass size and IOS value was not observed (data not shown). Similar to the PMA set, there was again no statistically significant relationship between IOS and benign mass size ($p=0.31$, Table 12).

Table 12. PPMA subjects: Benign masses – regression analysis of IOS on mass size

Source	Deg. of Freedom	Sum of Squares	Mean Square	F-value	Pr>F
Model	1	643.26960	643.26960	1.05	0.3092
Error	61	37329.47704	611.95864		
Total	62	37972.74664			

- **Combined PMA and PPMA subjects (mass size)**

  The results for the combined dataset containing 105 malignant masses is consistent with the PMA set and again demonstrates that there is a statistically significant relationship between malignant mass size and IOS value (Tables 14, 15, $p<0.0001$) whereas there is no relationship with the benign masses (Table 16, $p=0.87$). These results support the hypothesis that the BCS 2100 works by detecting the increased physiological activity associated with malignancy.

Table 13. Combined PMA and PPMA subjects: Sensitivity and specificity by mass size

Size	Number of masses			Sensitivity			Specificity		
	Malig.	Benign	Total	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
0<size<0.5cm	2	12	14	(100.0%)	(22.4%)	(100.0%)	16.7%	3.0%	43.8%
0.5cm<=size<=1cm	50	188	238	98.0%	90.9%	99.9%	13.3%	9.4%	18.1%
size>1cm	53	185	238	100.0%	94.5%	100.0%	25.4%	20.2%	31.2%
Total	**105**	**385**	**490**	**99.0%**	**95.6%**	**100.0%**	**19.2%**	**16.0%**	**22.8%**

** Cohorts in which the range between UCB and LCB exceeded 50 points were omitted from trend pattern consideration. Values for these cohorts appear in parentheses.*

Table 14. Combined PMA and PPMA subjects: IOS by mass size

Size	IOS					
	Malig.	LCB	UCB	Benign	LCB	UCB
0<size<0.5cm	45.1	18.0	72.1	39.4	28.7	50.1
0.5cm<=size<=1cm	47.9	45.5	50.4	43.4	41.2	45.6
size>1cm	57.8	54.1	61.5	40.8	37.9	43.7
Total	**52.8**	**50.5**	**55.2**	**42.0**	**40.2**	**43.8**

Table 15. Combined PMA and PPMA subjects: Malignant masses – regression analysis of IOS on mass size

Source	Deg. of Freedom	Sum of Squares	Mean Square	F-value	Pr>F
Model	1	5568.57750	5568.57750	36.37	<0.0001
Error	103	15768.18197	153.08915		
Total	104	21336.75947			

Table 16. Combined PMA and PPMA subjects: Benign masses – regression analysis of IOS on mass size

Source	Deg. of Freedom	Sum of Squares	Mean Square	F-value	Pr>F
Model	1	13.63585	13.63585	0.03	0.8629
Error	383	174896.55951	456.64898		
Total	384	174910.19536			

4.4 Effectiveness Related to Breast Density

It was demonstrated that breast density was associated with IOS for malignant masses in that increasing average IOS values were found when proceeding from the almost entirely fat category to the extreme density category. These data are shown in the PMA dataset (Tables 18, 19, p=0.02) and the combined dataset (Tables 22, 23, p=0.02). In contrast, regression analyses relating breast density to IOS for benign masses did not produce statistical evidence of a relationship for benign masses in the PMA dataset (Tables 18, 20, p=0.22), the PPMA dataset (data not shown) or the combined dataset (Tables 22, 24, p=0.14). The ability of the device to detect malignant masses appears to be somewhat better in denser breasts, but this phenomenon is not well understood, and is undergoing further research. A clinical study that will investigate this issue more thoroughly has been instigated at the Massachusetts General Hospital in Boston.

- **PMA subjects (breast density)**

Table 17. PMA subjects: Sensitivity and specificity by breast density

Density	Lesions			Sensitivity			Specificity		
	Malig.	Benign	Total	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Almost entirely fat	7.83	24.5	32.3	100.0%	68.2%	100.0%	8.2%	1.5%	23.5%
Scattered fibroglandular density	39.5	121	160.5	100.0%	92.7%	100.0%	14.6%	9.6%	20.9%
Heterogeneous density	36.5	134	170.5	100.0%	92.1%	100.0%	21.0%	15.3%	27.6%
Extreme density	6.17	39.3	45.5	100.0%	61.5%	100.0%	25.8%	14.8%	39.8%
Total	**90**	**322**	**412**	**100.0%**	**96.7%**	**100.0%**	**18.0%**	**14.6%**	**21.9%**

Table 18. PMA subjects: IOS by breast density

Density	IOS					
	Malig.	LCB	UCB	Benign	LCB	UCB
Almost entirely fat	48.6	45.1	52.1	43.6	38.2	49.1
Scattered fibroglandular density	51.3	48.4	54.1	44.0	41.1	46.9
Heterogeneous density	56.4	52.1	60.6	41.3	38.3	44.4
Extreme density	61.3	42.1	80.5	39.4	32.9	46.0
Total	**53.8**	**51.4**	**56.2**	**42.3**	**40.4**	**44.2**

Table 19. PMA subjects: Malignant masses – regression analysis of IOS on breast density

Source	Degrees of Freedom	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	1035.58439	1035.58439	5.77	0.0184
Error	88	15793.94906	179.47669		
Total	89	16829.53345			

Table 20. PMA subjects: Benign masses – regression analysis of IOS on breast density

Source	Degrees of Freedom	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	652.98830	652.98830	1.53	0.2163
Error	320	136172.13398	425.537920		
Total	321	136825.12228			

- **PPMA subjects (breast density)**

There was no statistical evidence relating breast density to IOS in either the benign or malignant data for this set of patients. As mentioned previously when discussing the lack of statistical relationship between mass size and IOS, the PPMA malignant set is small consisting of 15 masses.

- **Combined PMA and PPMA subjects (breast density)**

Table 21. Combined PMA and PPMA subjects: Sensitivity and specificity by breast density

Density	Number of masses			Sensitivity			Specificity		
	Malig.	Benign	Total	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Almost entirely fat	9.2	28.0	37.2	100.0%	72.1%	100.0%	13.1%	4.3%	28.3%
Scattered fibroglandular density	48.8	145.3	194.2	100.0%	94.0%	100.0%	14.0%	9.5%	19.6%
Heterogeneous density	40.8	163.5	204.3	97.6%	88.9%	99.9%	23.1%	17.8%	29.2%
Extreme density	6.2	45.3	51.5	100.0%	61.5%	100.0%	26.8%	16.3%	39.7%
Total	**105**	**385**	**490**	**99.0%**	**95.6%**	**100.0%**	**19.2%**	**16.0%**	**22.8%**

Table 22. Combined PMA and PPMA subjects: IOS by breast density

Density	IOS					
	Malig.	LCB	UCB	Benign	LCB	UCB
Almost entirely fat	46.4	41.1	51.6	43.1	36.8	49.5
Scattered fibroglandular density	51.1	48.2	53.9	44.3	41.6	47.0
Heterogeneous density	55.1	51.0	59.3	40.4	37.5	43.3
Extreme density	61.3	42.1	80.5	39.8	33.7	46.0
Total	**52.8**	**50.5**	**55.2**	**42.0**	**40.2**	**43.8**

Table 23. Combined PMA and PPMA subjects: Malignant masses – regression analysis of IOS on breast density

Source	Deg. of Freedom	Sum of Squares	Mean Square	F-value	Pr>F
Model	1	1177.73363	1177.73363	6.02	0.0158
Error	103	20159.02584	195.71870		
Total	104	21336.75947			

Table 24. Combined PMA and PPMA subjects: Benign masses – regression analysis of IOS on breast density

Source	Deg. of Freedom	Sum of Squares	Mean Square	F-value	Pr>F
Model	1	970.00504	970.00504	2.14	0.1447
Error	383	173940.19032	454.15193		
Total	384	174910.19536			

4.5 Summary of Results

There were 490 evaluable masses in the clinical trial. Of these, 385 were found by biopsy to be benign; 105 were found to be malignant. Of the 385 benign masses, 74 received a negative test result, giving an overall specificity of 19% compared to the study baseline of 0%. Of the 105 malignant masses, 104 received a positive test result, giving an overall sensitivity of 99% compared to the study baseline of 100%. There were 415 positive and 75 negative IR test results. Of the 415 positive IR test results, 104 were associated with malignant masses, giving a positive predictive value (PPV) of 25%. Of the 75 masses receiving negative IR test results, 74 were associated with benign masses, giving a negative predictive value (NPV) of 99%.

The results for the combined PMA and PPMA dataset demonstrated a statistically significant relationship between malignant mass size and the IR test score, IOS, ($p<0.0001$), but not between benign mass size and IR test score. These results indicate that increasing amounts of malignant tissue produce increasing levels of IR radiation, while benign tissue, in whatever amount present, does not produce an increased IR level. This supports the hypothesis that the BCS 2100 identifies benign tissue by confirming the absence of increased physiological activity associated with malignancy.

It was also determined that there is an apparent relationship between breast density and IR test results. In the PMA dataset and the combined PMA and PPMA dataset, increasing breast density appeared to be associated with increasing IOS values in malignant masses ($p=0.02$ for both groups), but not in benign masses. Thus, the ability of the device to detect malignant masses appears to be somewhat better in denser breasts, but this phenomenon is not well understood, and is undergoing further research.

4.6 Conclusions

The study hypothesis, that benign tissue can be differentiated from malignant tissue based on the relatively lower strength of the IR signal in benign tissue was tested and demonstrated in all evaluable suspicious breast masses.

The ability of the device to avoid biopsies of masses which turned out to be benign was demonstrated in the PMA dataset and confirmed by the PPMA dataset, with a specificity of 18% in the PMA dataset and 19.2% in the combined PMA and PPMA dataset, and a narrowing of the confidence interval from 7.3% to 6.8%. In the combined dataset containing 385 benign masses, seventy-four received a negative IR test result, and could have been assigned to follow-up rather than a biopsy. This 19% improvement over the 0% baseline value offers the exceptional capability to avoid biopsies of approximately one-fifth of benign masses.

The ability of the device to correctly assign positive IR test results to masses that turned out to be malignant was also confirmed. A positive IR test result was assigned to all PMA masses, and to fourteen of the fifteen malignant PPMA masses. This resulted in a correct assignment of a positive IR test result to 104 of the 105 malignant masses, resulting in an overall sensitivity of 99%.

The strongly significant correlation of IR score to malignant mass size supports the premise that an increased IR score may indicate an increase in physiological processes associated with malignancy. It should be noted, however, that the current indication being sought for the BCS2100 is the confirmation of benignity, not malignancy. Thus, the BCS2100 currently functions only to confirm benignity based on the absence of increased IR radiation in benign masses.

In conclusion, the 19% improvement in specificity over the standard clinical practice combined with a 99% sensitivity, demonstrates that the BCS 2100 has been shown to be an effective and safe device for the indication of providing information to guide a biopsy decision for suspicious masses targeted by mammography.

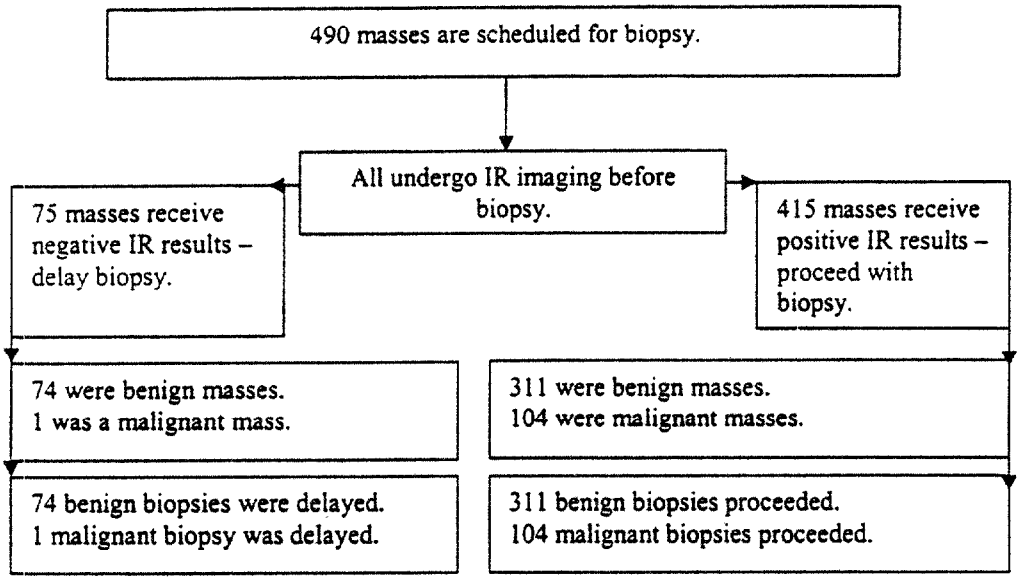
5. CLINICAL UTILITY

Approximately 1.2 million breast biopsies are performed every year in the United States. If the results of the clinical trial are consistent with general practice, approximately 75 to 80%, or 900,000 to 960,000 can be expected to yield benign results. The CTI BCS 2100 offers an opportunity to reduce this number, with a very high assurance that a negative IR test result reflects a truly benign condition.

The following shows the patient outcomes if the results of the clinical trial of the CTI BCS2100 were to be applied to clinical practice. It makes the following assumptions.

- The device is used to assess only subjects with lesions described as masses.
- All subjects would have gone to biopsy had the device not been used.
- Truth for malignancy or benignity is based on the pathology that would have been obtained if biopsy had proceeded.
- Each IR imaging positive or negative test result was based upon the threshold designated prior to the time the study blind was broken.
- A negative IR imaging result caused biopsy to be delayed.
- A positive IR result caused biopsy to proceed.
- Results are on per lesion basis.

Illustration. Net flow of subjects with breast masses who were converted from biopsy recommendation to follow-up recommendation



6. SAFETY DATA

Investigators at five sites enrolled 2,407 subjects in the clinical study during the period of October 1997 through April 2001. Four adverse events were reported during the study, and are itemized in the table below. Two of the events were assessed as possibly related to the device. Both were associated with patient discomfort during positioning on the device prior to imaging. Both events were rated as "mild" by the site investigator and resolved. One subject discontinued participation in the study due to the adverse event, and did not undergo the IR imaging procedure.

The remaining two adverse events were assessed as not likely to have been related to the device. One subject was hospitalized for treatment of a pre-existing metabolic disorder. Because this subject was hospitalized after IR imaging but before lesion biopsy, the hospitalization was reported as an adverse event during the study period. The investigator assessed the event as a serious event that resolved and was not related to the device. The second event that was assessed by the site investigator as not likely to be related to the device occurred in a subject who experienced dizziness when sitting up after IR imaging. The dizziness resolved within fifteen minutes after drinking apple juice. The investigator assessed the event as a mild event that resolved and was not related to the device.

At no time was any unanticipated adverse device effect (UADE) reported in association with the BCS2100 at any clinical site.

The small number and mild nature of reported adverse events in a population of 2,407 subjects demonstrates that the CTI BCS 2100 is a safe device.

Table 25. Safety data by site

	Total subjects enrolled	Total adverse events	Adverse events related to device	Adverse events unlikely related to device
Site 1a	204	3	2 NC1119 7/13/99 Subject experienced discomfort during positioning on the device. Subject discontinued prior to thermal imaging procedure. Rated as "mild". Resolved. NC1073 10/21/98 – 10/22/98 Subject experienced exacerbation of previously diagnosed sciatic nerve of the hip. Rated as "mild". Resolved.	1 NC1053 8/24/98-8/28/98 Subject was hospitalized due to complications of pre-existing hypothyroidism. Hospitalization was assessed by investigator as unlikely to be related to study, but took place during study period, between thermal imaging date and biopsy date, and was, therefore, reported as an adverse event for the study. Rated as "serious". Resolved.
Site 1b	165	0	0	0
Site 2	626	0	0	0
Site 3	428	0	0	0
Site 4	814	1	0	1 SA 0175 11/30/99 At completion of exam, patient sat up, had headache and felt dizzy. BP 130/50. Patient drank apple juice and "felt herself"after 15 minutes. Rated as "mild". Resolved.
Site 5	170	0	0	0
Total	2407	4	2	2

7. PATIENT COMPLAINTS

Three subjects reported complaints during the study. These subjects were enrolled into the study, but declined to undergo IR imaging because of anticipated difficulties in positioning themselves on the device due to pre-existing physical conditions. These subjects did not attempt to position themselves on device, and did not suffer any adverse events prior to withdrawing from the study.

Table 33. Patient complaints

Site	Subject Code	Complaint
3	MS0318	Not able to lie on stomach
5	LC0111	Had no cartilage in right knee and physically felt unable to get up on imaging table
5	LC0121	Not able to lay due to back pain

8. LABELING CONSIDERATIONS

8.1 Indication for Masses:

Because device effectiveness was demonstrated in breast lesions that included "mass" as a descriptor, the BCS2100 labeling will recommend that use of the device be indicated for breast lesions that include "mass" as a lesion descriptor. Presence of another lesion descriptor does not contraindicate use of the device, if the lesion is also described as a mass.

8.2 Recommendation for Short Interval Follow-up:

A mass identified as benign by IR imaging has a very high probability of being benign, as shown by the PMA and PPMA clinical data. However, in order to assure the safety of the rare subject with a malignant mass that is assigned a false negative IR test result, it is recommended that the appropriate recommendation for care for all patients receiving a negative IR test result be similar to the recommendation for care of a mass that is assigned to a mammographic BI-RAD category of 3. That is, a short interval follow-up is recommended in order to establish the stability of the finding. It is recommended that this follow-up assessment occur from three to six months after an IR procedure is performed that yields a negative test result. As the BCS2100 is incorporated into clinical practice, data will accumulate that will assist in determining the most appropriate time interval for follow-up. Labeling will be revised as necessary to reflect the most recent and complete data regarding recommendations for care after IR imaging.

9. SUMMARY OF SAFETY AND EFFECTIVENESS DATA

(As revised and submitted to FDA May 24, 2002)

I. GENERAL INFORMATION

Applicant's Name:
Computerized Thermal Imaging, Company
1719 West 2800 South
Ogden, UT 84401

Registration Number:
Pending

Submission Correspondent:
John Brenna
President
Computerized Thermal Imaging, Company
(801) 776-4700 Voice
(801) 337-8188 Fax

Device Generic Name:
Dynamic infrared imaging system

Device Trade Name:
CTI Breast Cancer System 2100

Device Classification:
System, Telethermographic

Device Class
Class III

Product Code:
IYM

CFR Section:
884.2980

Model:
Rev. 1

PMA Number:
P010035

Environmental Impact:
Computerized Thermal Imaging, Company claims categorical exclusion to the requirement to prepare an EA or an EIS for the device addressed in this Premarket Application original submission based on 21CFR 25.34.

Classification Panel:
Obstetrics and Gynecology Devices

Reviewing Panel:
Radiological Devices

Date of Panel Recommendation:
To be determined

Date of Notice of Approval to Applicant:
To be determined

II. INDICATIONS FOR USE

The CTI BCS2100 is a dynamic computerized infrared (IR) based image acquisition and analysis system intended for use as an adjunct to mammography to safely avoid biopsy of benign breast masses that would otherwise have undergone biopsy. The CTI BCS2100 provides additional information to guide a breast biopsy recommendation.

The CTI BCS2100 was tested and shown to be effective in the evaluation of breast masses scheduled for biopsy, achieving 99% sensitivity and 19% specificity in 490 breast masses. Because demonstration of device effectiveness was limited to breast lesions that included "mass" as a lesion descriptor, use of the CTI BCS2100 should be limited to the evaluation of breast lesions that include "mass" as a lesion descriptor. Presence of another lesion descriptor does not contraindicate use of the CTI BCS2100, if the lesion is also described as a mass.

Because larger malignant mass size was associated with increased IR indices of suspicion, or IOS, in masses ($p<0.0001$), the ability of the CTI BCS2100 to detect malignant masses appears to increase as the size of the mass increases.

The ability of the CTI BCS2100 to detect malignant masses also appears to be somewhat better in denser breasts, as evidenced by increased IOS values ($p=0.02$). However, this phenomenon is not well understood, and is undergoing further research.

It is not recommended that results from the CTI BCS2100 be used to delay biopsy of any mass if the physician feels that a clear indication exists for biopsy. The decision to proceed with, or delay, biopsy must ultimately be based on the physician's clinical judgment. Factors that may contribute to this decision include the mammographic assessment, the patient's involvement in the health care decision, family history of breast cancer, other known risk factors, physical findings or findings from other diagnostic testing.

A mass identified as negative by IR imaging has a very high probability of being benign, as shown by the clinical data. However, in order to assure the safety of a subject with a malignant mass that is assigned a false negative IR test result, it is recommended that the appropriate recommendation for care for all patients receiving a negative IR test result be similar to the recommendation for care of a mass that is assigned to a mammographic category of 3. That is, a short interval follow-up is recommended in order to establish the stability of the finding. It is recommended that this follow-up assessment occur from three to six months after an IR procedure is performed that yields a negative test result.

III. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

Contraindications:

- None known

Warnings:

- The CTI BCS2100 should not be operated in the presence of flammable anesthetic gases.
- Electrical shock will result if the operator touches the signal input or signal output ports on the computer, UPS, monitor, printer, or similar type device and the patient simultaneously.
- Patients weighing over 300 pounds should not be tested with the CTI BCS2100 because of the weight limit of the patient table.
- The CTI BCS2100 should be operated only by medical professionals who have completed training in its use.

Precautions:

- The CTI BCS2100 does not replace conventional methods for detection or diagnosis of breast cancer.
- A physician must evaluate the results of the procedure in conjunction with the patient's history, physical examination, mammography and other test results.
- The CTI BCS2100 was not studied in pregnant women due to the anticipated difficulties that pregnant women might experience lying prone for the duration of the IR imaging procedure.
- Power should never be turned off without first shutting down the system via the mouse and / or keyboard commands.
- Processor unit hardware and / or software should not be added or replaced by the user.
- The patient should not move during the imaging procedure.
- The patient should not talk during the procedure, as this could cause movement.
- Care must be taken to prevent any fluid from dripping into the equipment through the imaging aperture since this could damage the mirror or other internal components.
- Patients with limited mobility may require assistance in positioning themselves on the table.
- The CTI BCS2100 must be used in accordance with the instructions provided with the device.
- Installation and repair must be performed by CTI or its designated agent.
- The CTI BCS2100 Physician's Evaluation Subsystem must not be placed closer than 1.83 meters (6 feet) to the Data Acquisition Subsystem.
- The Data Acquisition Subsystem processor unit should not be opened or modified in any manner.
- The Physician's Evaluation Subsystem processor unit should not be opened or modified in any manner.

IV. DEVICE DESCRIPTION

The CTI BCS2100 contains two major subsystems, the Data Acquisition Subsystem (DAC) and the Physician's Evaluation Subsystem (PEV). The DAC is used to image the patient's breast and store the images. The images are transferred to the PEV for image analysis and evaluation. The CTI BCS2100 acquires a sequence of digital IR images of a patient's breast while the breast surface is cooled with refrigerated air. Image acquisition requires approximately 3.5 minutes per breast. The system then performs digital processing of the images to extract image features necessary for subsequent computer aided analysis. A graphical user interface allows a physician to select a region of interest (ROI) on the breast for analysis of malignancy likelihood. The likelihood value pertaining to the ROI is displayed electronically to the physician as an Index of Suspicion (IOS) value. The capability to electronically archive and print the IR images and image analysis results is also provided

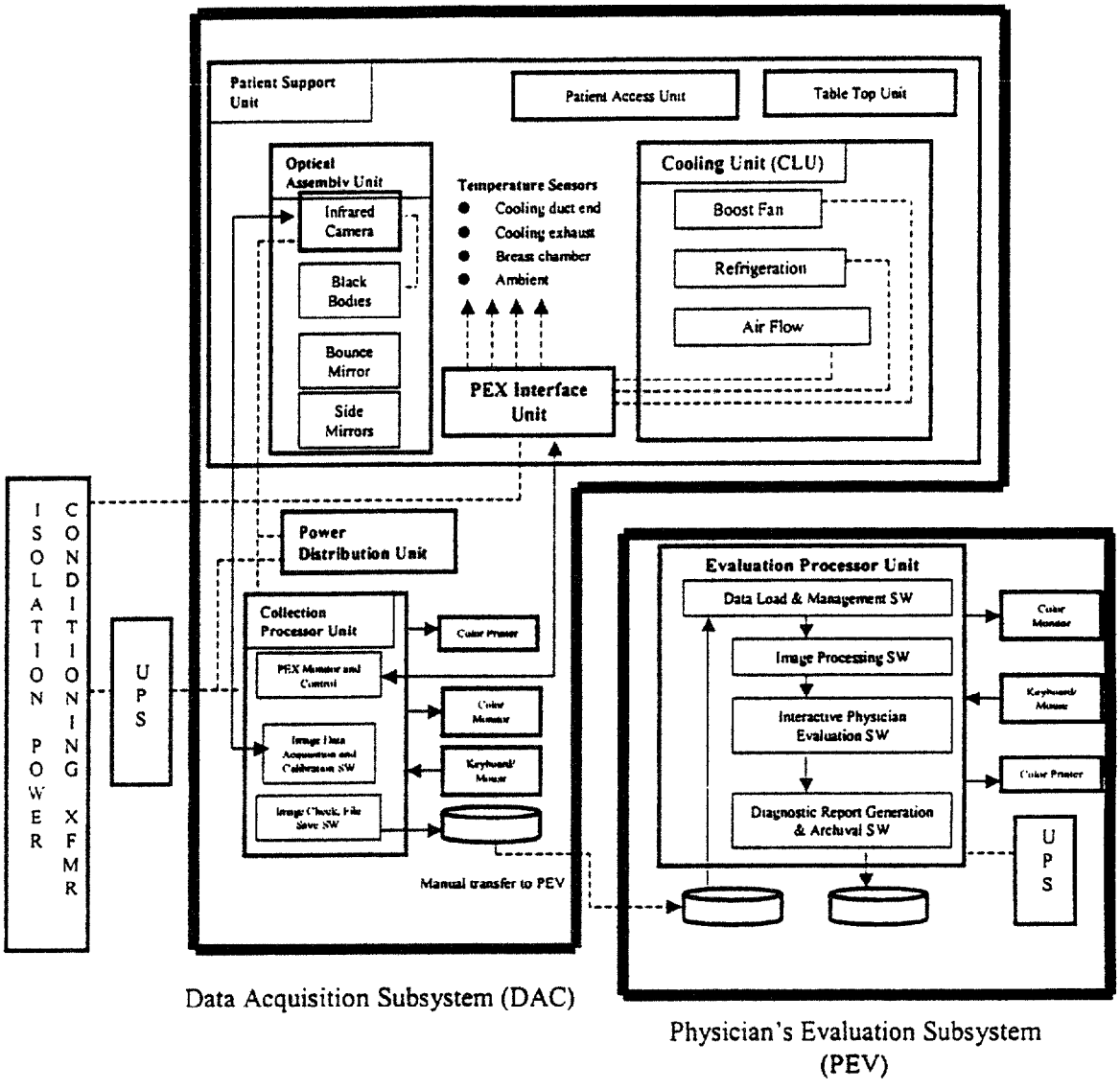


Illustration. A Block diagram of the CTI BCS 2100 showing the main components

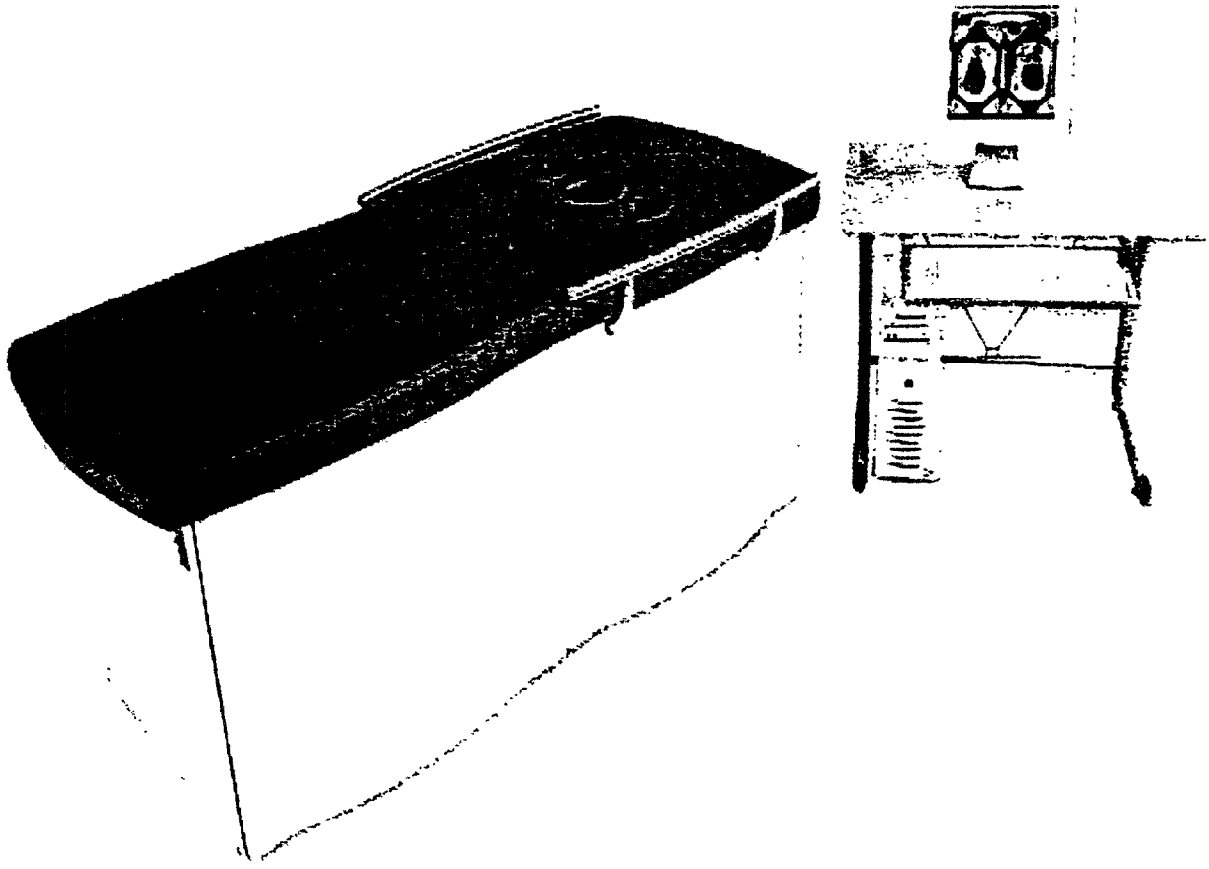


Illustration -- BCS2100

V. ALTERNATIVE PRACTICES AND PROCEDURES

Other methods used to aid in the detection and diagnosis of breast lesions include breast self-examination, clinical breast examination, mammography, ultrasonography, magnetic resonance imaging, positron emission tomography, electrical impedance scanning, fine needle aspiration and core and tissue biopsy.

VI. MARKETING HISTORY

The device has not been marketed in the United States. CTI has conducted exploratory discussions with government health officials and medical equipment importers to assess markets in Canada, Mexico, Brazil, Argentina, Chile and Kuwait. A purchase order was received, but later cancelled, for the purchase of ten systems for placement in Mexico. No systems have been shipped either domestically or internationally, other than the units used in the clinical trial to support the PMA.

VII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

There are no known potential adverse effects of the CTI BCS2100 on patient health when used according to prescribed labeling.

VIII. PRECLINICAL STUDIES

The following studies were conducted to determine that the CTI BCS2100 meets system design specifications dictated by systems requirements, electrical safety requirements, electromagnetic compatibility requirements, biocompatibility requirements, and reliability and durability requirements.

1. Bench Testing

Validation protocols were conducted for the mechanical, electro-mechanical, PEV software function, DAC software function, and camera requirements to demonstrate that the CTI BCS2100 operates within all documented requirements, specifications and parameters established by CTI. The resultant data generated from these protocols validated the non-clinical test requirements for safety and efficacy of the CTI BCS2100 system.

2. Biocompatibility Testing

CTI concluded that, based on the Biocompatibility Flow Chart for the Selection of Toxicity Tests for 510(k)s, biocompatibility requirements were met for the patient contact materials. This was based on material selection and selection of material that is used in a similar device that is legally marketed. Therefore, toxicology tests outlined in the "Use of International Standard ISO-10993", "Biological Evaluation of Medical Devices Part-1: Evaluation and Testing," (#G95-1, 5/1/95) were not conducted.

3. Electrical Safety Testing

CTI performed dielectric strength testing per EN60601-1 Clause 20, continuous leakage currents testing per EN60601-1 Clause 19, and protective earthing (ground continuity) per EN60601-1 Clause 18 on the BCS2100. These tests successfully passed the requirements of EN60601-1, per testing conducted by DNB Engineering.

During device development, CTI expanded the electrical safety testing scope from the basic electrical safety tests of IEC-601-1 to the full gamut of safety requirements for medical electrical systems per EN60601-1. Canadian Standards Association (CSA) International conducted these tests. The CTI BCS2100 passed the requirements of EN60601-1 and was issued a Certificate of

Compliance (Certificate No. 1147841) and a CB Test Certificate (Certificate No. CA 2530) that allows the device to bear the CSA monogram with U.S. and Canadian compliance.

4. Electromagnetic Compatibility Testing

CTI conducted the following electromagnetic compatibility testing on the CTI BCS2100:

- EN60601-1-2 (Medical Equipment)
- EN55011 Class A Group 1 (Radiated and Conducted Emissions)
- EN61000-4-3 Radiated Immunity (3V/M 80-1000MHz)
- EN61000-4-4 Electrical Fast Transients
- EN61000-4-5 Surge
- EN61000-4-6 Conducted Immunity (3V .15-80MHz)
- EN61000-4-8 Magnetic Field Immunity
- EN61000-4-11 Voltage Dips and Variations
- FDA 510(k) Magnetic Field Emissions (reference Mil-Std 461D RE101)
- FDA 510(k) Magnetic Field Immunity (reference Mil-Std 461D RS101)
- FDA 510(k) Conducted Susceptibility (reference Mil-Std 461D CS114)
- FDA 510(k) Slow Sags and Surges
- FDA 510(k) Over voltage / Under voltage
- FDA 510(k) Quasi-Static Discharge
- FDA 510(k) Voltage Dropout

The CTI BCS2100 passed the electromagnetic compatibility requirements of the standards and tests listed above, per testing conducted by DNB Engineering.

5. Reliability and Durability Testing

Continuous life cycling of a CTI BCS2100, Revision 0, demonstrated the reliability and durability of the system to meet a Mean Time To Failure (MTTF) goal of ≥2000 hours set by CTI. This reliability and durability goal was based on the ≥2000 hour MTTF specification set by the manufacturer of the IR imaging camera. The continuous life cycle was concluded when the IR imaging camera failed after 2639 hours of operation. This cycling simulated the testing of 12,979 patients.

A CTI BCS2100 system, configured as a Revision 1, started life cycling on March 7, 2001 to determine the reliability, durability, and the expected life of the components contained within the Revision 1 system. CTI set a new reliability and durability goal of the ≥5000 hours MTTF for the Revision 1 system. The manufacturing of the IR imaging camera has incorporated the use of a new RC2 Detector / Micro-Cooler assembly that has a MTTF of ≥5000 hours. As of May 21, 2002, the system had logged 10,465 hours, which simulated the testing of 41,309 patients without failure.

6. Stress and Wear Testing

Continuous life cycling of a CTI BCS2100, Rev. 0, demonstrated the stress and wear of the system to meet a MTTF goal of ≥2000 hours set by CTI. This reliability and durability goal was based on the ≥2000 hour MTTF specification set by the manufacturer of the thermal imaging camera. The continuous life cycle was concluded when the thermal imaging camera failed after 2639 hours of operation. This cycling simulated the testing of 12,979 patients.

Continuous life cycling of a CTI BCS2100, Rev. 1, is being conducted to demonstrate the stress and wear of the system to meet a MTTF goal of ≥5000 hours set by CTI. This reliability and durability goal is based on the ≥5000 hour MTTF specification set by the manufacturer of the thermal imaging camera. The manufacturing of the IR imaging camera has incorporated the use of a new RC2

Detector / Micro-Cooler assembly that has a MTTF of ≥5000 hours. As of May 21, 2002, the system had logged over 5000 hours without failure. Life cycle testing will continue until failure.

IX. SUMMARY OF CLINICAL STUDIES

A. Overview:

The protocol was entitled "Clinical Study of the Examination of Breasts for Identification of Suspicious Tissue Using Clinical Examination and Mammography With and Without the CTI Thermal Imaging System." Five centers participated in the clinical study from 10/23/97 through 4/30/01. A total of 2,407 subjects were enrolled. The studies were conducted as nonsignificant risk studies under 21CFR812 in consultation with the FDA and the reviewing IRBs.

B. Protocol:

Protocol title:

"Clinical Study of the Examination of Breasts for Identification of Suspicious Tissue Using Clinical Examination and Mammography With and Without the CTI Thermal Imaging System"

Study hypothesis:

The study hypothesis was that the CTI BCS2100 could safely differentiate benign breast masses from malignant breast masses based on the relatively lower strength of the IR signal in benign tissue, thereby demonstrating that the BCS2100 is a safe and effective device when used adjunctively to mammography to avoid biopsy of benign masses that would have otherwise undergone biopsy.

Study objectives:

The following objectives were established to provide evidence to confirm the study hypothesis.

- Efficacy objective: To demonstrate that the BCS2100 can be used to avoid a large number of biopsies of benign masses, without significantly affecting the outcomes of subjects with malignant masses. This objective was demonstrated in a group comprised of all masses that could be localized with mammographic films and that had evaluable IR images.
- Safety objective: To demonstrate that the BCS2100 is a safe device. All subjects who enrolled in the study were analyzed for safety and complaints.

Study design:

The study design incorporated a blinded multi-center study that compared the levels of suspicion of malignancy of suspicious breast lesions before and after IR imaging, using the pathology findings from biopsies of the identified lesions as the "gold standard" references.

Patient population:

Patients at five clinical sites throughout the United States who were recommended for breast biopsy based on abnormal findings on clinical physical examination and/ or mammography were given the opportunity to enroll in the study.

Patient inclusion / exclusion criteria:

Inclusion criteria:

- Subject underwent a mammogram, results were interpretable and a surgical or core biopsy within sixty days had been recommended, or

- Subject underwent a clinical examination, results were available and a surgical or core biopsy had been recommended, and
- Subject signed an Informed Consent Form

Exclusion criteria:

- Subject had previous surgery in breast of interest within last year
- Subject had breast implants
- Subject had breast reduction
- Subject had previous radiation therapy in breast of interest
- Subject's body weight was over three hundred pounds (table limit)
- Subject was pregnant
- Subject had histologically proven cancer in breast of interest

Procedures:

- Subjects who met initial entry criteria were invited to participate.
- Subjects who agreed to participate provided appropriate written informed consent.
- Information regarding previous mammographic procedures, if applicable, was collected.
- A subject history was taken that included breast cancer risk factors, nicotine, alcohol and caffeine use, and demographic data.
- Site investigators recorded the type and size of each lesion to be biopsied.
- A physical examination was performed of the subjects' breasts.
- Subjects underwent IR imaging of their breasts with the CTI BCS2100.
- Safety data regarding the investigational device and procedure were collected.
- The subjects were released and underwent biopsy as previously planned.
- IR data, appropriate case report forms (CRFs), and mammographic films and reports were transferred from the sites to CTI.
- IR imaging data were correlated to case report form and mammographic information.
- IR imaging files were prepared for physician analysis by independent blinded radiological technologists
- Independent radiologists, using mammography films for localization, attempted to assess IR images and assign IOS values to all evaluable masses.
- Independent radiologists also assessed breast density while reviewing each lesion's mammographic films.

C. Demographics:

Because of the nature of the study, the majority of the enrolled subjects were female; less than 1% with breast lesions were male. Over one-half of enrolled subjects were between the ages of 50 and 60, with approximately one-third greater than 60 years of age. Less than 12 % were under 40 years of age. Approximately 60% of the enrolled subjects were Caucasian, followed by African Americans, Latinos, Asians, and others.

D. Safety results:

Four adverse events were reported during the study. Two of the events were assessed as possibly related to the device. Both were associated with patient discomfort during positioning on the device prior to imaging. Both events were rated as "mild" by the site investigator and resolved. One subject discontinued participation in the study due to the adverse event, and did not undergo the IR imaging procedure.

The remaining two adverse events were assessed as not likely to have been related to the device. One subject was hospitalized for treatment of a pre-existing metabolic disorder. The investigator assessed the event as "serious", and resolved. The second event assessed by the site investigator as

not likely to be related to the device occurred in a subject who experienced dizziness when sitting up after IR imaging. The dizziness resolved within fifteen minutes after drinking fruit juice. The investigator assessed the event as "mild" and resolved.

No unanticipated adverse device effect (UADE) was reported for any subject.

E. Efficacy results:

Overall efficacy in masses:

The primary objective, to demonstrate that the CTI BCS2100 could be used to lower the large number of biopsies that are performed every year on benign masses, was demonstrated by assessing the performance of the IR imaging device when used as a follow-up procedure after a suspicious mass had been identified through mammography.

The ability of the device to avoid biopsies of masses that turned out to be benign was confirmed, with a sensitivity of 99% and a specificity of 19.2%. A total of 74 biopsies of masses that turned out to be benign would have been avoided. One malignant mass would have been assigned to short-term follow-up.

Table 26. Study results in masses: Sensitivity and specificity

Lesion type	Number of masses			Sensitivity			Specificity		
	Malig.	Benign	Total	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Mass	105	385	490	99.0%	95.6%	100.0%	19.2%	16.0%	22.8%

Table 27. Study results in masses: Negative and positive predictive values

Lesion type	Positive predictive value			Negative predictive value		
	Pt. Est.	LCB	UCB	Pt. Est.	LCB	UCB
Mass	25.1%	24.2%	25.9%	98.7%	96.5%	100.0%

Efficacy by mass size:

It was demonstrated that malignant mass size was associated with IOS ($p<0.0001$). In spite of the fact that the CTI BCS2100 correctly would have sent small malignant masses to biopsy, there were too few very small malignant masses in the clinical trial to be able to determine if there was a lower size limit beyond which the device would not be effective The smallest malignant masses correctly assigned a positive IR test result in the clinical trial were 0.1cm and 0.4cm. One malignant mass that measured 1.0 cm was incorrectly assigned a negative IR test that was very close to the positive / negative test threshold. Regression analysis relating IOS to benign mass size did not produce statistical evidence of a relationship ($p=0.86$). These data validate the hypothesis that the BCS2100 works by detecting increased physiological activity associated with malignancy.

Efficacy by breast density:

It was demonstrated that breast density was associated with IOS for malignant masses ($p=0.02$). Regression analysis relating breast density to IOS for benign masses did not produce statistical evidence of a relationship for benign masses ($p=0.14$). The ability of the device to detect malignant masses appears to be somewhat better in denser breasts, but this phenomenon is not well understood, and is undergoing further research.

Efficacy applied to clinical utility:

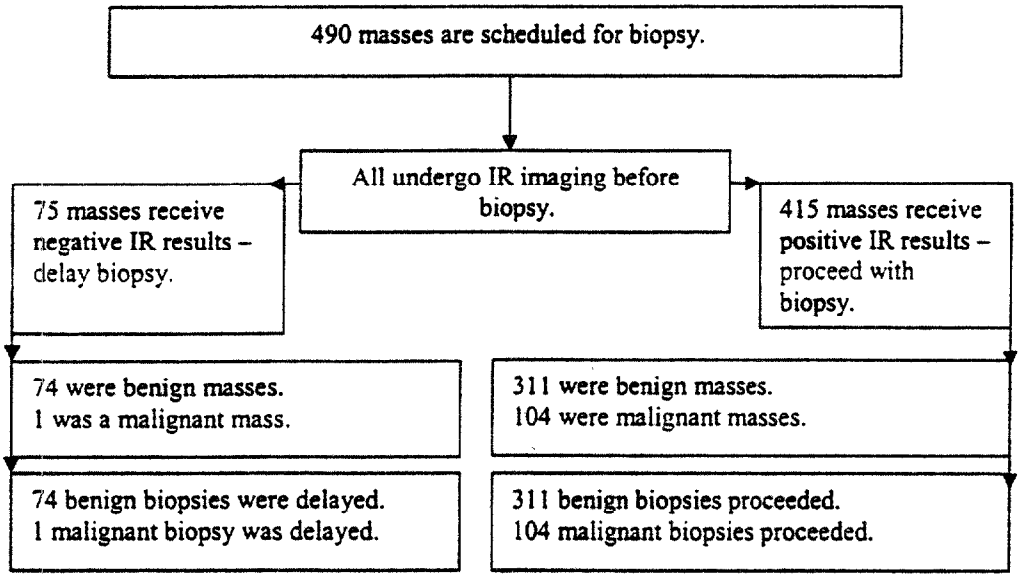
Approximately 1.2 million breast biopsies are performed every year in the United States. If the results of the clinical trial are consistent with general practice, approximately 75 to 80%, or 900,000

to 960,000 can be expected to yield benign results. The CTI BCS2100 offers an opportunity to reduce this number, with a very high assurance that a negative test result reflects a benign condition.

The following shows the patient outcomes if the results of the clinical trial of the CTI BCS2100 were to be applied to clinical practice. It makes the following assumptions.

- The device is used to assess only subjects with lesions described as masses.
- All subjects would have gone to biopsy had the device not been used.
- Truth for malignancy or benignity is based on the pathology that would have been obtained if biopsy had proceeded.
- Each IR imaging positive or negative test result was based upon the threshold designated prior to the time the study blind was broken.
- A negative IR imaging result caused biopsy to be delayed.
- A positive IR result caused biopsy to proceed.
- Results are on per lesion basis.

Illustration. Net flow of subjects with breast masses who were converted from biopsy recommendation to follow-up recommendation



There were 490 evaluable masses in the clinical trial. Of these, 385 were found by biopsy to be benign; 105 were found to be malignant. Of the 385 benign masses, 74 received a negative test result, giving an overall specificity of 19%. Of the 105 malignant masses, 104 received a positive test result, giving an overall sensitivity of 99%. There were 415 positive and 75 negative IR test results. Of the 415 positive IR test results, 104 were associated with malignant masses, giving a positive predictive value (PPV) of 25%. Of the 75 masses receiving negative IR test results, 74 were associated with benign masses, giving a negative predictive value (NPV) of 99%.

X. CONCLUSIONS DRAWN FROM THE STUDIES

The results of the clinical studies demonstrate that the CTI BCS2100 is a safe and effective device when used adjunctively to mammography to avoid biopsies of benign masses that would otherwise have undergone biopsy.

XI. PANEL RECOMMENDATIONS

To be determined.

XII. CDRH DECISION

To be determined.

XIII. APPROVAL SPECIFICATIONS

To be determined.

10. BIBLIOGRAPHY

1. Smart CR, Byrne C, Smith RA, et al. Twenty-year follow-up of the breast cancers diagnosed during the Breast Cancer Detection Project. *CA Cancer J Clin* 1997; 47: 134-149

2. Tabar L, Fagerberg CJ, Chen HH, et al. Efficacy of breast cancer screening by age: New results from the Swedish Two County Trial. *Cancer* 1995; 75: 2507-2517

3. Fletcher SW, Black W, Harris R, Rimer BK, Shapiro S. Report of the International Workshop on Screening for Breast Cancer. *J Natl Cancer Inst* 1993; 85: 1644-1656

4. Shapiro S. Screening: assessment of current studies. *Cancer* 1994; 74: 231-238

5. Leitch AM, Dodd GD, Costanza M, et al. American Cancer Society guidelines for the early detection of breast cancer: update 1997. *CA Cancer J Clin* 1997; 47:150-153

6. U.S. Preventive Services Task Force. *Guide to clinical preventive services.* Baltimore: Williams & Wilkins, 1996-

7. Liberman L, Abramson AF, Squires, FB, et al. The Breast Imaging Reporting and Data System: positive predictive value of mammographic features and final assessment categories. *AJR* 1998; 171: 35-40

8. Orel SG, Kay N, Reynolds C, et al. BI-RADS categorization as a predictor of malignancy. *Radiology* 1999; 211: 845-850

9. Liberman L. Clinical management issues in percutaneous core breast biopsy. *Radiol Clin North Am* 2000; 38: 791-807

10. Brenner RJ, Sickles EA. Surveillance mammography and stereotactic core breast biopsy for probably benign lesions: a cost comparison analysis. *Acad Radiol* 1997; 4: 419-425

11.Burkhardt JH, Sunshine JH. Core-needle and surgical breast biopsy: comparison of three methods of assessing cost. *Radiology* 1999; 212: 181-188

12.Bodai BI, Boyd B, Brown L, Wadley H, Zannis VJ, Holzman M. Total cost comparison of 2 biopsy methods for nonpalpable breast lesions. *Am J Manag Care* 2001; 7: 527-538

13.Adler DD, Carson, PL, Rubin JM, Quinn-Reid D: Doppler-ultrasound color flow imaging in the study of breast cancer: preliminary findings. *Ultrasound Med Biol* 16; 553-559, 1990

14. Dixon JM, Walsh J, Paterson D, Chetty U: Colour Doppler ultrasonography studies of benign and malignant breast lesions. *Br J Surg* 79; 259-260, 1992

15.Hanahan D, Folkman J: Patterns and emerging mechanisms of the angiogenic switch during tumorigenesis. *Cell* 86(3); 353-364, 1996.

16.Gasparini G, Harris AL: Clinical importance of the determination of tumor angiogenesis in breast carcinoma: Much more than a new prognostic tool. *J Clin Oncol* 13; 765-782, 1995.

17. Weidner N, Semple SO, Welch WR, Folkman J: Tumor angiogenesis and metastasis-correlation in invasive breast carcinoma. *N. Engl J Med* 324; 1-8, 1991

18. Los M, Voest EE: The potential role of antivascular therapy in the adjuvant and neoadjuvant treatment of cancer. *Semin Oncol* 21(1); 93-105, 2001.

19. Anbar M: Clinical thermal imaging today: shifting from phenomenological thermography to pathophysiologically based thermal imaging. *IEEE Engineering in Medicine and Biology*. 17 (4):25-33, July/August 1998

20. Anbar M: Hyperthermia of the cancerous breast – analysis of mechanism. *Cancer Letter* 84; 23-29, 1994

21. Thomsen LL, Miles DW, Happerfield L, Bobrow LG, et al: Nitric oxide synthase activity in human breast cancer. *Br J of Cancer* 72(1); 41-44, 1995

22. Vaupel P, Hockel M. Blood supply, oxygenation status and metabolic micromilieu of breast cancers: characterization and therapeutic relevance. *Int J Oncol* 17(5); 869-79, Nov 2000.

23. Parisky Y, Sardi A, Hamm R, Hughes K, Esserman L, Rust S, Callahan K: Efficacy of computerized infrared imaging analysis when evaluating mammographically suspicious lesions. *AJR* in press Jan 2003