1. Phase 1 Final Report (DE-FG02-04ER83962) Cervical SPECT Camera for Parathyroid Imaging

1.1 Identification and Significance of the Problem or Opportunity and Technical Approach

Hyperparathyroidism is a clinical syndrome of systemic symptoms and signs such as renal stones, muscle weakness, psychiatric disorders, bone pain and abdominal pain. Hyperparathyroidism is becoming more prevalent recently with an estimated 2 out of every 1,000 American women over the age of 40 suffering from the disease \((1)\). Primary hyperparathyroidism (PHPT), characterized by excessive secretion of parathormone (parathyroid hormone \([PTh]\)) by one or more enlarged parathyroid glands, has become one of the most common endocrine diseases in the world \((2)\). Its estimated prevalence in the United States is 0.5 per 1,000 (51% asymptomatic) in over 40 year old (yo) men \((3), (4)\). Based on US census 2000 bureau reports \((5)\) there are thus approximately 160,000 new cases of PHPT per year in the US. Considering that about one tenth of all patients with PHPT undergo the current treatment plan for parathyroidectomy surgery, there are approximately 16,000 resulting surgeries per year. Parathyroidectomy has a notable mortality rate because the anatomy of the anterior neck compartment is very complex and the parathyroid has close proximity to vital and fragile structures increasing the risk of mortality to the patient during surgery. Complicating this matter is the variability of parathyroid location due to its embryologic location.

Normally, there are 2 pairs of parathyroid glands in adult humans. Each gland measures approximately 6 x 4 x 2 mm and weighs approximately 30–50 mg (total weight, approximately 130–140 mg). Although supernumerous parathyroid glands are present in approximately \(2\%–5\%\) of the population, the presence of <4 glands is a rarity. One pair of glands is typically located at the posterolateral surface of the lower lobes of the thyroid. The second pair is typically positioned at the posterolateral surface of the upper poles of the thyroid lobes.

Migration of the parathyroid glands during fetal development from their original location to the final juxtathyroidal location explains why the surgical approach to the parathyroid glands can be intricate and variable. In most cases, normal upper glands are located posterior to the middle and upper third of the thyroid lobe and posterior to the recurrent laryngeal nerves, cranially to the inferior thyroid artery. The location of normal inferior parathyroid glands, however, is more variable, probably as a consequence of the more complicated migration process, which brings them from a cranial position to a caudal position relative to the other pair of parathyroid glands. In approximately 50% of explorations, the lower parathyroid glands are found posteriorly or laterally to the lower pole of the thyroid lobe, usually within a 20-cm radius. With decreasing frequency, they are found within the thyrothymic ligament, within the thymus in the mediastinum, and intrathyroidal. When parathyroid glands become adenomatous or hyperplastic and enlarge, their location may change somewhat. \(80\%–85\%\) of parathyroid adenomas are found adjacent to the thyroid gland in their normal location, \(15\%–20\%\) are ectopically placed (Fig. 1).

![FIGURE 1. Anatomic locations of abnormal parathyroid glands found at reoperation by single group. Most common ectopic sites mirror routes of descent of upper parathyroid glands (short migration path) and of lower parathyroid glands (longer migration path in association with thymus) (modified from (6)).](image)

When no preoperative imaging was available, bilateral exploration was mandatory, because discrimination between single-gland and multigland disease was solely based on macroscopic appearance of all glands. Parathyroidectomy is complicated by the variability in the number of parathyroid glands, the different locations of normal and abnormal glands as described above, and problems in distinguishing normal glands from those that are diseased. The utilization of parathyroid imaging introduced the prospect of focused, minimal surgeries.

Early imaging attempts involved US and \(^{201}\text{Tl}^{\text{Tc}}\text{-pertechnetate subtraction scintigraphy. Recently}^{\text{Tc}}\text{sestamibi scintigraphy has shown its superior ability to identify and locate the parathyroid adenoma preoperatively.}

The accuracy of the parathyroid tumors’ localization by US varies as a function of the size and location of the adenoma. The sensitivity of US identification of parathyroid adenomas ranges between \(70\%\) and \(80\%\) \((7), (8)\). The sensitivity of US evaluation falls to \(40\%\) in patients who have had prior failed surgical exploration \((9), (10)\). US is
highly sensitive in detecting parathyroid adenomas located behind the thyroid gland or located beyond the lower contour of the thyroid, but finds difficulty visualizing upper parathyroid glands located medially, deep in the neck in the para- and retropharyngeal space (11), (12), (13), or close to the carotid bifurcation (14), (15). Moreover, parathyroid enlargement can be mimicked by other structures in the neck, such as muscles, vessels, enlarged lymph nodes, and esophagus (14). Therefore, the rate of false-positive ultrasound (US) results is not negligible, with specificities reported between 40% and 100% (7), (8), (9), (10), (11), (12), (13), (15), (16).

US has lower sensitivity and accuracy than scintigraphy for detecting parathyroid tumors. However, when used in combination with other imaging procedures such as thyroid scintigraphy, it is useful to differentiate enlarged parathyroid glands from thyroid nodule(s) (9), (10), (13), (17). This combination also appears to be of value in detecting parathyroid enlargement in patients with secondary hyperparathyroidism (9), (10), (13).

The overall sensitivity of CT for preoperative identification of hyperplastic parathyroid glands ranges between 46% and 80%. The sensitivity consistently approaches 80% with intravenous contrast enhancement because adenomas and hyperplastic parathyroid glands are hypervascular. Prior neck surgery affects the sensitivity of CT imaging. Artifacts caused by metallic clips from previous surgery ("sparkler" effect) lower the sensitivity of CT to 46%–58% (18), (19). There has been some speculation that if CT was combined with SPECT that it may increase the sensitivity for parathyroid adenomas and hyperplasia detection. However in a recent study by Gayed et al, (20) at University of Texas M.D. Anderson Cancer Center, they found no significant clinical value of adding CT. They in fact stated that eliminating the CT spared patients additional time, radiation exposure, and expense (20). In the detection of ectopic thyroid glands there was only a minimal improvement in detection rate of 2% (20).

Imaging of normal parathyroid glands by MRI is poor due to their small size (<5 mm) (21). However, its ability to characterize nodular lesions on the basis of intensity make this technique particularly attractive (22), however these image patterns do not distinguish parathyroid adenomas from either simple hyperplasia or carcinoma.

Paired evaluations in the same patients have shown that the sensitivity of MRI is equivalent to that of parathyroid scintigraphy. However, the specificity has been found to be consistently lower (23), (24), (25), (26). Most authors believe that MRI is worth performing when parathyroid scintigraphy is negative or equivocal or when it suggests an ectopic gland (23), (24), (27). However, some authors suggest the systematic use of combined MRI and parathyroid scintigraphy (despite the associated high costs) because this approach should increase the accuracy and reliability of preoperative identification and localization of parathyroid lesions (24), (28).

Due to the less-than-optimal accuracy of the then conventional imaging techniques, the National Institutes of Health consensus statement on the treatment of PHPT in 1990 (28) concluded that preoperative localization in patients without prior neck surgery was rarely indicated and not proven to be cost-effective, recommending 4-gland bilateral exploration with discrimination between single-gland and multi-gland disease based solely on macroscopic appearance of the glands as the operation of choice. However, the success of surgery, as measured by return to normal calcium levels, continued to depend primarily on the experience and the judgment of the surgeon in recognizing the difference between enlarged or normal-sized glands, although the size of the parathyroid gland does not always correlate well with the secretion of PTH. Thus efforts towards improved imaging techniques continued and recently a paradigm shift towards minimally invasive parathyroidectomy (MIP) in the surgical treatment of PHPT brought about by the introduction of Tc-99m Sestamibi parathyroid imaging has emerged. A 2000 survey of the members of the International Association of Endocrine Surgeons indicated that, as of 2000, $^{99m}$Tc-sestamibi-based MIP had been adopted by >50% of the surgeons worldwide (59% from America, 56% from Australia, and 49% from Europe and the Middle East).

**Parathyroid Scintigraphy**

$^{99m}$Tc-sestamibi, a myocardial perfusion agent, exhibits significant uptake and retention in the abnormal parathyroid glands of patients with PHPT (29). Successful utilization of $^{99m}$Tc-sestamibi imaging for localizing abnormal parathyroid glands has been confirmed by numerous reports (30), (31), (32), (33), (34) and, with some protocol modifications, has become the parathyroid imaging technique worldwide (35).

The localization of $^{99m}$Tc-sestamibi in the parathyroid tissue is a function of metabolic activity, accumulation occurring specifically in the mitochondria. The overall uptake in hyperplastic or adenomatous parathyroid glands is linked to the blood flow, gland size, and mitochondrial activity (36). Like other radioactive imaging agents (such as


$^{201}$Tl, $^{99m}$Tc-sestamibi accumulates both in the thyroid and in the parathyroid tissue within minutes after intravenous administration. However, what makes this tracer especially useful for parathyroid imaging is its different washout rate from the 2 tissues, as $^{99m}$Tc-sestamibi is released much faster from thyroid than from parathyroid tissue. Planar imaging of the neck and thorax is recorded starting 15 min and then 2–3 h after the intravenous injection of $^{99m}$Tc-sestamibi (approximately 740 MBq [20 mCi]) (Fig. 2). The scan is considered positive for parathyroid disease when an area of increased uptake that persists on late imaging is found (29). High-quality scintigraphy with $^{99m}$Tc-sestamibi can accurately localize parathyroid adenomas in 85%–95% of patients with PHPT (37), (38), (39), (40), (41).

Image Subtraction is a second technique combining dual-phase $^{99m}$Tc-sestamibi imaging with a second radiopharmaceutical that accumulates specifically in the thyroid gland and not in the parathyroid tissue. The images are subtracted from one another to allow detection of focal uptakes specific for abnormal parathyroid tissue. One such application is the $^{99m}$TcO$_4^-$/99mTc-sestamibi, dual-tracer subtraction technique (42). However, this technique has its own shortcomings.

SPECT Imaging with Standard Whole Body SPECT

Factors affecting the diagnostic accuracy of $^{99m}$Tc-sestamibi imaging of parathyroid glands include regional perfusion, gland size and functional activity, cell cycle phase, and prevalence of mitochondria-rich oxyphil cells (43), (44). As little as 100 mg hyperfunctioning parathyroid glands can be detected with application of an appropriate imaging protocol and technique(11), (45), (46), (47), (48) The use of a pinhole collimator for parathyroid imaging, with a trade-off in image acquisition time, increases imaging resolution. SPECT offers the advantage of better discrimination of focal $^{99m}$Tc-sestamibi retention in thyroid nodules and the parathyroid tissue and an improvement in the overall detection rate of parathyroid adenomas (49), (50). Most authors now favor a wider application of this imaging modality, especially in patients with recurrent hyperparathyroidism after prior surgery (13), (15), (44), (50), (51), (52), (53), (54).

However, in a busy clinical practice this technique is rarely used for evaluating the neck alone. SPECT utilizing standard whole body scanners suffers from sub-optimal imaging geometry and poor resolution with a parallel hole collimator. Pinhole collimation offers improved spatial resolution, but with worse sensitivity due again to the sub-optimal geometry resulting from applying a large whole body scanner to the neck region. These problems can be overcome with the use of a dedicated cervical SPECT camera for parathyroid imaging.

Minimally Invasive Parathyroidectomy

The gold standard approach of bilateral neck exploration in the treatment of PHPT is gradually shifting to a more minimally invasive approach (20), (55), (56), (57). Most surgeons believe that a bilateral neck exploration is an over treatment especially in cases were there is a solitary parathyroid adenoma (56). Minimally invasive surgery may entail a mini open approach through a 2-3cm unilateral incision, or a videoscopically assisted surgery, or an endoscopic, or a radioguided technique (57). Regardless of the approach of Minimally Invasive Parathyroidectomy, preoperative localization is mandatory assuming the hyperparathyroidism is caused by a solitary parathyroid adenoma (56). However recent studies have shown that using SPECT imaging with other imaging modalities (20), (47), (55), (47), (56), (57) can improve detection for single or multiple adenoma detection.
Dedicated Parathyroid Imaging

The introduction of a dedicated imaging device for parathyroid imaging could offer the surgeon the ability to narrow the surgical procedure by precise pre-surgical localization of the parathyroid adenomas, single or multiple, including those in the ectopic sites. Additionally, by combining minimally invasive parathyroidectomy with dedicated imaging, all pathological parathyroid can be localized at the initial surgery preventing the need for any additional surgeries from a missed lesion. Through this newly proposed instrumentation the surgeon could for the first time determine whether a MIP procedure is warranted and plan a far less invasive surgery. Less invasive surgery offers minimal scars, decreased risk of damaging vital vessels and nerves and less hospital time. Thus the newly proposed device has the potential to yield enormous savings in the cost of medicine in the United States.

1.2 Anticipated Public Benefits

PHPT disorder has become one of the most common endocrine diseases in the world (1). During the last 40 years, its estimated prevalence in the United States jumped from about 0.08 per 1,000 (18% asymptomatic) to about 0.5 per 1,000 (51% asymptomatic) (2,3). The anterior neck compartment is very complex; the parathyroid has close proximity to vital and fragile structures that have the potential for extensive mortality to the patient during surgery. Complicating this matter is the variability of parathyroid location due to its embryologic location. The standard treatment of PHPT today is still bilateral neck exploration. This procedure is highly invasive and has a non-negligible mortality risk. New minimally invasive parathyroidectomy to be achieved by high-resolution, high-sensitivity parathyroid SPECT will allow the physician to effect less invasive surgery. The introduction of the proposed dedicated imaging device for parathyroid imaging will allow the surgeon to fine tune the surgical procedure by finding the exact location of all parathyroid adenomas. The surgeon can then use a minimally invasive procedure and plan the surgery accordingly. Less invasive surgery offers minimal scars, decreased risk of damaging vital vessels and nerves and less hospital time. Dedicated parathyroid imaging also offers easy imaging acquisition and frees up the conventional gamma camera for the daily duties of a nuclear medicine department. One additional benefit of combining MIP with dedicated imaging is the promise of locating all pathological parathyroids at the initial surgery preventing the need for any additional surgeries from a missed lesion.

Thus the newly proposed device has the potential to yield enormous savings in the cost of medicine in the United States.

1.3 Degree to Which Phase I Demonstrated Technical Feasibility

1.3.1. Summary of Phase I Accomplishments

During Phase I of this project, we were able to accomplish our objectives and successfully demonstrate the feasibility and practicality of using a pixelated CZT camera for thyroid and parathyroid imaging. The goals in phase I of this project have been met or exceeded. We addressed each of the specific aims listed in the Phase I proposal. These specific goals of the Phase I project are:

Task 1: Detector Design

We have successfully designed and implemented advanced and unique solid state cross-grid CZT detector modules for the cervical SPECT imaging application. To our knowledge these are the first such structures implemented on CZT.

Task 2: Detector Mounting

Ceramic carrier boards have been successfully designed, fabricated and mounted to the cross-strip detector modules. They provide not only the mechanical support of the detector material, but also the electronic connections between the readout electronics and detector unit.

Task 3: Readout Electronics

Readout electronics with 16 channel ASIC circuitry was incorporated into the system and its performance has been successfully evaluated.

Task 4: Detector Fabrication and Evaluation
6 prototype modules have been fabricated using this design and experiments have been conducted to characterize the detector.

**Task 5: Pixelated CZT Detector Evaluation**

The pixelated CZT detector modules developed in Phase I were thoroughly tested. The test results showed the feasibility of employing pixelated CZT detector module for this project.

**Task 6: Phantom Measurements**

A thyroid phantom was purchased for this project and modified by adding a small (3 mm) fillable sphere attached to the “thyroid” part of the phantom to simulate a parathyroid nodule. The phantom was filled with Tc-99m and imaged using a rotational mechanical movement to acquire projection data.

**Task 7: Scanner and Gantry Design**

The scanner, dedicated SPECT gantry, pinhole collimator, camera mounting support, scanner driving mechanism and patient bed have been designed and a prototype system is ready to be manufactured in Phase II.

1.3.2. Detailed Report of Phase I Accomplishments

1.3.2.1 Task 1: Detector Design

We have developed position-sensitive cross-strip CdZnTe (CZT) detector as proposed shown in Figure 3 and have fabricated six detectors during the Phase I period of this project. Each detector module was built on a 25 mm by 25 mm single CZT crystal. Among the six detectors, three of them have the thickness of 2 mm and the other three are 3 mm thick.

![FIGURE 3. Cross grid concept detector](image)

1.3.2.2 Task 2: Detector Mounting

![FIGURE 4. Detector to ASIC interface](image)
Figure 5 shows the original design of the detector assembly (from the Phase I proposal). This design has been realized as shown in Figure 5. Figure 5.a shows the cathode side of the detector, which is considered the top side of the detector module. The anode side (bottom side) of the detector is mounted directly to a custom designed ceramic carrier. Figure 5.b shows the anode side of the detector with carrier board mounted.

Sixteen conductive strips were attached to each side of the detector with the strips on the cathode side being orthogonal to those on the anode side, resulting in a grid pattern of 256 pixels. All strips were made of 1.46 mm wide platinum. The pitch size is 1.56 mm with 0.1 mm gap between strips. Each strip is connected to a small wire, which runs parallel to the wires from other strips to a smaller connector on the ceramic carrier board on the anode side. The carrier board on the anode side has traces for transporting both the anode and cathode signals to a 40-pin connector located on the back side of this carrier. The detector is always illuminated from the cathode (top) side. The cathode strips are implemented by an array of parallel conductive traces on thin flexible circuit, which also serves as a flexible data bus to route the cathode signals to the ceramic carrier board.

Such a design resulted in a vertical assembly of the cross-strip device with all interconnections lying behind the active area of the detector. This assures that high packing fractions will be obtained in 4-side mounting devices.

1.3.2.3 Task 3: Readout Electronics

Figure 6 shows the detector module testing jig with one detector module mounted. Figure 6.b shows a sealed testing jig for one detector module mounted.
A multiPIX detector module testing jig, as shown in Figure 6, with one 16-channel charge-sensitive ASIC (eV Products, Saxonburg, PA) was used to test the detector module. The cathode strips were biased through 10 Mega-ohm resistors and cathode signals were AC-coupled to ASIC inputs. Signals from anode strips were DC-coupled to ASIC providing a low impedance DC path to ground. As the ASIC is 16 channels, we decided to have 8 AC-coupled cathodes signals and 8 DC-coupled anodes signals from the cross-strip CZT array each amplified by a channel in the 16 channel ASIC module. Thus all the signals from one quadrant of the detector area were processed and collected. To assure proper condition of the detector bias the remaining 8 anode strips were connected to common ground.

Figure 7 is the diagram of the entire electronics for the detector module testing system. The ASIC output voltage signals are fed into a specially designed charge division circuit. This board was then used to convert the cathode and anode signals into four position encoding signals. The position encoding readout circuit is based on current division method used in two-dimensional position-sensitive proportional counters. Two symmetrical circuits are used for anode and cathode strip position identification, respectively. The anode strip circuit comprises two anode summing amplifiers driven by signals from each anode while each cathode strip signal is fed to two cathode summing amplifiers. The network of 16 resistors for each anode and cathode strips and gain of amplifiers were chosen to obtain the linear encoding of strip position versus output voltage. The charge division circuits provide four outputs representing signals from +X and –X direction for cathode strips and from +Y and –Y direction for anode strips. The signals are then fed into shaping amplifiers and digitized with ADCs located on data acquisition board. The ADCs were triggered by the sum signal from anode strips processed by Tennelec TC 451CF Timing SCA.

1.3.2.4 Task 4: Detector Evaluation

1.3.2.4.1 Current-Voltage Characteristics

The current-voltage characteristics of the entire device were measured by connecting all of the cathode strips together and split anodes strips into two groups, each of 8 strips. A negative bias voltage was applied to the cathode strips and the detector current was measured from anode strips by two picoamp-meters, each connected to 8 anode strips.

The purpose of splitting of anode strips was to evaluate the leakage current uniformity over detector active area. Both groups of anode strips showed similar values of leakage current. An average leakage current of 5 nA per strip was measured with 600 V bias at room temperature. This corresponds to a dark current of 0.3 nA/mm². This is a reasonable level.

1.3.2.4.2 Gamma-Ray Response Measurements
The ASIC output signals were amplified, shaped using a NIM module linear amplifier and fed to a multi-channel analyzer (TRUMP-PCI-2K) to study the spectrum of the signals from anode and cathode. Different shaping time was used to achieve the best energy resolution, throughput and photo-peak efficiency. Figure 8 shows the typical signal from one anode strip (Figure 8.a) and one cathode strip (Figure 8.b).

A Co-57 source was used to irradiate the CZT detector with gamma rays at 122 keV. Figure 9 shows the typical spectra from one anode strip (Figure 9.a) and one cathode strip (Figure 9.b). It is apparent that the anode spectrum shows much better energy resolution and less tailing of the photo peak. This is due to the more complete electron collection at the anode than hole collection at the cathode.

Gaussian functions were fitted to recorded full energy peaks to determine their position and energy resolution. The energy spectra from anode strips of the CZT array were recorded for biases from 300 V to 600 V and peaking time ranging from 0.6 to 4 μs. Energy resolution, noise performance and photo-peak efficiency were evaluated. The energy resolution was evaluated as the full width at half maximum (FWHM) of the photo peak. We believe that the measured resolution is very reasonable for this novel device and is quite encouraging.

Table 1 lists the energy resolution, as well as the photo peak efficiency with different shaping times of Co-57 spectra from one anode strip with 600 V bias applied to the detector. The peaking time ranged from 0.6 to 4 μs. We observed a significant increase in the number of events recorded in strip spectra with increasing peaking time. The total number of events above 18 keV energy recorded at a 4 μs spectrum is larger than that recorded at 0.6 μs by a factor of 2.5. Thus, the combination of sensitivity, photo peak efficiency and energy resolution rendered 4 μs peaking time an optimal choice.

![Figure 8](image1.png)

**a. Anode signal from detector**

**b. Cathode signal from detector**

Figure 8 typical waveform of an anode strip signal (a) and a cathode strip (b) signal after ASIC preamp. Notice that cathode signal has a negative polarity.

![Figure 9](image2.png)

**a. Co-57 Spectrum from one anode strip**

**b. Co-57 spectrum from one cathode strip**

Figure 9. Typical Co-57 spectra from one anode strip (a) and one cathode strip (b).
Table 1. Photo peak efficiency with different shaping time

<table>
<thead>
<tr>
<th>Peaking Time [μs]</th>
<th>Photopeak FWHM [keV]</th>
<th>+/-10% Energy window</th>
<th>+/-15% energy window</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
<td>13.4</td>
<td>47.0</td>
<td>57.7</td>
</tr>
<tr>
<td>1.2</td>
<td>12.7</td>
<td>48.2</td>
<td>58.0</td>
</tr>
<tr>
<td>2.4</td>
<td>12.5</td>
<td>52.4</td>
<td>61.7</td>
</tr>
<tr>
<td>4.0</td>
<td>13.5</td>
<td>56.6</td>
<td>65.6</td>
</tr>
</tbody>
</table>

1.3.2.4.3 Imaging Measurements

As shown in Figure 7, the anode and cathode signals from the detector module were encoded to generate 4 weighted signals, namely +X, -X, +Y, and −Y, such that the rather simple “back-end” data acquisition system described could be easily and directly deployed to acquire images from each detector module. The encoded +X (from anode) and +Y (from cathode) signals are demonstrated in Figure 10.

Figure 10. Amplified encoded signals from anodes (c) and cathode (d) before feeding to ADC board.

a. Amplified and encoded X1 signal from anode
b. Amplified, inverted and encoded signal from cathode

Figure 11. Intrinsic image one quadrant of the cross grid detector module using LumaGEM software.

a) Intrinsic flood image
b) Identified pixels from intrinsic flood image
Figure 12. Spectrum of one representative pixel.

Figure 13. Summed spectrum of cross grid detector module. The overall energy resolution of the entire detector is 28 keV, or 20% FWHM.

1.3.2.5 Task 5: Pixelated CZT Detector evaluation

While the results of the novel cross-grid array device developed in Phase I were extremely interesting and show great promise, at the same time as the cross grid CZT detector was being evaluated, we were also working to improve the Company’s base 2-D pixel technology by using corporate funds to invest heavily into finer pitch 2-D arrays. We have been able to move the state of the art forward considerably so that the superior energy resolution of pixilated CZT is now combined with significantly smaller pitch size of 1.5 mm (prior state of the art at 2.5mm x 2.5mm was approximately 300% larger area than what we have now developed and was at the time unusable for the parathyroid SPECT project). However, we are in the very good position now of comparing the two technological approaches and suggesting the best method to move forward in Phase II. This choice involves consideration of what will lead to the greatest chance of success with the Phase II full system prototype. Towards this goal we investigated the potential of employing the fine pitch 2-D CZT arrays for the thyroid imaging application.

Each 1.5 mm pitch CZT detector module measures 1 inch by 1 inch and consists of 16 by 16 pixels, and 64 (6 by 8) modules are employed in each of Gamma Medica’s next generation Molecular Breast Imaging systems (LumaGEM 3200S 12K). Thus we have been able to evaluate this approach thoroughly and to characterize the performance of the small pitch size pixeled CZT detector module.
First, spectra from several isotopes covering the energy range from 20 keV to 250 keV were measured and compared with the measurements on our current 2.2 mm and 1.5 mm pixelated NaI(Tl)/PSPMT (Position Sensitive Photomultiplier Tube) technology to evaluate the energy resolution of the pixelated CZT detector module. Figure 14 displays the spectra of these tested isotopes, and the energy resolution for each photo peak in Figure 14 is plotted in Figure 15. The energy resolution was < 5% at energies ranging from 120-170 keV, superior by a factor of two or more to that of any of our in house scintillator based gamma camera technologies (or any in the world for that matter) and superior to the cross grid CZT detector we have investigated in this work. This outstanding energy resolution offers great opportunity of having a narrow energy window for imaging resulting in significantly enhanced contrast, and also multiple isotope imaging capability.

The detector sensitivity was measured using a Tc-99m source when equipped with both high resolution and high sensitivity collimators. The resulting sensitivity of the detector with different energy cutoff windows is plotted in Figure 16. Similarly, the data from 1.5 mm pitch and 2.2 mm pitch NaI(Tl) gamma camera were compared in this figure as well. The graph shows that the sensitivity of the 1.5 mm CZT detector is always better than scintillator based gamma camera, regardless of the window size around the photo peak. Furthermore, due to the excellent energy resolution from CZT detector, it can use a much narrower window around the photo peak without losing sensitivity. Hence, signal to noise ratio is expected to be higher in acquired data and image quality should be improved.
Conclusion regarding the Choice of Detector Technology for Phase II

As a result of our evaluation of both cross grid CZT detector and pixelated CZT detector, we believe that the small pitch pixelated CZT module is the best candidate for the Phase II realization of the prototypical gamma camera system for this project.

1.3.2.6 Task 6: Anthropomorphic Phantom Measurements

To test the components of the camera we conducted preliminary phantom testing on a Lucite thyroid phantom. An average thyroid measures 2.5-4cm in length, 1.5 - 2cm in width, 1 - 1.5cm in thickness, weighing approximately 20 grams. The average parathyroid measures $6 \times 4 \times 2$ mm and weighs approximately 30-50 mg. The thyroid Lucite phantom was obviously the best choice for preliminary testing. The phantom is constructed from Lucite and simulates a 30-40 gram thyroid and has the dimensions of $10.2 \times 10.2 \times 2.2$ cm. The phantom can be filled with the appropriate amount of radiotracer concentration to replicate an active thyroid. The phantom contains both hot and cold nodules to mimic abnormal thyroid nodules. Figure 17 shows the picture of the thyroid phantom. These dimensions permit precise duplication of clinical conditions.

Figure 17. Thyroid phantom
The thyroid phantom was filled with Tc-99m aqueous solution at a concentration of 0.064 mCi/ml. One 0.26 ml button was filled, sealed and attached to posterior portion of the thyroid phantom with a concentration of 0.64 mCi/ml; 10 times the concentration in the simulated thyroid body.

The camera was equipped with a 1.0 mm pinhole collimator with a focal length of 7.0 cm and ROR of 6.0 cm. The phantom was mounted onto a circular automated gantry that was previously developed for small animal imaging by Gamma Medica. Tomographic SPECT data were obtained in a step and shoot mode. A total number of 64 projects over 360 degrees were acquired with each projection accumulating 30 seconds of data. Figure 18 is the setup for this imaging acquisition. The CZT camera is stationary while the thyroid phantom rotates, driven by a computer controlled motor. The red spot on the phantom is the small cup simulating a parathyroid nodule.

Figure 19 shows two typical projection images at different rotating angles. An OSEM iterative pinhole image reconstruction algorithm was used to reconstruct the phantom image. The resulting image is shown in Figure 20 and 21. The simulated parathyroid nodule can be clearly identified in the reconstructed image. The cold buttons inside the body of the main thyroid phantom can also be clearly separated in the reconstructed image.

The imaging experiments described above using the thyroid phantom successfully shows the feasibility of achieving our goals of significantly enhanced parathyroid imaging using small pitch pixelated CZT detector and pinhole aperture.
Figure 19. Projection image of the thyroid phantom.

Figure 20. Sagittal slices of the thyroid phantom reconstructed image.
Figure 21. Three standard views and projection views of reconstructed thyroid phantom image.

1.3.2.7 Task 7: Scanner and Gantry Design

a. Camera ring at opening position  
b. Camera ring at closed position
We have finished the design of the scanner and gantry. As shown in Figure 22. The scanner consists of a patient bed and two C-arms which hold two half-ring detector structures. These two C-arms will be mounted onto a rail and driven by a computer controlled motor. During operation of the scanner, the two C-arms will move towards each other simultaneously to form a single ring structure. The inner diameter of the ring is 149 mm. This diameter was chosen to offer an optimal inner circumference to adjust for various neck sizes supporting the general patient population. Figure 22.a and 22b demonstrates the operation of the scanner between open and closed position.

Inside each C-arm, there are 4 cameras equipped with pinhole collimator. When the entire ring is formed, all 8 cameras from both arms are evenly distributed over 360 degree angle. There is a Gonioimetric cradle driving mechanism behind each C-arm. They are synchronized to rotate both C-arms in both directions up to 45 degrees, which is the angle between two adjacent cameras. Thus the projection of patient thyroid at any angle can be sampled by rotating the C-arms to a proper angle position.

Figure 22.c shows the two C-arms that are mounted onto the rail and rotated simultaneously in one direction. Figure 22.d is the inner structure of one C-arm. Four gamma cameras are evenly spaced in the C-arm, driven by a Gonioimetric cradle (yellow and green part). Except the upper and lower opening for purpose of camera rotation, the C-arm and Gonioimetric cradle are sealed inside a frame, thus no moving parts will be in contact with the patient. The detector ring layout during the operation of the scanner is given in Figure 22.e.
Reference List


