Design and development of a Compact Gamma Camera for the Detection of Malignant Sentinel Lymph Nodes

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Abstract

Breast cancer is most often treatable when detected in the early stages, before the primary disease spreads to sentinel lymph nodes in the axilla and supraclavicular region. A sentinel lymph node is the closest adjacent lymph node to receive lymphatic drainage from a primary breast tumor. It is from these nodes that cancer cells metastasize throughout the lymphatic system, spreading the disease. This work details the design and optical Monte Carlo modeling of an ultra compact, nuclear medicine gamma camera that will be used intra-operatively to detect sentinel lymph nodes. This development will improve the identification and localization of these sentinel nodes, thereby facilitating improved techniques for auxiliary lymph node dissection (ALND), and sentinel lymph node biopsy.

I. Introduction

Breast cancer is most often treatable when detected in the early stages, before the primary disease spreads to sentinel lymph nodes in the axilla and supraclavicular region. A sentinel lymph node is the closest adjacent lymph node to receive lymphatic drainage from a primary breast tumor. It is from these nodes that cancer cells metastasize throughout the lymphatic system, spreading the disease. This work details the design and optical Monte Carlo modeling of an ultra compact, nuclear medicine gamma camera that will be used intra-operatively to detect sentinel lymph nodes. This development will improve the identification and localization of these sentinel nodes, thereby facilitating improved techniques for auxiliary lymph node dissection (ALND), and sentinel lymph node biopsy. The closest adjacent draining nodes to the site of a primary tumor are known as sentinel lymph nodes. The sentinel lymph node is the point of origin from which cancer cells metastasize throughout the lymphatic system, spreading the disease. In the case of breast cancer, these lymph nodes are located in the axilla and supraclavicular regions. It is proposed that if these diseased lymph nodes could be precisely spatially mapped using an imaging technique offering high specificity, and then it would be possible to surgically excise only the diseased nodes, making the surgery considerably less invasive than would be the case with axillary lymph node dissection (ALND). A major limitation of conventional gamma cameras is that they are not designed to be used intra-operatively. Due to their extremely large footprint and shielding mass, mobile gamma cameras are not commonly found in current clinical practice. For this reason, intra-operative clinical nuclear medicine studies have seldom if ever been performed in the OR. At the Royal Jubilee Hospital on Vancouver Island, diagnostic imaging is performed pre-operatively and post-operatively, but never during surgery. However, because the proposed camera under discussion is so compact, it can be used in the operating theatre to create diagnostic quality images in real time. This is different from a standard intra-operative gamma probe such as a Neoprobe or C-Trak, which does not provide an image. Our camera performs an external mapping of the region of interest, allowing the surgeon to perform a more precise excision during surgery.

II. The Theory of Operation

The operation of a conventional gamma camera involves the conversion of a number (N) of gamma-ray photons into an image on a computer screen. The process starts with a radiopharmaceutical such as ^{99m}Tc-Sestamibi being injected into the patient, which is preferentially taken up by the tumor, making the tumor more radioactive than the surrounding tissue. Attached to the camera head, a collimator (which is simply a plate of lead with holes in it) blocks gamma rays, which are not normally incident to the imaging plane. Gamma rays, which penetrate the collimator, enter a scintillator, causing flashes of visible light, which are allowed to spread in a pyrex light spreader and then are detected by a close-packed hexagonal array of photomultiplier tubes. The resulting data is fed into a computer where Anger Logic is used to reconstruct an image, within which a particularly bright spot corresponds to the site of a primary or a meta-static tumor.

The development of a hand-manipulated ultra-compact gamma camera is made possible through a fusion of totally new hybrid technology, which permits miniaturization of the conventional gamma camera.

In our objective to miniaturize the conventional gamma camera, we required a device that would operate in a similar way, but be much smaller. The detector that was specifically chosen for this application is a Multi-pixel Hybrid Photodiode (M-HPD) manufactured by Delft Electronic Products. The M-HPD is a position-sensitive vacuum photo-tube employing a hybrid of photo-multiplier and photodiode technology, and has a sensitive area of 25 mm diameter with an overall diameter of 52.7 mm (Figure 1). The detector has a fiber optic entrance window, which constrains visible light spread. The imaging plane of the M-HPD is made up of a close-packed array of 73 hexagonal PIN photodiodes (reproducing the structure of the photo-multiplier tubes in the conventional camera). Each hexagonal photodiode element measures 2.68 mm across flats. The signal is read out through an array of 112 small pins on the underside of the detector (Figure 2).

Collimated gamma-rays incident from within the patient interact through photoelectric absorption and Compton scattering in a scintillator, which is optically coupled to the M-HPD's entrance window, causing a flash of optical light. Many of these optical photons penetrate the fiber optic entrance window and strike the photocathode where they are converted into photoelectrons. The electrons are then accelerated towards the anode by an applied electric potential of 12 kV. The impact ionization of 3.62 eV in the silicon anode results in a gain of approximately 3000. Since the charge generated within each anode pixel can be read out individually, the location of the vertex of each gamma-ray interaction within the scintillator may be found using one of two algorithms. The first, allowing sub-pixel resolution, is centroiding. This process relies upon finding the "center of gravity" of the charge signals read out from a group of anode pixels. The other method, known as the "Winner Take All" algorithm requires a much simpler calculation. This algorithm requires that the pixel with the most deposited charge be assigned the sum of the charge read out on all 73 pixels. Spatial resolution becomes limited to the pixel size (2.68 mm), but the algorithm is fast, and can handle charge distributions, which may lead to misleading results if decoded using centroiding. The position of interaction determined using either of the two methods in turn correlate with the source of collimated gamma rays originating from the radiotracer located in the sentinel lymph nodes.

III. Testing and Measurements

The first part of the camera that gamma-rays encounter is the collimator. The collimator is usually constructed from lead or tungsten with parallel holes drilled in it. Gamma rays, which are not at or near normal incidence to the collimator are absorbed and dissipated as heat.

The collimator has a strong effect on the camera's operation. If its holes are too large, the resulting resolution is poor, meaning that some detail in the image may be lost. If the holes are too small, the resulting sensitivity is poor, meaning that it takes a long time to aquire an image. Because of this, an optimization must be performed so that a design is achieved which allows an appropriate trade-off between resolution and sensitivity. Our optimization yielded a collimator design with holes 1 mm in diameter drilled in a 1 cm thick slab of lead. Using simulation plots and planning on the use of a Winner Take All algorithm, we chose an acceptable resolution value of 3.2 mm (only marginally larger than the M-HPD's anode pixel size). To allow the flexibility of using either reconstruction algorithm, we also wanted the holes to directly map to the anode pixels of the M-HPD. In conjunction with a MATLAB program, we chose a hole diameter of 1 mm, with a hole separation of 1.34 mm and a hole length of 1 cm. Since these holes were separated by exactly half of the anode pixel diameter, and since they were in a hexagonal array, the holes were placed such that exactly 4 of them would map to each anode pixel. The result is a good count rate of 7.1 kHz with a hole alignment that will allow the Winner Take All algorithm to function while keeping misleading results to a minimum.

After the gamma rays penetrate the collimator, they enter a small puck-shaped crystal called a scintillator. The purpose of the scintillator is to absorb the high-energy gamma-ray photons, and release a burst of visible light. Light that it produces can be detected by the M-HPD since the scintillator is mounted in direct contact with the M-HPD's entrance window.

The first thing that must be decided in this phase of the project is which type of scintillator to choose. Each scintillator type produces a slightly different wavelength of light, and each photon detector type best detects a particular wavelength of light. Since the photon detector type was chosen early on in the project, this decision was based on finding a scintillator whose output wavelength best matched the peak sensitivity of the detector. This scintillator type is called Thallium doped Cesium Iodide, CsI(T1). It has an output wavelength of 565 nm, which is in the green region. The scintillator's diameter was chosen to match the diameter of the M-HPD's photocathode (27 mm), which is just slightly larger than the sensitive area of the detector. However, determination of thickness required further investigation.

Software donated by Lambda Research Corporation called TracePro was used to determine the optimal thickness of the scintillator. As the thickness of the scintillator decreased, the light produced inside it was not permitted to spread very far before entering the M-HPD. As expected, as the thickness of the crystal was allowed to increase, the plot shows that the width of the light pool also increased. This is due to light being allowed to spread to a greater extent before leaving the scintillator. From the TracePro plots, it was determined that the optimal thickness of crystal would be 4 mm. This would allow the light to spread enough that a centroiding technique could be used, but not so much that a Winner Take All algorithm would yield meaningless results. Looking further into the light spread function, and knowing the characteristics of the gamma ray, the scintillator, and the M-HPD, it was possible to simulate the distribution of electrons in the pixellated anode of the M-HPD. This investigation revealed that almost 200,000 electrons would be generated in the central pixel of the detector, a value that could only be guessed at without this method.

For the electronic parts of the system, the detector plugs directly into an interface board, which in turn plugs directly into a "front-end board" (Figure 3). The head of the camera is shielded against gamma rays coming from any direction except through the collimator (Figure 4). The front-end board acts as a preamplifier for the small signals produced by the detector. These signals then pass to a controller board, which acts as an interface between the computer and the front-end board. It also is responsible for sending control signals to the front-end board. Finally, the signals are passed to an analogue to digital converter, which resides inside of a computer. Once the information is inside the computer, it is decoded and reconstructed in order to produce an image, which is viewed by a surgeon.

The electronics for this project were custom designed specifically for this project by a Norwegian company called Integrated Detector and Electronics (IDE). IDE understood our requirements to have the circuitry fit into a camera with dimensions appropriate for hand-manipulation, and designed the electronics specifically to "hide" behind the M-HPD. Only the electronics that needed to be near the detector were placed on the front-end board, thus minimizing the size. All other control electronics were placed in a remote box on the control board, which was referred to on the previous panel. This board is called the MCRI board (see Figure 5).

On the front-end board (a close-up is shown in Figure 6) can be found 3 chips manufactured by IDE called VA/TA chips (Figure 7). Each chip can handle 32 input channels; so three of them are daisy-chained together to allow the capture of 96 input channels (of which we only use 73). These chips do the work of triggering the readout sequence to begin, as well as amplifying the extremely small signals produced by the M-HPD. Our electronics are capable of a read-out frequency of 5 million samples per second, which is more than enough for this project and allows for the possibility of higher activity detection in the future.

As visible light traverses material boundaries, reflections can be minimized if the material the light is entering has a refractive index equal to or higher than the material it is leaving. This concept was used while looking to the future of our camera. We found that the use of a segmented CsI(T1) scintillator (index=1.79) coupled to a Cerium doped YAP, M-HPD entrance window (index=1.94) increases light collection efficiency of the camera from 46.6% to 82.5%. Potentially, this could allow the camera to produce sharper images due to the higher intensity light.

While the unusual looking light spread function (shown left) produced by this setup was a surprise, we soon theorized that it may be possible to use the lobes of the function to expand the sensitive area of the camera beyond the sensitive area of the detector. The charge distribution simulation (right) confirmed these conceptual design principles, which will be incorporated into our next generation gamma camera.

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Figure 1: The Multi-pixel Hybrid Photo Diode

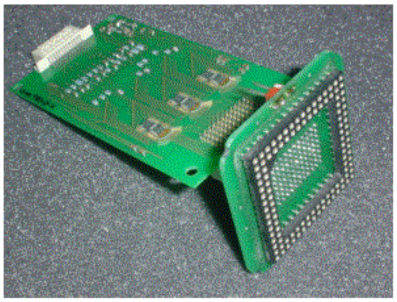

Figure 2: Interface and Front-End Boards

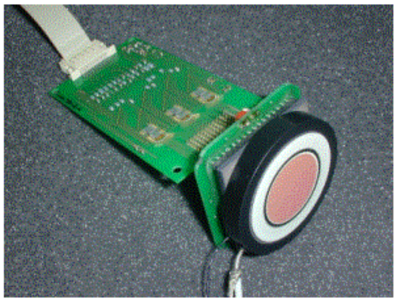

Figure 3: M-HPD Connected to Front-End Electronics

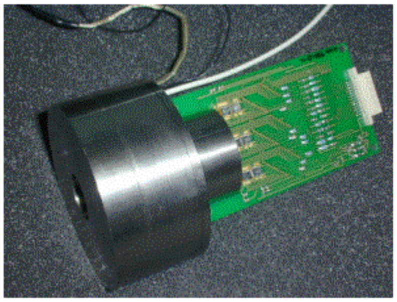

Figure 4: Camera Head Shielding

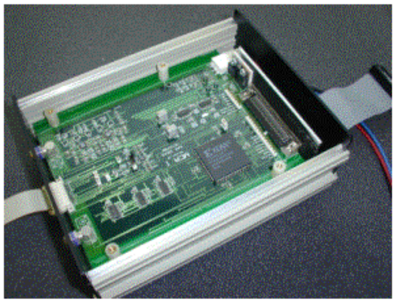

Figure 5: MCRI Controller Board

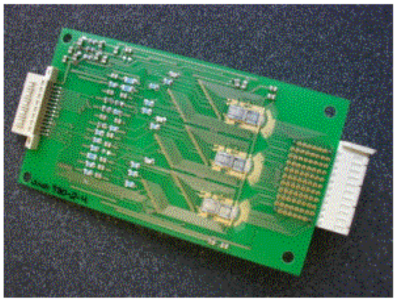

Figure 6: Front-End Board Close-Up

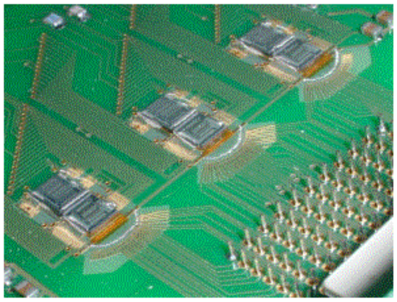

Figure 7: VA/TA Chip Close-Up