論文の内容の要旨

論文題目： **DEVELOPMENT OF DIGITAL ANIMAL DOUBLE-PHOTON EMISSION TOMOGRAPHY USING TIME-OVER-THRESHOLD METHOD**

（高分解能 PET 用新規 DOI 検出手法に関する研究)

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This research was particularly done towards developing high-resolution coincidence imaging systems including positron emission tomography (PET) and double-photon emission computed tomography (DPECT) with full digital readout schemes using time-over-threshold (ToT) methods. Particularly in PET, since the trend for high-resolution imaging is reducing the detector pitch and implementing dual-ended readout for depth of interaction (DOI) identification, the number of channels is increasing generation by generation. In chapter 4 of the thesis, it is explained that why individual readout is necessary in order achieve sub-mm resolution. The conventional multiplexing network (electronic encoding) limits the spatial resolution to 1-mm and no further improvement can be done by reducing the crystal size. Quantitively speaking, for a system with 2-mm-pitch pixelated detectors and electronic encoding (b = 1 in the principle formula for the spatial resolution of a PET scanner), the spatial resolution in the center of the ring is 1.4 mm, while 1-mm resolution is expected from a system with a 2-mm detector-pitch. On the other hand, reading out the large number of channels without multiplexing is not feasible. With the conventional analog-to-digital conversion (ADC) approach, each channel will be digitized in 12 bits, which multiplies the number of outputs by 12. ToT is an alternative ADC method that provides a single-bit output for each channel. It is also very compact since it has only one comparator. Therefore, it can be implemented for a large number of channels on a small application-specific integrated circuit (ASIC) board. Since each channel has only one-bit signal, digital multiplexing is feasible, and it does not make any distortion in demultiplexing because the signal is encoded digitally and decoded in the data processing.

In this work a digital readout scheme based on the conventional time over threshold method was evaluated for a 2-mm pitch PET system without DOI capability. This system has1152 channels that is enough for the first evaluation. A modular PET system with a 2-mm detector pitch was assembled. Each module was 12 × 12 detector array (144 channels). Details about this system and materials are presented in chapter 4 of the thesis. Even though the ToT ASIC boards were partially broken, and the threshold level could not be adjusted (leading to very poor energy resolution), the data was recorded, decoded, coincidence data was extracted, and a ~ 1-mm spatial resolution was assessed in the center of the ring. In this digital multiplexing scheme, miscoding happens sometimes due to some noise or pulses from neighboring channels. In such cases, that pulse cannot be decoded, it will be skipped, and therefore, it does not lead to mispositioning of the original detector. In this sense, this readout scheme is robust against the noise from other channels, while in conventional PET systems such noises lead to distortion in positioning the original signal, and consequently poorer spatial resolution in the image.

The next digital animal PET system with sub-mm resolution was aimed to have detectors twice the number of detectors in previous system. Therefore, the pitch should be around $\sqrt{2}$ so that within the same dimensions the number of channels will be twice. KETEK GmbH manufactures SiPM arrays (PM1125) with 1.36-mm pitch which is close to $\sqrt{2}$. This can provide 0.7 mm spatial resolution in the center of the ring, however, in order to develop a submillimeter PET imager, it is essential to apply a DOI estimation method to the system. Since the detector has smaller pitch and longer length (for better detection efficiency), parallax error is more severe. In the 2-mm system (with 15-mm long crystals) the spatial resolution at the edge of FOV is ~ 4 mm (center of the ring: ~ 1 mm), while in the 1.36 mm system (with 20-mm long crystals), it is ~ 6 mm (center of the ring: ~ 0.7 mm). Thereby, it is necessary to remove or reduce this vast variation in the spatial resolution of the image in the next animal PET system.

In chapter 5 of the thesis, the parallax error and DOI identification approaches are discussed. Among all the methods, dual-ended readout method has been proven to be the most effective approach to estimate the depth of interaction of gamma photons inside the scintillator crystals. Also, one of the great advantages of this method in our system is that it can be easily implemented with the proposed digital readout scheme. In this study, the dual-ended method (for pixelated crystals) for a 1.2 × 1.2 × 20 mm^3 Ce:GAGG (cerium-doped $Gd_3Al_2Ga_3O_{12}$) crystal was explored. DOI resolution as fine as crystal pitch was experimentally achieved that would results in the total elimination of parallax error in the image. In other words, the spatial resolution at the edge of FOV would be the same as that in the center (0.7 mm). It is worth mentioning that this fine DOI resolution was obtained without subtracting the collimation uncertainty, and the actual resolution must be even better. Moreover, there were no report of such a fine DOI resolution in the literature. The closest experimental report is [1] with 1.76-mm resolution for unpolished LYSO crystal with 0.62 mm width (half as wide as our crystal), where 0.7 mm DOI resolution is expected. The reason behind this fine resolution is that, first, GAGG crystal has higher light yield (almost twice). As making contrast between the two outputs of the dual-ended readout is done by introducing light loss, the higher light yield is beneficial and provides an acceptable energy response. Second, in all published works, it was believed that increasing the roughness of crystal lateral surfaces improves DOI resolution while there was no thorough study on the roughness of latera sides as a variable for DOI. Mostly, polished and unpolished crystals were compared. In addition, very fine electronic collimation and event selection might have influenced the results; i.e., it might be closer to the actual DOI resolution, since the actual resolution is usually better than the measured values due to collimation width in the measurements.

Nonetheless, there are still some area open for investigation. One important note is that this resolution is achieved for a $1.2 \times 1.2 \times 20\ mm^3$ GAGG crystal. An interesting topic of research is to study roughness-to-width (or length or total lateral area) ratio of the crystal as a variable for DOI resolution. Also, the cutting direction might affect the surface structure. In fact, the surface structure might influence DOI resolution since different polishing methods make different patterns on the surface even though the average roughness is around the same.

A great challenge in DOI PET, is DOI calibration. There will be 2024 detectors in the 1.36-mm system which all should be calibrated individually. For the calibration purpose, the same procedure explained in chapter 5 the thesis should be taken with some modification so that the measurement for all the detectors of one module be done at the same time. The precision in the alignment of irradiated point is very important since misalignment leads to a wrong DOI function and would affect the overall performance of the system.

Another issue is the ToT method that is going to be applied to the dual-ended method. In the 2-mm system, the energy of the signals was not of great importance and normal ToT could still provide good digital signals. However, since DOI identification in dual-ended method is done by comparing the energy of the two outputs, it is important to preserve the energy of the signals. Therefore, normal ToT is not a good choice. Slew-rate ToT method could be an option that is under study and will be evaluated with the 2-mm system. Dynamic ToT (dToT) is another alternative since it can provide a linear response over a vast range of energies. In other words, ToT pulse-width generated by dToT is proportional to the energy of the analog signal over a wide range. Therefore, it can preserve the contrast between outputs and hence the DOI resolution of the detector.

In order to show the great capability of this digital readout method in energy preservation, the performance of a collimator-based double-photon imager coupled to a dynamic ToT board for digital readout was evaluated. In DPECT, energy resolution is of a great importance since photons with different energies are emitted. The collimator-based DPECT itself is a new imaging modality. Its concept and the preliminary design of the collimator are discussed in chapter 6 and possible double-photon emitting radionuclides are introduced. The system was used to scan an ^{111}In source. Results show a very good energy response in the sense that even 26-keV X-ray emission upon electron capture of ^{111}In nuclides can be distinguished thanks to the great energy preservation capability of the dToT method. The results showed a better signal-to-background ratio (SBR) compared with the single-photon analysis. Also, the image was closer to the actual shape and dimensions of the source. However, further optimization of the design is required to achieve a reliable image. Particularly, the coincidence count rate was too low in these experiments. Only 64 central holes of the collimator were coupled to the detectors. If all 256 holes are covered, the coincidence count rate increases by a factor 16. Also, the size of the collimator could be expanded to introduce more channels and increase the solid angle coverage. Doubling the dimensions (2D) increases the coincidence count rate by a factor 16. The focal distance of the collimator (70 mm) is too long for animal studies where 30 mm is enough. Another parameter to be optimized is the collimator thickness which was 30 mm in this current design. A 20-mm thickness (lead) is enough in the case of ^{111}In to stop 171-keV and 245-keV photons. These two modifications together reduce the distance of the detector plane to the focal point to half (from 100 mm in the current design to 50 mm), which increases the coincidence count rate by a factor 16 again. It should be noted as well that the source activity was 1 MBq, while in animal studies 40-50 MBq is generally used that means the count rate would be 40-50 times better.

All these measurements and investigations will lead to a digital animal DOI-PET aiming at sub-mm resolution currently under development. Two important components of this system are dual-ended detectors and digital readout. The dual-ended readout with GAGG crystal provides 1.2 mm intrinsic DOI resolution. The digital readout component must preserve this DOI capability. The finer pitch along with implementing dual-ended detectors increases the number of channels by a factor 4 which brings up the need for ToT readout method. The proposed digital approach is excellent in encoding and decoding the signals, however, the challenge is energy resolution of the method. In order to preserve DOI capability of the detectors, the readout system must preserve the energy resolution, and to this end, slew-rate ToT method is under investigation as well as dynamic ToT method that was evaluated for DPECT system.

[1] Z. Kuang, X. Wang, C. Li, X. Deng, *et al.*, "Performance of a high-resolution depth encoding PET detector using barium sulfate reflector," *Phys. Med. Biol.,* vol. 62, p. 5945–5958, 2017.